ESOT Congress

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LONDON | 29 JUNE–2 JULY 2025

Abstract Book

22nd CONGRESS OF THE EUROPEAN SOCIETY FOR ORGAN TRANSPLANTATION

29 June – 2 July 2025

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Nurturing a Sustainable Transplantation Journey

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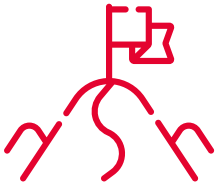
About the European Society for Organ Transplantation

The European Society for Organ Transplantation (ESOT) was founded nearly 40 years ago and has been dedicated to pursuing excellence in organ transplantation ever since.

Facilitating a wealth of international clinical trials and research collaborations over the years, ESOT remains committed to its primary aim of improving patient outcomes in transplantation.

With a community of transplant professionals from around the world, ESOT is an influential international organisation and the facilitator of the biennial ESOT Congress. ESOT attracts the foremost transplantation experts to work in its committees and sections. It has an impressive track record in supporting research, extensive education and promoting changes in European policy.

Our Mission



To improve outcomes for patients with terminal organ disease through transplantation, organ regeneration and substitution.

Our Vision

To promote sustainable scientific advancement through multidisciplinary communities of healthcare professionals

To deliver first-class education, training and career advancement opportunities to all healthcare professionals, with specific training programmes for low-income countries

To work with partner organisations, professional bodies and competent authorities to improve public and institutional awareness of the latest research in the field

To develop and promote policies for equitable access to transplantation and related therapeutic strategies

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ESOT LEONARDO DA VINCI TRANSPLANT RESEARCH INNOVATION AWARD

LDV_1 DECEASED-DONOR INITIATED CHAIN: SIX-YEAR RESULTS ON BEHALF OF THE ITALIAN KIDNEY PAIRED DONATION GROUP

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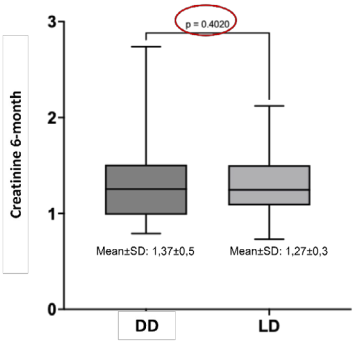
Background: The DECeased-donor initiated Kidney Paired Exchange (DECK) program is demonstrating how the domino effect of living donor (LD) transplant (TX) chains can be harnessed, despite a shortage of altruistic, non-directed donations, by using a deceased donor (DD) to initiate LD TX chains among immunologically incompatible pairs. After a pilot phase of 5 chains using 5 DDs from a inter-regional area and enabled 14 TX, the program was approved in July 2019 as part of the national Italian Kidney Paired Donation initiative.

Methods: Data from all TX chains performed in the DECK program from March 2018 to December 2024 were analysed.

Results: Thirty chains were carried out, involving over 15 Italian Centres: 79 TX were performed, 52 from LD. In 27 cases, the chains adhered to the principle of the program: upon closure of the chain, a kidney from a LD was returned to the regional TX list manager of the region where the initiating DD was located. In 3 cases, the chain early stopped, after the first TX from DD: in one case for LD's clinical contraindication, in another case for a primary non function (PNF) in the recipient, in the last case for new onset psychological issues. Thirteen chains were short, involving 2 TXs: 1 incompatible pair and 1 waiting-list (WL) recipient. The other chains involved a maximum of 3 couples, with an average length of 98.5 days. Reasons for enrolling pairs in the program were: ABO incompatibility (25), HLA incompatibility (19) and ABO+HLA incompatibility (6). No complications were reported in LDs who participated in the program; a total of 4 graft losses occurred (2 arterial thrombosis, 1 rejection, 1 PNF). No differences were observed in serum creatinine at 6-month post-TX between LD recipients and DD recipients (fig 1).

Conclusions: The success of the program is primarily based on the active collaboration of TX Centres that enrol immunologically incompatible pairs for LD TX in the DECK program. The program represents not only a significant treatment opportunity for patients who otherwise would not be able to undergo TX but also a research platform for optimizing matching algorithms aimed at increasing the number of TXs, immunological compatibility, outcome quality, and addressing the gap between available organs and the growing number of patients on the WL, prioritizing long-waiters and sensitized patients.



DD: recipient from deceased donor (22 patients)
LD: recipient from living donor (30 patients)

	DD	LD
Number of values	22	30
Minimum	0,7900	0,7300
Maximum	2,740	2,120
Range	1,950	1,390
Mean	1,365	1,272
Std. Deviation	0,4963	0,2954
Std. Error of Mean	0,1058	0,05393

LDV_2 IMPACT OF PRE-DONATION CARDIAC ARREST ON LIVER TRANSPLANTATION

Dharesh Raj Amarnath[1], **Samuel James Tingle[2], Georgios Kourounis[3], Chris Freise[4], Garrett Roll[5], Seiji Yamaguchi[6], Charles Rickert[6], Colin Wilson[7]**

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Background: Liver transplantation is the definitive treatment for end-stage liver disease and some cancers, but organ shortages necessitate maximising donor use. The use of livers from donors following pre-donation cardiac arrest (PDCA), especially with prolonged downtime duration, has been limited due to fears over presumed inferior outcomes from ischemic injury. Conversely, some suggest PDCA may induce ischemic preconditioning, which could improve post-transplant outcomes. However, this elusive phenomenon has proved difficult to translate into human studies. This study aims to assess the impact of PDCA occurrence and downtime duration on liver transplantation.

Methods: This population-cohort study used the UNOS registry on adult liver-only transplantation (2010-2023). Multivariable regression models, with interaction terms, were used to analyse the associations. Multiple imputation was used for missing data, and restricted cubic spline modelling to account for non-linear relationships.

Results: Among 74,592 recipients, 32,631 (43.7%) received a liver from a PDCA donor. PDCA occurrence was associated with a small improvement in graft survival (aHR=0.914, 95% CI=0.851-0.982). This benefit was more pronounced among DCD donors and those with moderately raised ALT (Figure 1(A)). The effect was only seen in donors with a short admission-to-donation time (Figure 1(B)) and in older donors (Figure 1(C)). Increasing PDCA downtime duration was also associated with a small improvement in graft survival (aHR per doubling of duration=0.953, 95% CI=0.917-0.991). Similar associations were seen with our secondary outcomes.

Conclusions: The use of livers from donors with PDCA, including those with prolonged downtime duration, is a safe and simple approach to expand the donor pool. Interaction terms and non-linear modelling provided clinical evidence for ischemic preconditioning from PDCA, which represents the largest real-world demonstration of this phenomenon.

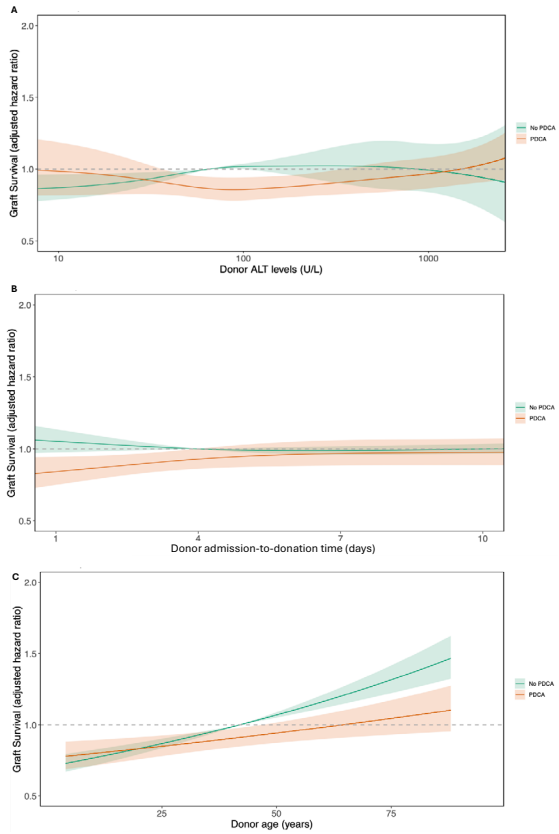

Figure 1: (A) Interaction model between PDCA and donor ALT on 1-year graft survival. (B) Interaction model between PDCA and time from admission to organ donation on 1-year graft survival (C) Interaction model between PDCA and donor age on 1-year graft survival.

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LDV_3 ADVANCING PEDIATRIC HEART TRANSPLANTATION USING THE VP.S ENCORE PEDS DEVICE

Kristina Andrijauskaite[1], Rafael Veraza[2], John Kucera[3], Seth Wolf[3], Riley Lopez[2], Isabella Cano[2], Exal Cisneros[2], Chelbee Farnen[2], Zachary Maxwell[2], Berk Aykut[3], Hiba Ghandour[3], Maria Basurto[2], Tyler Dean[2], George Lamberson[2], Leonid Bunegin[2], Douglas Overbey[3], Joseph Turek[3]

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Background: Pediatric patients remain among the most underserved populations in medical device innovation. Approximately 1,000 children annually are added to the cardiac transplant list, yet half receive a transplant. Infants under one year old face the highest mortality rates due to scarcity of suitable donor hearts. Furthermore, there is no currently approved organ perfusion system for donors less than 40 kilograms. To address this critical gap, we sought to evaluate the safety of a novel, portable, simple-to-use hypothermic cardiac preservation device, the VP.S ENCORE® PEDS™ (Pediatric Enhanced Delivery System), specifically designed to fit pediatric cardiac grafts.

Methods: Pediatric-sized porcine hearts (n=6) were preserved in the device for up to 8 hours. Robust perfusion parameters including pressure, flow, and temperature were established to meet the metabolic demands of small pediatric hearts. Post-preservation, hearts were evaluated for left ventricular function during the re-perfusion phase on the Langendorff apparatus, metabolism, gene expression, and histological assessment. Feasibility and organ viability were assessed via heterotopic heart transplant in matched recipients (n=2) at Duke University.

Results: The average recorded temperature during preservation was 7.8 +/- 1.5°C with a mean pressure of 11 ± 1.4 mmHg and a flow of 22 ± 14 mL/min. The heart weight before preservation ranged from 56 to 218 g (116 ± 61 g) with no edema observed. Our prolonged heart preservation experiments demonstrate strong left ventricular function (>2000 dP/dT), low lactate levels (<3 mmol/L), reduced expression of inflammatory markers ($p < 0.0001$), and preserved endothelial integrity. Our preliminary transplant data show 100% recipient survival, excellent post-transplant metabolic measures, normal cardiac activity in heterotopic transplant at time of implantation, and normal porcine behavioral scale ratings.

Conclusions: The study's results suggest the VP.S ENCORE® PEDS™ can effectively preserve pediatric-size hearts and holds potential for enhancing heart transplant rates among pediatric patients. Future studies will focus on orthotopic transplant models and clinical trials to validate safety and efficacy, bringing us closer to revolutionizing pediatric heart transplantation

LDV_4 DUODENODUODENOSTOMY IN PANCREAS TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

Alba Torroella[1], Rongrong Hu Zhu[2], Ramón Rull[3], Rocío García[3], Clara Bassaganyas[4], Carlos Perez Serrano[5], Martí Manyalich[6], David Saavedra[7], Emma Folch Puy[8], Víctor Emilio Holguin[7], Pedro Ventura-Aguiar[9], Antonio J Amor[10], Fritz Diekmann[11], Mª Angeles Garcia-Criado[12], Josep Fuster[3], Joana Ferrer-Fàbrega[13]

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Background: Duodenoduodenostomy as an exocrine drainage reproduce more accurately the physiology of the native pancreas and enables more conservative management of postoperative complications. We present our experience with duodenoduodenostomy (DD) for exocrine drainage, analyzing intestinal complications and their impact on patient and graft survival.

Methods: All pancreatic transplants performed between May 2016 and November 2024 were included. For exocrine secretion, enteric drainage was performed "side-to-side" with DD anastomosis.

Results: A total of 170 transplants were performed using DD. Recipients' median age was 43 years [IQR 36 - 39], with 56.7% being male. Median cold ischemia time was 8 hours [IQR 6.1-10.1].

According to the Clavien-Dindo classification, complications were: 7.6% Grade I, 17.1% Grade II, 2.4% Grade IIIa and 21.8% Grade IIIB. The median hospital stay was 12 days [IQR 10 - 19.2]. Prevalence of intestinal complications was 10%, which included: intestinal occlusion (n=4); paralytic ileus (n=5); post-transplantectomy duodenal dehiscence (n=1); DD dehiscence (n=5); anastomotic bleeding (n=2). Eleven cases required surgical treatment due to intestinal complications: adhesiolysis (n=3); Hartmann's procedure in an occlusive stercoraceous colitis (n=1), primary closure of the dehiscence (n=3); transplantectomy after failed primary closure (n=2); redo of the enteric anastomosis (n=2). After a median follow-up of 39.79 months [IQR 18.1- 69], pancreas graft survival was 86.7% at 1, 3 and 5 years, and patient survival was 100%, 99.2% and 99.2% at 1, 3 and 5 years, respectively.

Conclusions: Duodenoduodenostomy for enteric drainage in pancreas transplantation is a feasible and safe technique, offering competitive outcomes in terms of graft and patient survival.

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LDV_5 LOSS OF REGULATION OF ANTIGEN SPECIFIC IFNG-PRODUCING T CELLS PRECEDES THE APPEARANCE OF DE NOVO DSA POST TRANSPLANT

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Background: While de novo donor specific antibodies (dnDSA) associated with graft loss in the OuTSMART trial, optimised immunosuppression post-DSA did not improve transplant survival. Furthermore it is unknown why only some patients develop dnDSA. The longitudinal analysis of OuTSMART samples provided a unique opportunity to understand whether loss of regulation of allo-responses was a prerequisite for dnDSA formation.

Methods: Peripheral blood mononuclear cells were available from multiple time-points prior to first DSA development (t0) from 52/82 patients; initially DSA- but developed dnDSA during the trial. HLA Pure Proteins (PP) representing either DSA or control donor antigens were used to stimulate CD8 depleted PBMC to evaluate indirect alloresponses. Using FluoroSpot, antigen specific IFNγ & IL17 CD4+ production (ASR) were compared, including additional conditions depleting CD19+ & CD25hi cells. These cytokines associate with adverse transplant outcomes, germinal centre alloresponses & may pre-empt DSA formation.

Results: ASR were detectable to either control/DSA PP in 67.9% (95/140) of IFNγ assays & 35.7% (50/140) for IL17. Notably ASR were measurable in >50% of samples even up to 32 months at all timepoints prior to t0. Fig 1a) indicates overall ASR to control mismatches were more regulated (50%, 33/66) than to DSA protein (36.5%, 27/74) but was not statistically significant. Fig 1b) demonstrates similar proportions of regulated IFNγ responses to both control & DSA PP until 8 months prior to t0. However from -4 months, unregulated IFNγ responses to DSA predominated. This differed from the control protein where regulated responses were maintained. No similar patterns were discerned in responses to IL-17. A concomitant 36-colour flow cytometry panel highlights which regulatory cell subsets associate with ASR regulation & their changes prior to dnDSA.

Conclusions: This is the first systematic study of clinical samples prior to dnDSA. ASR were detectable even 32 months prior to DSA formation in >50% samples. There was differential loss of regulation of IFNγ production to DSA PP just prior to dnDSA detection. Conversely regulated control ASR responses predominated at all timepoints. This highlights a window of detectable T cell sensitisation prior to dnDSA potentially amenable to specific Treg cell therapy.

1a) Pure Protein stimulus	No IFNγ response from CD8-depleted PBMC		IFNγ response from CD8-depleted PBMC	
	No ASR	ASR only after depletion of CD19+ and/or CD25hi cells	ASR but evidence of regulation after depletion of CD19+ or CD25hi cells	ASR but no evidence of regulation after CD19+ or CD25hi cells
Control Samples: 66	19	24	9	14
DSA Samples: 74	26	23	4	21

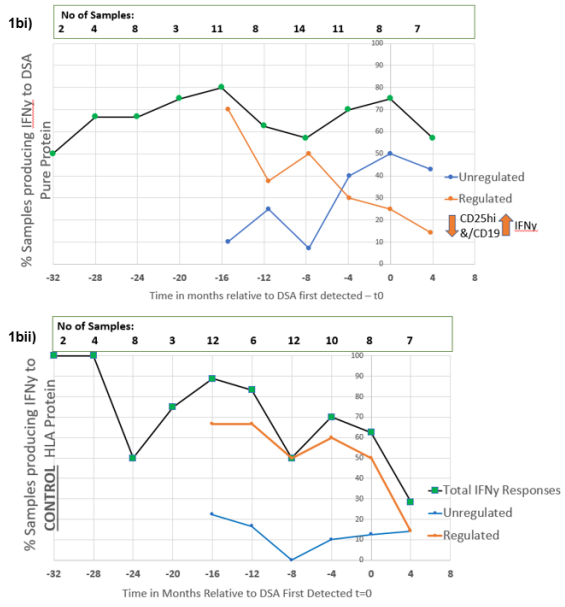

Figure 1a) Antigen specific IFNγ responses to HLA pure proteins with DSA specificity or control prior to appearance of DSA (t0) out of 140 functional experiments. 1b) Longitudinal analysis of antigen specific IFNγ in response to pure protein relative to DSA first appearing (t0) i) DSA PP ii) Control

LDV_6 OX118, A NOVEL FULLY HUMAN ANTI-OX40L MONOCLONAL ANTIBODY WITH OPTIMAL IMMUNE MODULATING PROPERTIES

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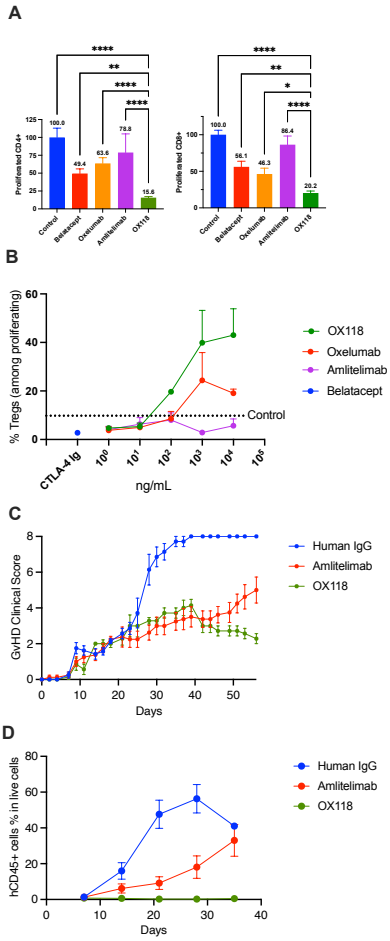
Background: Co-stimulatory pathways such as OX40/OX40L are essential for T-cell activation. The OX40/OX40L pathway is inducible rather than constitutive upon immunological stimulus. Clinical trials have demonstrated the safety of targeting OX40L, and non-human primate models of kidney and heart transplantation indicate promising therapeutic potential. Here, we present OX118, a fully human antibody optimized for ADCC-enhanced targeting of OX40L.

Methods: Allogeneic MLR (mixed lymphocyte reaction) assays were used to evaluate OX118 effects on $CD4^+$ and $CD8^+$ T-cell proliferation, bystander activation, and regulatory T-cell induction. A humanized graft-versus-host disease (GvHD) model assessed OX118's ability to mitigate GvHD development. Benchmarking included antibodies against hOX40L oxelumab (IgG1 wild-type), amlitelimab (IgG4 wild-type), and Belatacept.

Results: OX118 significantly inhibited $CD4^+$ (15.6% of control) and $CD8^+$(20.2% of control) T-cell proliferation (Fig 1A). OX118 treatment markedly increased regulatory T-cells (43% of proliferating $CD4^+$ T-cells vs 8.8% in control setting) compared to benchmarking agents (Fig 1B). Bystander activation in NK cells, B cells, and CD14+ cells was reduced with OX118 treatment (data not shown). OX118 attenuated GvHD development (Fig 1C), controlled proliferation (<1% chimerism, % hCD45 cells) by day 35 (Fig 1D), compared to ~33.0% with IgG4 anti-hOX40L. OX118 also reduced the number of $hCD45^+$ cells in tissues. Body weight trends inversely correlated with clinical scores, showing weight gain in OX118-treated animals by day 56. All control animals died within 39 days, and no deaths in OX118 or amlitelimab treated mice until study end at day 56.

Conclusions: OX118 represents a novel approach to co-stimulation blockade, offering unique immune modulation with balanced control over CD4+ and CD8+ T-cell proliferation and enrichment of regulatory T-cells. A Phase 1 clinical trial is starting shortly.



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LDV_7 RNASEQ CHANGES ASSOCIATED WITH POLYOMAVIRUS-ASSOCIATED NEPHROPATHY: FROM PATHOPHYSIOLOGY TO DRUG REPURPOSING

Alexis Piedrafita[1], Pierre de la Grange[2], Arnaud Del Bello[3], Nassim Kamar[4], Marc Raynaud[5], Brousse Romain[6], Maud Racape[7], Goutaudier Valentin[6], Agathe Truchot[8], Jessy Dagobert[9], Zeynep Demir[10], Fariza Mezine[11], Marta Sablik[12], Olivier Aubert[13], Carmen Lefaucheur[14], Alexandre Loupy[15]

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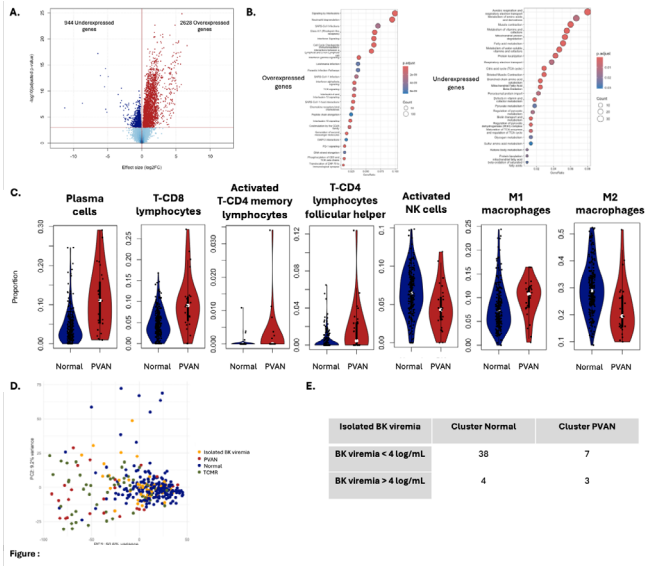
Background: Polyomavirus-associated nephropathy (PVAN) is a severe complication of kidney transplantation, difficult to diagnose, and lacking specific treatment. We hypothesized that whole-transcriptomic analysis could reveal molecular mechanisms, refine diagnosis, and identify drug candidates.

Methods: From a cohort of kidney biopsies with Illumina bulk mRNA sequencing data, based on Banff 2019 histological diagnosis and concomitant BK viremia, we selected BK virus-associated biopsies (n=78; PVAN, n=26; isolated BK viremia, n=52) and compared them to pure T-cell-mediated rejection (TCMR, n=52) and normal biopsies (n=198) without BK viremia. We conducted differential expression analysis using DESeq2, functional enrichment analyses, cell deconvolution analysis, and a drug repurposing approach using Connectivity Map.

Results: Among 21,013 analyzable genes, 3,572 were differentially expressed (DEG) between PVAN and normal biopsies (2,628 overexpressed and 944 underexpressed, **A**). Functional analysis identified dysregulated inflammation, cell proliferation, metabolism, and differentiation pathways (**B**). Cell deconvolution analysis revealed significant changes consistent with a polymorphic immune infiltrate (plasma cells, M1 macrophages, T lymphocytes, **C**). These abnormalities largely overlapped with TCMR (**D**). Isolated BK viremia biopsies showed heterogeneous transcriptomic changes consistent with low-grade inflammation (**D**). Transcriptomic profiling classified them as normal (n=42) or PVAN (n=10), irrespective of BK viremia levels (above or below 4 log/mL, **E**). A drug repurposing approach identified candidate drugs to antagonize the PVAN transcriptomic signature.

Conclusions: We identified a PVAN transcriptomic signature, consistent with its pathophysiology, and used it to identify candidate drugs. Isolated BK viremia, even at low levels, can be associated with PVAN-like abnormalities, enabling transcriptomic-based reclassification.



Isolated BK viremia	Cluster Normal	Cluster PVAN
BK viremia < 4 log/mL	38	7
BK viremia > 4 log/mL	4	3

Figure :

A: Volcano plot of differential expression analysis between PVAN and Normal.
B: Pathway enrichment analysis of DEG (up-/downregulated) between PVAN and Normal.
C: Proportion of differentially represented cells between PVAN and Normal, obtained from cell deconvolution.
D: Individual representation on the first two components of a principal component analysis (PCA1/2) on differentially expressed genes between PVAN and Normal samples.
E: Confusion matrix among BK viremia patients, comparing clustering on DEGs between PVAN and Normal samples and grouping according BK viremia > or < 4 log/mL.

LDV_8 THE IMMUNOSURVEILLANCE OF HYPOIMMUNOGENIC STEM CELL-DERIVED PANCREATIC ISLETS: IMPACT OF VIRAL INFECTION

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Background: Immune-evasive stem cell-derived islets are being developed as a promising cell therapy for type 1 diabetes. While abrogation of MHC-I prevents $CD8^+$ T cell killing, it exposes the graft to natural killer (NK) cell lysis via missing-self recognition. Prior strategies attempted to mitigate rejection by expressing inhibitory ligands, but this yielded inconsistent results due to the heterogeneity of NK cells. To address this challenge, we devised an alternative strategy targeting NK activation by genetically ablating B7-H3 and CD155 in MHC-I-null cells, creating triple knockout (T-KO) islets. T-KO islets successfully evaded T and NK cell-mediated rejection, and restored euglycemia in diabetic mice. However, the safety of hypoimmune islets in the context of infection remains unclear. Given this, we assessed *in vivo* immunosurveillance by challenging T-KO islets with lymphocytic choriomeningitis virus (LCMV-WE).

Methods: Mice transplanted with luciferase-expressing T-KO islets were humanized with NK cells (day 10) and infected with 1×10^6 FFU/mouse LCMV-WE (day 24). Acute infection was assessed by platelet count, while viral titers, immunophenotyping, and hC-peptide levels were evaluated at 3 and 7 days post-infection. Graft survival was analyzed by IVIS, and explanted organs were examined at the endpoint.

Results: Thrombocytopenia indicated occurrence of acute LCMV-WE infection. Humanized mice showed higher viral titers than their non-humanized counterparts. Interestingly, hC-peptide levels decreased significantly in infected humanized mice, correlating with the bioluminescence signal reduction of T-KO islets. Importantly, we found that NK cells were responsible for graft rejection, as $hCD56^+$ cells were detected at the graft site. Mechanistic evaluations confirmed that NK cell activation and recognition of islet cells were NKG2D-dependent, with LCMV-WE infection causing the upregulation of the activating ligands MICA/B and ULBP3 in T-KO islets.

Conclusions: This study highlights that the upregulation of activating ligands other than B7-H3 and CD155 enables NK cells to re-engage in missing-self recognition, targeting infected cells. Due to potential viral escape, further studies with islet-tropic viruses are needed to fully assess hypoimmune SC-islets' safety for clinical use

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FULL ORALS

From basic to translational immunology

FOS_01_1 SELECTIVE IN-VIVO EXPANSION OF REGULATORY T CELLS LEADS TO LONG-TERM TOLERANCE OF HEART ALLOGRAFTS

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Background: Chronic antibody-mediated rejection (ABMR) and cardiac allograft vasculopathy (CAV) are key causes of late graft failure in heart transplant recipients, with few effective treatments available. Regulatory T cells (Tregs) are essential for immune tolerance, suppressing both autoimmune and alloimmune responses. A promising approach to expand Tregs in vivo involves an interleukin-2 (IL-2) complex with an anti-IL-2 antibody (IL-2cplx), which boosts Treg proliferation. This study examines the potential of IL-2cplx-based immunomodulation in a murine heart allograft model.

Methods: Female C57BL/6 mice were transplanted with fully mismatched BALB/c hearts and treated with IL-2/anti-IL-2 (1µg/5µg) and rapamycin (1µg/gBW) administered on d-3/-2/-1 and thrice a week until d29, and short-term anti-IL-6 (600µg d-1; 300µg d4/6). Cardiac allograft survival was monitored. Flow-cytometric crossmatch was performed to detect donor-specific antibodies (DSA). Mixed lymphocyte reaction essays were performed to assess donor specific T-cell reaction and histological analysis was performed according to the ISHLT grading. Additionally, efficacy of this protocol was assessed in Tmem enriched mice (receiving T-cell transfer from donor type skin challenged mice) prior to HTX.

Results: IL-2cplx protocol treatment led to indefinite survival (>150 d) compared to untreated controls (MST=7.5d). Furthermore, IL-2cplx-based treatment significantly reduced formation of donor-specific IgG1 and IgG2ab. $CD4^+$ and $CD8^+$ cell proliferation against donor antigen was comparable between naïve and treated mice, indicating no donor specific T-cell hyperresponsiveness. Histologic grading revealed low rejection scores even at the end of follow up. We found less necrosis (p=0.02) compared to untreated controls. Even in presensitized mice, survival of the graft was significantly prolonged (> 70 d).

Conclusions: We demonstrated that selective in vivo expansion of Tregs using IL-2cplx, combined with rapamycin and short-term anti-IL-6mAb treatment, leads to operational tolerance in a clinically relevant model of cardiac transplantation, as evidenced by indefinite survival in the absence of continuous immunosuppression. Moreover, the potency of this approach is preserved in the presence of alloreactive memory

FOS_01_2 ORGAN-SPECIFIC HETEROGENEITY OF HUMAN LYMPHATIC VESSELS HAS IMPLICATIONS FOR TRANSPLANTATION

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Background: Lymphatic vessels, critical for tissue homeostasis, are present in all transplanted solid organs. Whilst resolving inflammation, lymphatics facilitate lymphocyte trafficking and immune surveillance. This dual role leads to ambiguity as to whether these vessels promote allograft survival or facilitate rejection. Limited understanding of molecular characteristics of lymphatic endothelial cells in human organs underpins this issue.

Methods: To characterize the molecular profile of organ lymphatics, we generated a single-cell RNA sequencing dataset spanning 140 human donors. This comprised 13,454 lymphatic endothelial cells from kidney, skin, breast, heart, lung and intestines. We focused on the kidney for in-depth validation using optical tissue clearing and 3D imaging of immunolabelled renal tissue from mice, healthy humans or patients with chronic mixed cellular- and antibody-mediated rejection.

Results: Human lymphatics demonstrated organ-specific molecular heterogeneity. Superficial organ lymphatics (skin, breast) exhibited an immunomodulatory profile, expressing pro-inflammatory cytokines, interleukins and chemokines. In contrast, visceral lymphatics in the kidney and heart lacked these immune-activating molecules. Prompted by our transcriptomic analysis, we generated a new short-domain antibody for the leukocyte trafficking receptor, LYVE1, which was minimally expressed by kidney lymphatics compared with other organs. During kidney transplant rejection, lymphatics expanded sevenfold and showed C4d deposition. We observed impaired T cell trafficking and emergence of tertiary lymphoid structures along the rejecting allograft lymphatic network.

Conclusions: This study provides the first molecular evidence for heterogeneity of organ lymphatics, implicating their organ-specific roles in transplantation. In the kidney, lymphatic dysfunction appears to be a hallmark of alloimmune injury, representing a novel therapeutic target to improve transplant outcomes.

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FOS_01_3 DUAL INHIBITION OF MTOR AND CALCINEURIN ALLEVIATES MISSING SELF-INDUCED MICROVASCULAR REJECTION

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Background: The inability of graft endothelial cells to deliver HLA-I-dependent inhibitory signals to recipient NK cells (i.e. missing self, MS), drives DSA-independent microvascular inflammation (MVI), ultimately leading to graft failure. This study aimed to validate these findings, elucidate the signalling pathways involved in MS-induced NK cell activation, and explore therapeutic strategies

Methods: MS-induced NK cell-mediated microvascular rejection was investigated in an independent cohort of kidney transplant recipients. Two experimental models were developed to mimic the pathological condition: *in vitro* cocultures of human NK cells with allogeneic microvascular endothelial cells and an *in vivo* murine heart transplantation model. A pilot clinical study was conducted involving 50 renal transplant recipients with MS-induced NK cell-mediated microvascular rejection, among whom 16 on CNI+MMF-based maintenance immunosuppression were switched from MMF to an mTOR inhibitor and compared to an historical cohort left on CNI and MMF.

Results: MS-induced detrimental impact on kidney graft survival was confirmed and analyses of graft biopsies identified calcium signalling pathways and mTOR as a key regulator of MS-induced NK cell activation. Our *in vitro* and *in vivo* models showed that while calcineurin inhibitor (CNI) alone had a limited impact, combining CNI with mTOR inhibitors (mTORinh) synergistically reduced NK cell activation and endothelial damage. Consistent with the presence of mTOR-activated NK cell infiltrating graft biopsies, patients who tolerated mTORinh introduced on top of CNI at diagnosis demonstrated reduced MVI lesions and improved graft survival compared to those left on CNI+MMF based treatment.

Conclusions: This translational study identifies mTOR inhibition as a pivotal adjunct to CNI in mitigating MS-induced NK cell-mediated rejection, potentially improving long-term graft outcomes.

FOS_01_4 SPATIAL INSIGHTS INTO CLAD REVEAL DIFFERENTIAL MODULATION OF IMMUNE CHECKPOINTS IN OBSTRUCTIVE VS RESTRICTIVE PHENOTYPE

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Background: Chronic lung allograft rejection (CLAD) is the leading cause of morbidity and mortality in lung transplantation, and there is still a gap of knowledge about immune-mediated rejection mechanisms. Therefore, we investigated panels of immune- and cell-signaling proteins at the spatial level in CLAD lungs.

Methods: Eight representative lung tissue blocks from 8 patients who underwent re-transplantation for CLAD, were retrieved. Four had BOS- and four had RAS-CLAD. Spatial proteomics of CD4, CD8, CD68, panCK, and CD20-pos cells was performed using the GeoMX platform and protein modules for immune cell profiling, immune checkpoints, cell death, PI3K/AKT and MAPK signaling (n=72 proteins) in both fibrotic and endoalveolar regions (ROI; CD4 and CD8), in peri-bronchial area (CD20), or in endoalveolar space (panCK and CD68).

Results: At unsupervised level, lung epithelial cells from BOS and RAS CLAD showed distinct regulation of proteins belonging to the MAPK, PI3K/Akt and Immune checkpoint families; specifically, epithelial cells in BOS upregulate phospho−MEK1, phospho−p38 MAPK, phospho−JNK and phospho−AKT1 whereas in RAS we could detected upregulation of immune checkpoints, namely PDL1, PDL2 and VISTA. Further, a higher quota of proliferating cells (Ki67pos) was detected in BOS lungs. Differential expression of immune checkpoints between BOS and RAS was evident for immune cell populations. CD4pos T cells from fibrotic ROI in RAS overexpressed OX40L, CD14 and IDO1, while in BOS there was a predominant overexpression of known repressors of the T cells function, such as PDL1/ 2, B7-H3, Tim3, VISTA and Lag-3. A similar trend was observed in CD8pos and CD68pos immune cells. B-cell (CD20pos) was the histotype with less dissimilarities between BOS and RAS for all the protein modules.

Conclusions: Our spatially resolved approach reveals the involvement of innate immune response in RAS, and this is specifically evident in fibrotic areas. On the other side, BOS lungs show predominant expression of immune checkpoints with a suppressive function both in T-lymphocytes and in monocyte cells within endoalveolar space. These profound immunological differences between the two phenotypes of CLAD support the need of a differentiated medical approach for patients with either forms of chronic rejection.

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FOS_01_5 INVESTIGATING IMMUNE INFILTRATES IN KIDNEY TRANSPLANT BIOPSIES FOLLOWING TREG CELL THERAPY

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Background: Regulatory T cell (Treg) therapy is a promising treatment with the potential to minimise reliance on standard immunosuppressive agents in transplantation. Interestingly, Treg therapy is associated with infiltration of immune cells into the graft. Our previous findings from kidney biopsies from two Treg cell therapy trials showed these infiltrates to have a unique composition, with a clear population of B cells. We aimed to characterise protein profile of these infiltrates in depth using multiplexed spatial approaches.

Methods: FFPE kidney biopsies (n=4) were compared with time-matched acute T-cell-mediated rejection samples. A further set of matched biopsies were compared before and after Treg treatment time points (n=4), as well as to a control time-matched non-Treg therapy group (n=2). A comprehensive protein profiling analysis was completed using Nanostring's spatial protein panel of 580 targets. Immune infiltrated areas were selected for downstream analysis. A dedicated multiplexed immunofluorescence (IF) panel was used for further identification and validation of the infiltrate composition.

Results: Infiltrates in cell therapy were distinct from those of rejection in the first study cohort. Differential protein expression analysis revealed a clear increase in B cell-associated markers such as CD20, CD38, CD22, CD79a, CD79b and CXCR5 in Treg-treated immune infiltrates, whereas in rejection plasma cell markers including Blimp1 and CD138 with other inflammatory markers are enriched. Similarly, the post-Treg treatment regions of samples from the second trial clustered separately compared to both control and pre-Treg infusion biopsies. Further IF analysis showed that the infiltrates exhibited features of organised tolerogenic tertiary structures.

Conclusions: We present here a comprehensive analysis of the spatial protein expression profile in focal infiltrates within kidney biopsies from Treg-treated transplant patients. The findings mirror emerging evidence that Treg therapy reshapes local immune microenvironment to support graft tolerance. The distinct enrichment of B cell-associated markers and potential formation of organized, tolerogenic tertiary lymphoid structures suggest a potential role for B cells as either mediators or biomarkers of immune regulation.

FOS_01_6 IN VITRO MODEL TO INVESTIGATE THE SYNERGISTIC ROLE OF LIL RECEPTORS IN HLA MOLECULE BINDING

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Background: Innate immune cells have long been relegated to a non-specific role in the rejection process. It has recently been proven in mouse models that monocytes, independently of the adaptive immune system, have allogeneic recognition abilities. They can cause rejection lesions following the recognition of the donor's major histocompatibility complex class I molecules by their paired immunoglobulin-like receptors (PIRs), also known as leukocyte immunoglobulin-like receptors (LILRs) in humans. Single-cell RNA sequencing analysis has also shown that the expression of blood and biopsy monocyte LILRs (LILRB1, LILRB2 and LILRB3 specifically) increases significantly in cases of rejection. In this work, we sought to explore the synergistic role of these LILRs in HLA molecule binding using an *in vitro* model.

Methods: We built a model of human monocytes (THP1 cells) overexpressing LILRs using a lentiviral strategy. We then selected various clones expressing either LILRB1, LILRB2 or LILRB3 or two or all of these LILRs by cell sorting. Finally, we assessed the ability of these LILRs to bind human leukocyte antigen (HLA) class I molecules using HLA pentamers.

Results: We first developed a polyclonal monocytic cell line transduced to express LILRB1 (71%), LILRB2 (57%) and LILRB3 (33%). Among these transduced cells, those expressing only LILRB3 did not bind HLA pentamers. In contrast, those expressing LILRB1 bound HLA-A2 (5%) and HLA-B27 (56%) pentamers. LILRB2 positive cells bound mainly HLA-B27 (53%). Whatsmore, HLA ligation increased when THP1 cells expressed more than two LILRs (8% of cells expressing both LILRB1 and LILRB2 bound HLA-A2 and 72% bound HLA-B27 pentamers).

Conclusions: We have demonstrated here the ability of LILRB1 and B2 to synergistically bind HLA-A2 and B27 molecules. Further experiments will be required to explore the different signaling pathways activated following the binding of HLA pentamers by cells expressing LILRB1 and/or LILRB2.

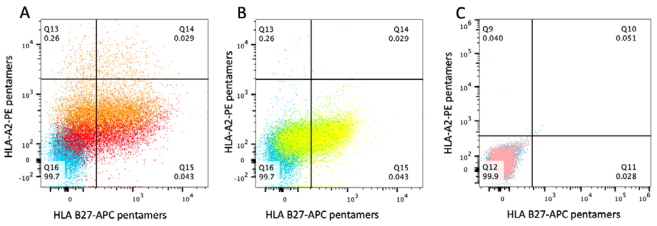

Figure - Flow cytometry analysis of HLA-A2 and HLA-B27 pentamer ligation by transduced THP1 clones: A: LILRB1 + clones (red and orange) vs wild type THP1 cells (blue). B: LILRB2 + clones (green and yellow) vs wild type THP1 cells (blue). C: Stained (pink) vs non stained (blue) polyclonal LILRB3 + cells

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FOS_01_7 DEVELOPMENT OF AN IN VITRO KIDNEY ALLOGRAFT MODEL USING KIDNEY ORGANOIDS TO STUDY RENAL GRAFT FIBROSIS

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Background: Renal graft fibrosis is common among transplant recipients with graft function exceeding 10 years and commonly measured together with tubular atrophy. However, the underlying mechanisms remain incompletely understood. The pathogenesis of renal graft fibrosis involves a cascade of events, in which macrophages play an important role, such as promoting inflammation and secreting pro-fibrotic cytokines. Reliable in vitro models are essential to elucidate these mechanisms and test potential therapeutic strategies. Here, we present a novel in vitro kidney allograft model utilizing human-induced pluripotent stem cell (iPSC)-derived kidney organoids and macrophages to study kidney allograft fibrosis.

Methods: Four iPSC clones were used to generate macrophages and kidney organoids. These kidney organoids, co-cultured with and without allogeneic macrophages, were subjected to various injuries mimicking transplantation-related conditions, including inflammation (IL-1β), ischemia-reperfusion injury (hypoxia), and calcineurin-induced cytotoxicity (tacrolimus). Gene and protein expression levels in these experimental groups were assessed using quantitative PCR and immunohistochemistry.

Results: Gene- and protein expression analyses demonstrated significantly elevated levels of fibrosis markers, including fibronectin and collagen 1, in kidney organoids subjected to hypoxia, IL-1β, and tacrolimus. While all transplant-related injuries individually resulted in fibrosis, their combination led to significantly more pronounced fibrosis. The inclusion of macrophages in the organoids further amplified the fibrotic responses and the expression of pro-inflammatory cytokine markers upon injury, compared to organoids without macrophages.

Conclusions: We are here providing a new model in the presence of macrophages to study allograft fibrosis. This platform can help to dissect mechanisms of allograft fibrosis and test novel interventional strategies. Our findings pave the way for future research into therapeutic interventions to mitigate fibrosis and improve kidney allograft outcomes.

FOS_01_8 MULTIMODAL PHENOTYPING OF PIG-TO-HUMAN HEART XENOGRAFTS' IMMUNE RESPONSE

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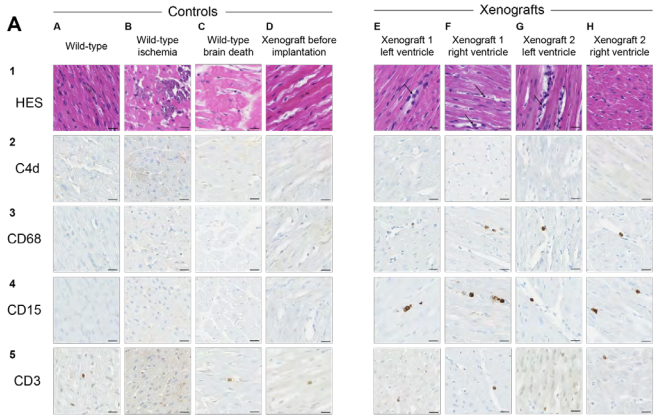
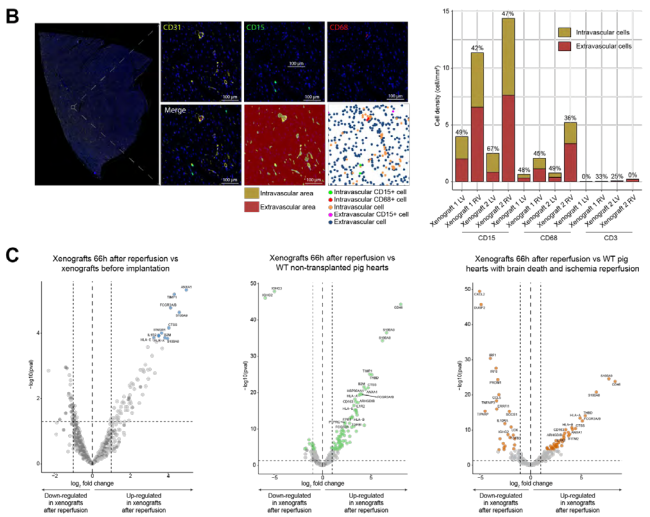
Background: Porcine genome editing has revolutionized xenotransplantation by allowing the first pig-to-human heart transplantations. However, the mechanisms driving the immune response in heart xenografts transplanted to humans remain poorly understood.

Methods: We analyzed two heart xenografts transplanted from 10-gene-edited pigs into brain-dead human recipients. Biopsies at 66-hour post-reperfusion were studied using a multimodal phenotyping approach combining: morphological evaluation, immunophenotyping, ultrastructural assessment, automated quantification of multiplex immunofluorescence staining and gene expression profiling. Xenografts before implantation, wild-type pig hearts with and without ischemia injury as well as wild-type pig hearts with brain death and ischemia reperfusion were used as controls.

Results: Both xenografts showed evidence of endothelial activation and mild microvascular inflammation without capillary C4d deposition. Immune infiltrates were mainly composed of CD15+ and CD68+ innate immune cells (A). Ultrastructural assessment showed endothelial swelling with occasional intravascular leucocytes. Deep-learning based automated multiplex immunofluorescence analysis confirmed that microvascular inflammation was primarily associated with CD15+ and CD68+ innate immune cells (B). Finally, both xenografts showed increased expression of genes associated with monocyte/macrophage activation, neutrophil activation, interferon-gamma response, natural killer cell burden, endothelial activation, apoptosis and injury repair (C). This phenotype was absent in control pig hearts, in ischemia and brain death models.

Conclusions: Multimodal phenotyping of pig-to-human heart xenografts revealed a pattern of mild humoral xeno-immune response, characterized by mild innate microvascular inflammation, endothelial activation, and molecular signature of antibody-mediated rejection. Integration of this approach into future clinical trials could facilitate real-time graft monitoring, mitigate rejection risk, and enhance xenotransplant outcomes.





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From basic to translational immunology

FOS_01_9 UNRAVELLING THE MECHANISMS OF IMMUNE PRIVILEGE IN GRAFT ENDOTHELIUM DURING TCMR

Thomas Barba[1], Martin Heinrich Oberbarnscheidt[2], Maud Rabeyrin[3], Candice Roufosse[4], Linda Moran[5], Alice Koenig[6], Virginie Mathias[7], Carole Saison[8], Valérie Dubois[9], Emmanuel Morelon[10], Yi-Chun Xu-Dubois[11], Jean-Paul Duong van Huyen[12], Antonino Nicoletti[13], Fadi Lakkis[14], Olivier Thaunat[15]

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Background: Graft endothelial cells express donor alloantigens and are exposed to cytotoxic T lymphocytes (CTL), yet they are generally spared during T cell-mediated rejection (TCMR), which predominantly targets epithelial structures. The mechanisms behind this vascular immune privilege are not well understood.

Methods and Results: Transcriptomic analysis and endothelial-mesenchymal transition (EndMT) assessments confirmed that the graft endothelium is preserved during TCMR. However, co-culture experiments with alloreactive CTLs showed that endothelial cells are as susceptible to lysis as epithelial cells, ruling out a cell-intrinsic protective mechanism. Intravital microscopy of murine kidney grafts and analysis of human renal allograft biopsies revealed that CTL interactions with endothelial cells were shorter than with epithelial cells. Single-cell RNA sequencing demonstrated that this difference is due to a chemotactic gradient produced by graft stromal cells, guiding CTLs toward epithelial cells. In vitro, chemotaxis was found to override TCR-induced cytotoxicity, protecting endothelial cells. These findings were supported by microfluidic models under shear stress, simulating flow conditions, where the presence of a CXCL12 gradient prevented endothelial damage. Finally, immunohistological and computer-assisted analyses of TCMR biopsies showed that the disruption of the chemotactic gradient was associated with endothelialitis lesions, linking gradient loss to endothelial damage.

Conclusion: Our findings challenge the traditional view of cell-intrinsic immune privilege, proposing a cell-extrinsic mechanism where chemotaxis plays a crucial role in preserving graft endothelium during TCMR. This mechanism may have broader implications beyond transplantation, potentially aiding in the preservation of vascular integrity across various pathological conditions.

Donor organ optimisation in cardiothoracic TX

FOS_02_1 DIFFERENT STEM CELL THERAPIES RESTORE ASPIRATION-DAMAGED LUNGS AND IMPROVE OUTCOMES IN SUBSEQUENT TRANSPLANTATION

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Background: Lung transplantation is the only viable treatment option for end stage pulmonary disease. However, its effectiveness is hindered by a shortage of donor lungs and low utilization rates. A common reason for rejecting donor lungs is damage caused by gastric aspiration, which increases the risk of developing primary graft dysfunction (PGD) and early mortality. Stem cell therapy can regulate inflammatory processes and has been investigated as a potential treatment for lung injuries. This study explores full-term amniotic fluid-derived stem cells (TAF-MSCs) and bone marrow-derived mesenchymal stromal cells (BM-MSCs), administered during ex vivo lung perfusion (EVLP) and post-LTx with the aim to improve aspiration-induced lung damage and reduce the incidence of PGD.

Methods: Pigs were randomized into four treatment groups (n=6): BM-MSCs single dose, BM-MSCs repeated dose, TAF-MSCs repeated dose, or placebo. Lung injury was induced over six hours by administration of gastric contents and lungs were harvested thereafter followed by four hours on EVLP. The left lung was then transplanted, and recipients followed for 72 hours. Finally, the left lung function was evaluated in isolation over four hours. Donor lung quality, postoperative outcomes and molecular signatures were analyzed. All recipients were assessed for PGD based on chest x-ray imaging and blood gas analysis.

Results: Lung injury was confirmed according to the Berlin criteria for ARDS and further validated by histopathological analysis showing increased immune cell infiltration, edema and thickening of the alveolar walls. Pulmonary vascular resistance and lung compliance improved in the group with repeated BM-MSC treatment and with trends towards additional improvement in the animals that received repeated doses of TAF-MSCs. In contrast to the placebo and single dose group, where the majority developed PGD grade 2-3, no animal treated with repeated doses of BM-MSCs or TAF-MSCs developed PGD. This was further validated by histopathological assessment and molecular analyses including advanced multiplexed imaging and proteomics.

Conclusions: Repeated doses of TAF-MSCs and BM-MSCs hold significant promise as therapeutic options for repairing aspiration-damaged donor lungs and reducing the occurrence of PGD after transplantation.

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Donor organ optimisation in cardiothoracic TX

FOS_02_2 FWIT IN DCD HEART TRANSPLANTATION, DEFINITIONS AND OUTCOMES IN A 9 YEAR SIGLE CENTRE EXPERIENCE

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Background: Functional warm ischemic time (FWIT) is important in donation after circulatory death (DCD) heart transplantation. FWIT is defined to start when systolic blood pressure (SBP) falls below 50 mmHg, but the end time is debated. We studied the impact of FWIT definitions and durations on DCD heart transplant outcomes.

Methods: We did retrospective study on 105 DCD hearts, retrieved using direct procurement and perfusion (DPP) and transplanted in a single UK center from February 2015 to July 2024. Patients who received multiorgan transplants or had incomplete data were excluded (n=9). Two definitions of FWIT were used: FWIT-CP (FWIT from SBP <50 mmHg to cardioplegia) and FWIT-OCS (FWIT from SBP <50 mmHg to organ care perfusion). FWIT was additionally analyzed in <30 versus >30 minutes subgroups. We compared baseline characteristics, the need for post-transplant mechanical circulatory support (MCS) or an intra-aortic balloon pump, and short—and long-term survival.

Results: The study included 96 DCD HTx recipients. As expected FWIT-OCS was significantly longer compared to FWIT-CP (p < 0.05). Median and inter-quartile range for all FWIT are presented in table 1. There was no difference in need for MCS, IABP or 1-year mortality between patients with an FWIT above or below 30 minutes, by either definition of FWIT (Table1). Kaplan-Meier survival analysis revealed no difference in survival between FWIT-CP <30min and FWIT-OCS <30min (p=0.7479) or between FWIT-CP >30min and FWIT-OCS >30min (p=0.2705) Fig 1

Conclusions: This study suggests that DCD hearts with FWIT exceeding 30 minutes, may be used without increased MCS use or 1-year mortality, irrespective of FWIT definition. Larger studies will determine whether a threshold for acceptable FWIT exists and whether a particular definition of FWIT should be favored. Carefully selected DCD hearts with longer FWIT may add to the donor pool.

Variables		FWIT – CP		p-Value	FWIT - OCS		p-Value
		<30min (N=89)	>30min (N=7)		<30min (N=75)	>30min (N=21)	
Age, years, median (IQR)	Donor	35 (27-41)	37 (35-46)	0.10	35 (27-40)	35.50 (28.25-44)	0.42
	Recipient	53.96 (47.12-60.48)	49.01 (29.13-52.82)	0.09	53.60 (46.52-59.89)	53.31 (46.48-59.90)	>0.999
BMI, median (IQR)	Donor	25.20 (22.58-28.73)	29.80 (23.90-31.10)	0.24	25 (22.40-28.70)	27.20 (23.90-30.93)	0.11
	Recipient	25.85 (23.53-29.53)	23.40 (21.60-31.09)	0.48	26.20 (24-29.10)	25.35 (21.60-31.35)	0.61
FWIT, median (IQR)		16.50 (14-21)	40 (32-48)	**<0.0001**	24 (22-27)	36.50 (33-38.25)	**<0.0001**
Total Ischemia time, Median (IQR)		71 (63-83)	88 (78-93)	**0.03**	70 (61.75-80.25)	85.80 (73-95)	**0.00**
ICU Stay, median (IQR)		7 (4-13.75)	8 (3-22)	0.90	7 (3-14.25)	7 (3.5-12.5)	0.97
Hospital Stay, median (IQR)		23.50 (18.25-33.50)	24 (17-54)	0.89	23.50 (18-35.25)	24 (18.50-30.50)	0.98
30-days mortality, N (%)		4 (4.4%)	0.00	>0.9999	3 (4%)	1 (4.5%)	>0.999
90-days mortality, N (%)		7 (7.9%)	0.00	>0.9999	6 (8.1%)	1 (4.5%)	>0.999
1-year mortality, N (%)		9 (11.3%)	0.00	>0.9999	7 (10.6%)	2 (9.5%)	>0.999
MCS, N (%)		21 (23.03%)	1 (14.3%)	>0.9999	16 (21.3%)	6 (27.3%)	0.57
IABP, N (%)		15 (16.7%)	1 (14.3%)	>0.9999	11 (14.7%)	5 (22.7%)	0.35

Table 1. Baseline Characteristics and Outcomes

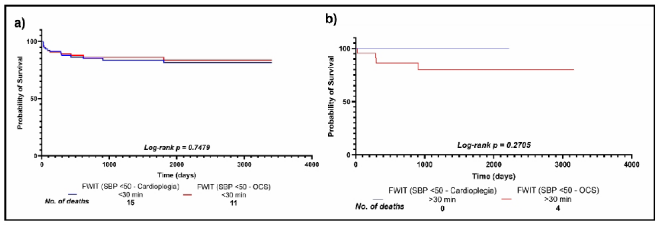

Fig 1. Long-term Survival Based on FWIT definition and duration

FOS_02_3 DOES DONOR AGE >70 VS <70 AFFECT LUNG TRANSPLANTATION OUTCOMES?

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Background: Lung transplantation (LTx) is a treatment for respiratory failure. Studies show that donor ages over 70 years did not adversely affect 1-year survival, but there is a lack of long-term outcomes. The aim of our study was to evaluate our cohort regarding the use of donors >70 compared to <70 after LTx.

Methods: We conducted a retrospective single centre study including all LTx performed between 2006 and 2024 (n=740). All-cause long-term mortality, 1-year mortality and forced expiratory volume in the first second (FEV1) were compared between groups based on donor age (A<70, B≥70). Risk factors for mortality were assessed using Cox regression. A propensity score matched analysis was performed to compare outcomes in the two groups.

Results: Recipients in group B (n=76, 10.3%) were shorter (p=0.023) and had a larger proportion with a history of smoking (p=0.0092) compared to group A. Recipients in group A were younger (52.4±14.3 vs 60.3±9.5, p<0.0001) and had a higher preoperative FEV1 (p=0.013). Donors of group B were more often women (p=0.004), had a shorter donor height (p<0.0001) and the cause of death was more frequently intracranial hemorrhage (p=0.0002). Postoperative duration of mechanical ventilation was shorter in group B (p=0.026). 1-year mortality was comparable though not statistically significant (group A 13.1%, group B 11.8%, p=0.76) between groups. FEV1 at 1 year was higher in group A (p=0.0077). In a Cox-regression analysis for long-term mortality recipient age (p>0.0001), BMI (p=0.031), donor age (per 10 y, p=0.029) and donor age ≥70 (p=0.026) were significant. Overall survival by Kaplan-Meier analysis was lower for group B (Fig 1). After propensity score matching two similar groups (n=63) were created and differences remained with poorer survival in group B (p=0.014).

Conclusions: This study shows that short-term survival using grafts from donors older than 70 years of age is comparable to those of younger donors, but long-term survival is inferior which indicates that grafts from older donors should be used in selected LTx patients.

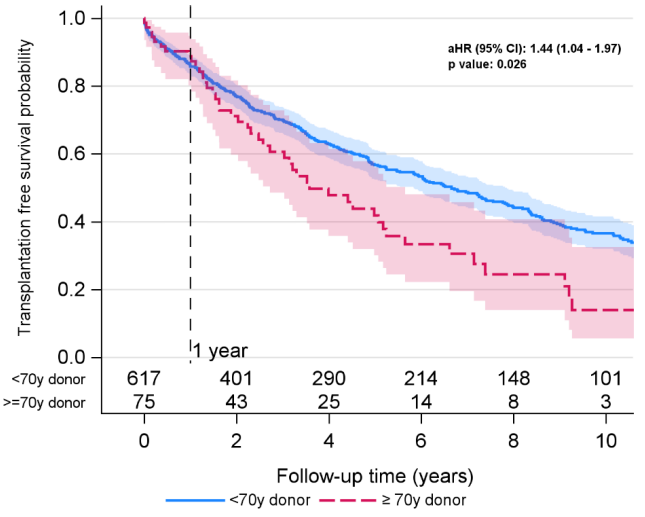

Fig 1. Kaplan-Meier Plot for composite of all cause death and re-transplantation by donor age groups. aHR adjusted for age and sex.,

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Donor organ optimisation in cardiothoracic TX

FOS_02_4 INTRODUCING FLEXIBILITY OF TRANSPLANT START TIMES USING CONTROLLED MODERATE HYPOTHERMIC DONOR LUNG PRESERVATION

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Background: Lung transplant centers are looking for new ways to add flexibility into their programs, whether it is to be successful in the CAS era or optimize their team's productivity. However, lung transplantation is limited by the short preservation window of donor lungs, with prolonged cold ischemic time (CIT) posing significant risks. In addition, nighttime transplants are associated with increased complications as well as logistical needs, while delaying surgery can contribute to the risks associated with CIT. Controlled moderate hypothermic lung preservation (LG) at 4-8 °C has shown promise in safely extending CIT beyond 8 hours. This multicenter study analyzed the impact of time-shifting practices on post-transplant outcomes when using the LG system for donor lung preservation.

Methods: Data from 437 adult lung transplant recipients transplanted between February 2021 and June 2024 from 9 transplant centers were analyzed in the GUARDIAN Lung Registry. We compared data from patients who received a lung transplant using a donor lung preserved in LG, with transplant occurring as soon as the lungs arrived at the recipient center (n=279, No Time-shifting), compared to data from transplants that were delayed for transplant (n=158, +Time-shifting).

Results: Time-shifting resulted in longer average total ischemic times, 10.7 versus 7.1 hours, $p<0.001$. The longer ischemic times were intentional, leading to planned incision start times, as the donor distance travelled was significantly shorter in the Time-shifting cohort (266 vs 401 miles, $p<0.001$). In Time-shifting procedures, there was a higher proportion of DCD donors (23.4% vs 9.0%, $p<0.001$) and donors >55 years of age (17.7% vs 8.2%, $p=0.005$). Despite total ischemic times averaging 3.6 hours longer, there was no difference in PGD3, and, while ECMO utilization appeared numerically higher in Time-shifting cases (17.1% vs 13.6%, $p=0.33$), the average days on ECMO was shorter (5.0 vs 8.0, $p=0.066$). One-year survival was similar.

Conclusions: The use of controlled moderate hypothermic lung preservation at 4-8 °C enables safe time-shifting of lung transplant procedures by extending preservation time without increasing the risk of adverse post-transplant events.

Table 1. Baseline characteristics and post-transplant outcomes

	No Time-shifting N = 279	+Time-shifting N = 158	*p*-value
Baseline Characteristics			
Donor Age (years)	36.4 ± 12.2	41.9 ± 15.4	<0.001
Donors >55 years	23 / 279 (8.2%)	28 / 158 (17.7%)	0.005
DCD Donor	25 / 278 (9.0%)	37 / 158 (23.4%)	<0.001
EVLP	0 / 279 (0.0%)	0 / 158 (0.0%)	>0.99
Total Ischemic Time (hours)	7.1 ± 1.7	10.7 ± 4.1	<0.001
Total Ischemic Time >8 hours	64 / 278 (23.0%)	113 / 158 (71.5%)	<0.001
Distance to Organ (miles)	400.7 ± 403.4	265.7 ± 298.5	<0.001
Average temperature	6.4 ± 2.3 °C	6.4 ± 1.9 °C	0.94
Recipient Age (years)	60.3 ± 10.6	60.0 ± 11.6	0.80
Recipient Age >70 years	27 / 279 (9.7%)	20 / 158 (12.7%)	0.34
Waitlist Duration, days	85.5 ± 160.1	79.1 ± 128.7	0.65
Post-transplant Outcomes			
Time Intubated (hours)	68.4 ± 145.7	54.9 ± 55.8	0.18
PGD Grade 3 at 72 hours	34 / 279 (12.2%)	20 / 158 (12.7%)	0.88
PGD Grade 2 or 3 at 72 hours	69 / 279 (24.7%)	41 / 158 (25.9%)	0.82
ECMO at 72 hours	24 / 279 (8.6%)	12 / 158 (7.6%)	0.86
Post-Transplant ECMO	38 / 279 (13.6%)	27 / 158 (17.1%)	0.33
Time on ECMO (days)	8.0 ± 7.8	5.0 ± 5.3	0.066
Vasodilator	118 / 279 (42.3%)	56 / 158 (35.4%)	0.19
Dialysis at Discharge	22 / 276 (8.0%)	16 / 157 (10.2%)	0.48
ICU Length of Stay (days)	13.6 ± 18.0	12.6 ± 13.2	0.52
Hospital Length of Stay (days)	30.5 ± 28.1	34.9 ± 34.4	0.18
In-hospital Survival	261 / 279 (93.5%)	150 / 158 (94.9%)	0.68
One-year Survival	202 / 231 (87.4%)	104 / 118 (88.1%)	>0.99
Acute Rejection* Within 1 Year	20 / 144 (13.9%)	5 / 69 (7.2%)	0.18

DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; EVLP, ex-vivo lung perfusion; ICU, intensive care unit; MCS, mechanical circulatory support; PGD, primary graft dysfunction.
** Acute rejection is defined as rejection grade A2-A4 (mild to severe) and the denominator at one year includes patients who have reached the one-year follow-up timepoint with a reported rejection status.*

FOS_02_5 COLD- STATIC DONOR LUNG PRESERVATION AT 10 DEGREE CENTIGRADE IN THE UNITED KINGDOM: A MULTI- CENTRE STUDY

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Background: Lung transplantation remains the only definitive treatment for patients with end-stage pulmonary disease, yet limited donor organ availability and preservation strategies present significant challenges. Cold static preservation at 10°C (CSP-10) has been proposed as a viable method for lung preservation, but its effectiveness and outcomes across centres has not been comprehensively evaluated in the UK context. This study was done at two major lung transplant centres in UK (Harefield Hospital and Royal Papworth Hospital).

Methods: A retrospective analysis was performed on UK lung transplant data (n=47) including Harefield Hospital (n=24) and Royal Papworth Hospital (n=23). The study evaluated donor characteristics, including age, sex, smoking history, and the total ischemic time (TIT), and compared outcomes based on preservation time at 10°C.

Results: Donor Characteristics-The mean age of donors was 51 years (range 32-59) at Harefield Hospital, 38 years (range 30-48) at Royal Papworth Hospital. Female donors accounted for 33% at Harefield and 43% at Papworth Hospital Donor smoking history was observed in 83% of Harefield, 70% of Royal Papworth hospital. Ischemic Time & CSP-10 Data-The median total ischemic time (TIT) for all cohorts was 672 minutes (range 567-824). At Harefield Hospital, the median time at 10°C was 623 minutes (range 733-942), while at Royal Papworth Hospital.Outcomes-30 days survival was 22 patients (92%) at Harefield Hospital and 22 patients (96%) at Royal Papworth Hospital and 1 year survival was 10 patients (80%) and 16 patients (81%) at both the hospitals respectively. There was no correlation observed between duration of preservation time at 10°C and post-transplant outcomes, including graft function and survival.

Conclusions: The use of cold static preservation at 10°C for donor lungs across the UK transplant centres is feasible and appears to provide comparable results, despite significant variability in ischemic times. Cold static preservation of lungs provide opportunity to accept more donor lungs and do transplant in semi-elective manner. Further prospective studies are necessary to confirm these findings and assess long-term graft survival and function.

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FOS_02_6 MITOCHONDRIAL TRANSPLANTATION DURING EX VIVO LUNG PERFUSION IMPROVED DAMAGED LUNGS AND TRANSPLANTATION OUTCOMES

Anna Niroomand[1], Nicholas B. Bechet[2], Aybuke Celik[1], Tibor Huzevka[1], Margareta Mittendorfer[3], Qi Wang[1], Embla Bodén[1], Gabriel Hirdman[1], Dag Edström[1], Gunilla Kjellberg[4], Haider Ghaidan[1], Snejana Hyllen[5], Franziska Olm[6], James McCully[7], Sandra Lindstedt[8]

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Background: Though there is a great level of demand for viable lung allografts, there is still a low rate of donor lung utilization owing to high discard rates secondary to donor-related injury, including aspiration-induced lung injury. To recuperate these potential grafts, advanced experimental therapies have been developed with the aim of mitigating ischemia-reperfusion injury and consequently the incidence of PGD. One promising approach involves delivering isolated exogenous mitochondria to the lungs prior to transplantation.

Methods: A porcine model of orthotopic left lung transplantation was leveraged to create a high-fidelity model of donor lung injury, followed by left lung transplantation and three days of recipient follow up. Aspiration of gastric contents induced lung injury in donor pigs and the subsequently explanted grafts were placed on ex vivo lung perfusion (EVLP) for four hours. Treatment followed with either exogenous mitochondria (n=6) or vehicle alone (n=6), and the left lung was transplanted into healthy recipients. PGD was evaluated based on blood gas measurements and chest imaging following the international guidelines. Lung tissue samples were used to histologically confirm lung injury, and further compare the groups at the conclusion of EVLP, and at the end of the experiment from the transplanted lungs.

Results: Mitochondrial transplantation resulted in a significantly increased PaO_2/FiO_2 ratio and reduced pulmonary vascular resistance compared to untreated lungs by the end of EVLP. At the conclusion of post-transplant follow up, all untreated recipients were found to have lower PaO_2/FiO_2 ratios and PGD grade 3, whereas only one recipient in the treated group experienced severe PGD. However, no lungs in the treated group were entirely free of PGD.

Conclusions: Mitochondrial transplantation was an effective therapy in mitigating aspiration-induced lung injury and resulting ischemia-reperfusion injury during EVLP. The treated grafts exhibited better lung function with lower incidence of PGD compared to untreated grafts following transplantation. Refinement of this advanced therapy will entail optimization of dosing and implementation of protocols to maximize therapeutic effect, though these results provide a basis for further pursuit of such work.

FOS_02_7 EX VIVO OPTIMIZATION OF DONOR LUNGS WITH INHALED SEVOFLURANE DURING NORMOTHERMIC LUNG PERFUSION

Shuqi Yang[1], Andrea Gentile[2], Mayara M de A Ramos[3], Sebastiaan Luttik[3], Jayant Jainandunsing[3], Dirk Bosch[3], Neeltina M Jager[4], Roland Hoffmann[5], Damien Richard[6], Matthieu Jabaudon[7], Matijs van Meurs[3], Michiel Erasmus[8], Michel Struys[3], Henri Leuvenink[9], Gertrude Nieuwenhuijs-Moeke[10]

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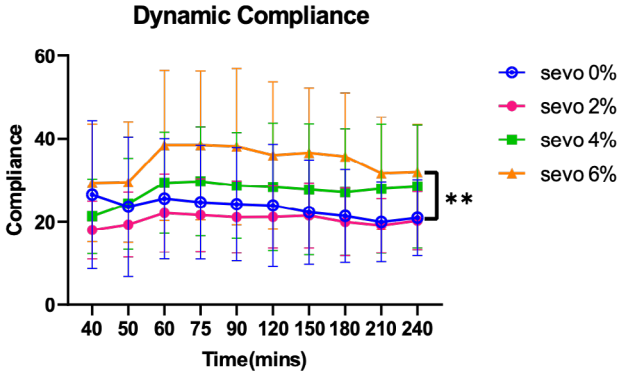
Background: Volatile anesthetics interfere with many of the processes underlying IRI and exerts lung protective properties in various models of injury and inflammation. Multiple points of engagement, are involved including prevention of opening of mitochondrial permeability transition pores, preservation of the glycocalyx, upregulation and stabilization of hypoxic inducible factors and direct effects on circulating immune. Ex vivo lung perfusion (EVLP) facilitates evaluation of potential grafts and extension of preservation time, and provides a therapeutic window of opportunity. We hypothesize that ventilation of donor lungs with sevoflurane during EVLP reduces injury and improves the quality of the transplanted lungs.

Methods: Thirty two lungs were randomized to 4 groups (n=8/group) ventilated with sevoflurane 0%,2%,4%,6% Cet during EVLP in a slaughterhouse sheep model. Lungs were harvested, flushed, and preserved cold storage for 3h, after which 4h EVLP was initiated. When a temperature of 32 ºC was reached ventilation was started. Functional measurements were recorded and perfusate and tissue samples were collected, at standardized timepoints. Normally distributed measurements were analyzed with one-way repeated measurements ANOVA and Friedman test was used for not normally distributed data.

Results: A steady state of the different target Cet sevoflurane was reached after 10 minutes. The Sevo-6% group showed remarkable increase dynamic compliance (p=0.006) compared to Sevo-0% group (Figure). After correcting the data to eliminate the effects of individual differences, Sevo-2%,4%,6% groups showed better compliance over time (p<0.0001) compared to Sevo-0% group. Sevo-6% group showed better oxygenation ability compared to Sevo-0% group (p=0.049). Wet weight/dry weight ratio and post-pre EVLP lung weight indicated no differences between groups. Sevo-4% group showed highest potassium levels in the perfusate (0% vs 4%: 4.33 vs 4.52,p=0.008) and Sevo-2% group showed lowest lactate levels in the perfusate (0% vs 2%: 0.93 vs 0.89,p=0.003). Sevo-2%,4%,6% groups' perfusate calcium levels were significantly reduced compared to Sevo-0% group (p<0.05).

Conclusions: Ventilating lungs with sevoflurane during EVLP showed better compliance and oxygenation ability, while no differences on edema.



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Donor organ optimisation in cardiothoracic TX

FOS_02_8 LACTATE CONCENTRATIONS DURING NORMOTHERMIC EX-SITU PERFUSION DO NOT CORRELATE WITH PGD IN DCD HEART TRANSPLANTATION

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Background: Normothermic ex-situ heart perfusion (ESHP) maintains donor hearts in a beating, metabolically active state outside the body. Lactate, a byproduct of anaerobic glycolysis, is a recognized marker of tissue hypoperfusion. An early study had demonstrated an association between lactate > 5mmol/L during ESHP of brain-dead donor hearts with poorer post-HTx outcomes. However, its reliability as a predictor of outcome in donation after circulatory death (DCD) heart transplantation (HTx) is uncertain. This study aims to evaluate lactate concentration during ESHP as a predictor of primary graft dysfunction (PGD) requiring veno-arterial extra-corporeal membrane oxygenator (VA-ECMO) support in DCD HTx recipients.

Methods: This is a single-centre retrospective study of consecutive DCD HTx procured using direct procurement and preservation (DPP) from March 2015 to July 2024. Patients without complete lactate profiles during ESHP were excluded from the analysis. The patients were divided in two groups according to the requirement for VA-ECMO post-HTx. Arterial and venous lactate levels and trends during ESHP in both groups were compared using logistic regression. Post-HTx outcomes in recipients with final arterial lactate on ESHP ≥5 mmol/L were also analysed.

Results: Of 103 DCD HTx included in the analysis, 25 (24.3%) required VA-ECMO support for PGD. There were no significant differences in arterial and venous lactate values or trends between the group with and without PGD. There were 52 (50.5%) DCD hearts with final arterial lactate concentration ≥5mmol/L. Recipients of DCD hearts with final lactate concentration <5 and ≥5 mmol/L had similar rates of PGD (21.6% vs 26.9%, p=0.53) and 90-day survival (92.2% vs 94.1%, p=0.7).

Conclusions: In our series of DCD hearts procured with DPP, lactate concentrations during ESHP did not correlate with the risk of PGD and requirement for post-transplant VA-ECMO. Our results suggest that carefully selected DCD hearts retrieved onto ESHP with final arterial lactate concentration ≥5mmol/L can be transplanted with good outcomes. However, we acknowledge that our study has an inherent bias, as only hearts that were used for transplantation were included, and further studies are required to investigate this topic.

FOS_02_9 A MACHINE PERFUSION SYSTEM FOR CARDIAC GRAFT ASSESSMENT AND TRANSPORTATIONS IN DONATIONS AFTER CIRCULATORY DEATH

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Background: Machine perfusion (MP) is emerging as a transformative technology for heart preservation and transplantation, particularly for donors after circulatory death (DCD). In this study, we developed and validated a portable ex-vivo MP system using slaughterhouse-sourced ovine hearts, simulating DCD conditions to assess organ viability and functionality.

Methods: Ovine hearts (n=10) were procured from a slaughterhouse following 15-25 minutes of warm ischemia. After initial cold cardioplegia perfusion, hearts were prepared and perfused in a closed-loop normothermic system using a novel customized perfusate. Myocardial function, metabolic recovery, and injury markers were evaluated in perfusate samples collected at predefined intervals. Myocardial tissue samples were analyzed for viability and injury.

Results: The perfusion system successfully resuscitated hearts, restoring pulsatile flow and achieving sustained contractile activity up to 7 ± 1.6 hours. Perfusate analysis showed lactate clearance (Lactate <4.75 ± 2.03 mmol/L), balanced pH (7.34 - 7.46), and stable electrolyte levels (Na^+: 136 ± 14 mmol/L, K^+: 4.9 ± 1.4 mmol/L). ECG monitoring showed sinus rhythm and consistent contractile function. Blood injury markers such as lactate dehydrogenase (366 ± 81 U/L), creatinine kinase (2804 ± 512 U/L) and troponin I (3.16 ± 1.1 µg/L) remained within clinically acceptable ranges. Infarct staining using TTC evidenced viable myocardium with less than 8% of infarct. Histological examination confirmed the preservation of myocardial architecture, with no evidence of edema, necrosis, or ischemic damage. Additionally, biochemical analysis indicated preserved mitochondrial function and reduced oxidative stress.

Conclusions: This study demonstrates the effectiveness of the developed portable MP system in maintaining organ viability and function during ex-vivo perfusion. The use of slaughterhouse-derived ovine hearts provides a cost-effective, ethical model for advancing DCD heart transplantation research. These findings highlight the potential of this system to expand the donor pool and improve transplantation outcomes.

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FOS_03_1 EVOLUTION OF TRANSCRIPTOMIC SIGNATURES ASSOCIATED WITH DONOR´S DIABETES IN NORMOGLYCEMIC TRANSPLANT RECIPIENTS

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Background: Deceased donors with diabetes are considered being suitable for kidney transplant recipients without diabetes, as long-term outcomes have generally been favorable however little is known about mechanisms supporting this approach. The assessment of zero-hour transplant biopsies, including transcriptomic analysis, represents an innovative tool to study molecular signatures associated with diabetes and their evolution in subjects with different glycemic control.

Methods: 288 deceased donor zero-hour kidney biopsies were prospectively collected in 2021-2022 and stored in RNAlater®. Transcriptomic profiles in biopsies of diabetic donors (n=43) and matched non-diabetic controls (n=86) were compared by microarray to identify diabetes-associated transcripts. Next, evolution of intrarenal transcriptome from zero-hour donor biopsy to 3-month protocol kidney graft biopsy was assessed by paired analysis in 50 diabetic and non-diabetic kidney transplant donors and recipients: Dd+/Rd-(n=13), Dd-/Rd+(n=11), Dd-/Rd-(n=26).

Results: Among the 47 upregulated (corresponding to 39 genes) transcripts discriminating diabetic donor kidneys from non-diabetic donor kidneys were aldo-ketoreductases (*AKR1C2, AKR1B10* and *AKR1B15*) and transcripts associated with fibrosis (*VNN1*, *VCAN*, *CXCL6* and *IGHM, IGHA1, JCHAIN*). Of 11 downregulated transcripts, three were from the kallikrein-kinin system (*KLK1*, *KNG1*, and *SERPINF2*). Assessments of transcriptome evolution from zero-hour biopsy to 3-months protocol biopsy in Dd+/Rd- revealed decrease in expression of aldo-ketoreductases (*AKR1C2, AKR1B10*) and *NQO1* (NAD(P)H quinone dehydrogenase 1) and increase of *SERPINF2* (serpin family F member 2), however there were no detected changes in the transcriptomic profiles in controls (Dd-/Rd-, Dd-/Rd+).

Conclusions: We identified four intrarenal transcripts associated with donor diabetes whose deregulated expression were normalized after successful kidney transplantation in non-diabetic recipients.

Support: Ministry of Health of the Czech Republic Grants NU21-06-00021 and by the project National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, Project No. LX22NPO5104) - funded by the European Union - Next Generation EU.

FOS_03_2 SGLT2I REDUCE THE EGFR SLOPE IN DIABETIC AND NON-DIABETIC RENAL TRANSPLANT RECIPIENTS

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Background: Renal graft function decline is an inevitable outcome in kidney transplant recipients (KTR). Non-immunological and immunological damage lead to glomerular loss, hyperfiltration, interstitial fibrosis, and tubular atrophy. Despite clinical-trial evidence proves that SGLT2i delay dialysis onset in diabetic and non-diabetic patients with CKD, and observational one shows safety in diabetic KTR, there is currently no data in non-diabetic KTR.

Methods: In this single-cohort study including all KTRs from Hospital Clínic Barcelona under SGLT2i, blood and urine tests at 12, 6 and 3 months before and after the initiation of an SGLT2i were collected. Demographic and clinical variables were obtained from medical health records. Estimated glomerular filtration rate, urine protein to creatinine ratio (UPCR), urinary tract infections (UTI) and treatment abandonment causes were recorded.

Results: From 2021 until 2023, 305 KTRs were prescribed an SGLT2i, 33 patients lost follow-up. 190 patients (62%) were male, 153 (50.2%) had diabetes [post-transplant diabetes in 61], 79 (26%) had a history of rejection. 59 (22%) were also receiving a GLP1 agonist. Eleven patients started treatment within 90 days of transplantation. The annual eGFR slope reduced from 1.58 before SGLT2i to 0.32 after, a decline of 1.2 ml/min/1.73m^2 (p = 0.049). UPCR significantly improved 6 months after treatment, going from an increase of 162 mg/g to a reduction of 64 mg/g (p=0.022). These results were independent from diabetes status. A total of 48 patients abandoned medication due to graft loss (16), UTI (4), erythrocytosis (2), diarrhea (3), renal function decline (3), unknown (4), struvite kidney stone (1), or died (15). 63 (21%) patients were admitted due to a UTI, 40 (13%) of them only once.

Conclusions: SGLT2 inhibitors slow renal function decline in diabetic and non-diabetic KTR. The observed improvements support their potential as an effective therapeutic option to preserve graft function.

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FOS_03_3 UNDERSTANDING THE IMPACT OF OBESITY ON LIVER TRANSPLANT OUTCOMES: A COMPREHENSIVE ANALYSIS

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Background: Exclusion criteria for liver transplant (LT) based on obesity vary throughout transplant centers, and morbid obesity is listed as a relative contra-indication in many transplant centers. The purpose of this investigation is to assess how effective it is to exclude individuals from LT by using BMI as a criterion.

Methods: A retrospective longitudinal analysis of liver transplant patient outcomes from January 2001 to May 2020 was conducted using the UNOS database. The cohort was categorized into subgroups based on transplant date and body mass index (BMI) of the recipients.

Results: A total of 118486 LT cases included in the study. Based on their BMI, patients were split into three groups: BMI<35 kg/m^2, 35≤BMI<40 kg/m2, and BMI≥40 kg/m2. The data analysis revealed a significant improvement in 10-year graft survival in the 2011-2020 group compared to the 2001-2010 group (Mean 70% vs. 53%, P<0.001). Interestingly, BMI above 35 kg/m^2 did not have a significant effect on the graft survival and in both time frames, there was no clinically significant difference between the recipients of different BMI spectrum. The patient's survival was also characterized by the same pattern. Primary graft failure was the most significant cause of allograft transplant failure in all the BMI spectrum, except recipients with a BMI<35 kg/m^2, in 2011-2020 group.

Conclusions: The long-term outcome of liver transplants in obese patients has been promising, particularly in the last decade. The outcomes of LT in patients requiring a LT are not significantly affected by BMI, considering the advancements in surgical techniques and post-operation improvements and excluding obese patients based on BMI alone would be inappropriate.

Graft failure causes (% total reported data)	2001-2010 (n= 8937)			2011-2020 (n=3095)			P-value[a]	P-value[b]	P-value[c]
	BMI<35 (n=8002)	35≤BMI<40 (n=647)	BMI≥40 (n=288)	BMI<35 (n=2572)	35≤BMI<40 (n=345)	BMI≥40 (n=178)			
Primary graft failure	1973 (24.6%)	169 (26.1%)	88 (30.6%)	352 (13.7%)	108 (31.4%)	57 (32%)	<0.0001	0.08	0.73
Recurrent disease	1434 (17.9%)	105 (16.2%)	37 (12.8%)	341 (13.3%)	36 (10.4%)	10 (5.6%)	<0.0001	0.01	0.01
Infection	1041 (13.1%)	90 (13.9%)	44 (15.3%)	417 (16.2%)	57 (16.5%)	32 (18%)	<0.0001	0.28	0.44
Vascular thrombosis	1158 (14.6%)	83 (12.8%)	41 (14.2%)	295 (11.5%)	32 (9.3%)	9 (5%)	0.0001	0.10	0.002
Chronic rejection	861 (10.7%)	69 (10.8%)	31 (10.8%)	287 (11.1%)	39 (11.3%)	15 (8.4%)	0.57	0.75	0.41
Biliary complications	731 (9.1%)	68 (10.5%)	25 (8.7%)	139 (5.4%)	8 (2.3%)	8 (4.5%)	<0.0001	<0.0001	0.09
Acute rejection	496 (6.2%)	40 (6.2%)	15 (5.2%)	250 (9.7%)	28 (8.1%)	23 (12.9%)	<0.0001	0.76	0.004
Hepatic artery thrombosis	82 (1%)	2 (0.3%)	0 (0%)	452 (17.6%)	34 (9.9%)	20 (11.3%)	<0.0001	0.0001	0.002
Patient non-compliance	226 (2.8%)	21 (3.2%)	7 (2.4%)	39 (1.5%)	3 (0.8%)	4 (2.3%)	0.0003	0.03	0.89

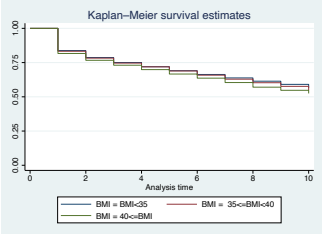

Figure 1. Graft Survival rate comparison between different BMI ranges in the 2001-2010 cohort (P=0.009)

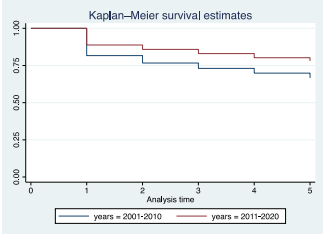

Figure 1. Graft Survival rate comparison between different BMI ranges in the 2011-2020 cohort (P=0.21)

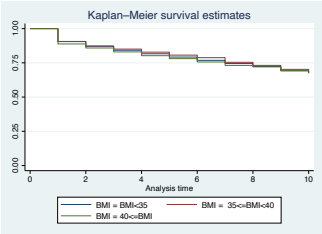

Figure 1. Graft survival rate comparison for 35≤BMI<40 kg/m^2 ᵗecipients between the 2001-2010 and 2011-2020 cohorts (p<0.001)

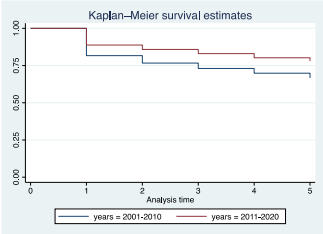

Figure 1. Graft survival rate comparison for BMI>=40 kg/m^2 recipients between the 2001-2010 and 2011-2020 cohorts (p<0.001)

FOS_03_3 MAJOR ADVERSE CARDIOVASCULAR EVENTS AFTER LIVER TRANSPLANTATION IN ENGLAND

Felicity Evison[1], Fatima Malik[2], Charlotte Stephens[3], Charles Ferro[4], Jonathan Townend[4], William Moody[4], Matthew Armstrong[5], Adnan Sharif[6]

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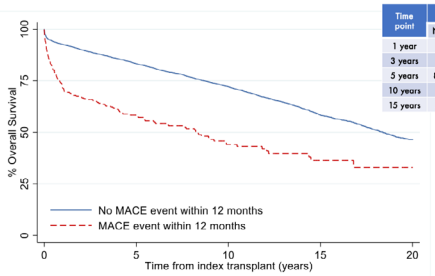
Background: Rates of major adverse cardiovascular events (MACE) early after liver transplantation are not well described in the literature.

Methods: In this retrospective cohort study, we studied every eligible liver transplant procedure performed in England between 1st April 2002 and 31st March 2023. Data was obtained from Hospital Episode Statistics, a data warehouse containing records for all patients admitted to the NHS in England. The primary outcome of interest was MACE defined as; any hospital admission with myocardial infarction, stroke, unstable angina, heart failure, any coronary revascularisation procedure and/or any cardiovascular death. Survival analyses were conducted with specific regression models (logistic, Cox and competing risk) for various survival explorations.

Results: After exclusions, 10,213 liver transplant recipients were available for analysis. MACE occurred in 268 liver transplant recipients within the first year after transplantation (2.6% of all liver transplant procedures). Of these 268 events, 125 occurred during the first month after liver transplantation surgery (representing 46.6% of all first-year MACE and 1.2% of all liver transplant procedures). Fatal MACE episodes within the first year were low at 0.1% (n=11). The commonest observed MACE was stroke (n=129), followed by myocardial infarction (n=89). Liver transplant recipients who experience MACE within the first year were older and had more co-morbidity, diabetes and pre-existing cardiovascular disease. After adjustment, MACE within the first year was associated with increased risk for long-term death (Hazard Ratio 1.37, 95% CI 1.05-1.79), p=0.021). In a competing risk regression model, with non-cardiac death a competing risk, the following were associated with increased risk for MACE; increasing age, male sex, diabetes, cardiac events in previous year (myocardial infarct, stroke, hypertension) and higher Charlson co-morbidity score.

Conclusions: MACE rates within the first year after liver transplantation in England are lower than reported in the literature. Although infrequent, non-fatal MACE within the first year is independently associated with increased risk for death in the long-term (see Figure) and more commonly associated with age, male sex and higher burden of medical co-morbidities.

Figure. Overall Survival by MACE at 12 months (MACE treated as time dependent)



Time point	Patient survival (95% CI)	
	No MACE within 1 year	MACE within 1 year
1 year	92.7% (92.1%-93.2%)	71.6% (65.8%-76.6%)
3 years	87.9% (87.2%-88.5%)	64.1% (58.0%-69.6%)
5 years	83.3% (82.5% - 84.0%)	58.3% (51.9%-64.2%)
10 years	72.2% (71.1%-73.1%)	44.1% (36.9% - 51.0%)
15 years	58.3% (56.9%-49.7%)	36.3% (28.1% - 44.6%)

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FOS_03_5 SAFE KIDNEY TRANSPLANTATION IN PATIENTS WITH HISTORY OF MULTIPLE MYELOMA: A FRENCH REGISTRY STUDY

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Background: Long-term outcome of kidney transplantation (KT) in patients with a history of multiple myeloma (MM) remain poorly characterized.

Methods: Based on the national Renal Epidemiology and Information Network registry, paired with the National Health System database, we analyzed MM patients under 70 years who underwent KT (MM+) between 2010 and 2020. A control group of KT recipients without MM (mm-) was matched on age, year of dialysis initiation, diabetes and cancer. The primary endpoints were patient and allograft survival within 5 years after KT.

Results: In MM+ and mm- group, 52 and 1364 patients were identified respectively. Table 1 depicted patient's characteristics at the time of transplantation. Time from dialysis to kidney transplantation was significantly longer in MM+ group (3.66 (IQR:2.04-4.85) vs 2.33 (IQR:1.21-3.80) years, p <0.001). Patient survival was similar in MM+ and mm- group (78.8% (59.7%-89.6%) vs 85.0% (82.7%-86.9%), p=0.49) (Figure 1.A.). Kidney allograft survival was significantly lower in MM+ group (72% (54.3%-83.8%) vs 90.0% (88.2%-91.6%), p <0.001) (Figure 1.B.). In MM+ group, 30.5% (17.8%-49.1%) of patients have MM relapse within 5 years after KT. Infection rate at 5 year was lower in MM+ than mm- group (17.1% (8.3-33) vs 31.8 (29.2-34.6), p=0.04). In multivariate analysis, history of MM was neither an independent risk factor for death (HR 1.28 (95% CI: 0.52,3.19)) nor for allograft loss (HR 2.37 (95% CI: 0.85,6.62)).

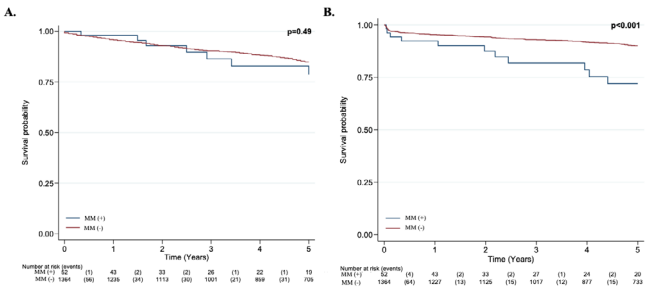
Conclusions: KT appears to be safe for patients with a history of MM showing no significant difference in overall survival compared to the general KT population and a satisfactory 5-year kidney allograft survival. However, this group may only represent low risk hematological profile.

Figure 1. Kaplan–Meier estimated (A) overall and (B) kidney allograft survival curves at 5 years for patients with history of myeloma (MM (+), blue) and no history of myeloma (MM (-),red)

Table 1. Characteristics of patients according to history of myeloma status

Baseline characteristic	MM+ N=52[1]	mm- N=1364[1]	p-value[2]
Age at initiation of dialysis, years	56.7 [48.9;62.0]	60.3 [53.3;64.9]	**0.005**
Male sex	34 (65.4%)	819 (60.0%)	0.44
Diabetes	2 (3.8%)	66 (4.8%)	>0.99
Coronary artery disease	0 (0.0%)	114 (8.4%)	**0.029**

[1]n (%); Median [25%;75%]



FOS_03_6 CARDIOVASCULAR OUTCOMES IN SOLID-ORGAN TRANSPLANT RECIPIENTS OF THE SWISS TRANSPLANT COHORT STUDY

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Background: Solid-organ transplantation (Tx) is the preferred treatment option for end-stage organ disease. Tx and immunosuppressive treatments are associated with an increased risk of cardiovascular disease (CVD), impacting morbidity and mortality of transplant recipients.

Methods: STCS is a comprehensive nationwide cohort study enrolling all solid-organ transplant recipients since May 2008. Clinical data from consecutive, first-time, single-organ Tx recipients was collected until December 2019. We assessed the primary composite CVD outcome of CVD-related deaths and CVD events (coronary, cerebrovascular and peripheral artery disease).

Results: Out of the 4254 included transplant recipients, 2429 were kidney, 1022 liver, 449 lung, and 354 heart recipients **(Table 1).** At Tx, the mean age was 53.2 (SD 13.2) and 1483 (34.9%) were women. The mean body mass index was 25.7 (SD 4.8) kg/m^2, systolic blood pressure 132.4 (SD 23.3) mmHg, LDL cholesterol 2.2 (SD 1.1) mmol/L, and 44% had never smoked. Pre-Tx CVD events were more frequent in heart recipients (51.3%) compared to kidney (30.0%), lung and liver (both 16.4%) transplant recipients (p<0.01). The main etiologies of the disease leading to Tx are shown in **Table 1**. After a median follow-up of 4.2 years (interquartile range 1.9–7.5), the risk for CVD events was 15.4% (650 events) and the risk for CVD-related deaths 4.4% (188 events). The overall incidence of the composite CVD outcome was 43.3 per 1000 person-years (95% confidence interval 40.4-46.4), which was highest in heart transplant recipients over the first 2.5 years post-Tx **(Figure 1,** log rank test p<0.001) and was decreasing over time in all Tx groups.

Conclusions: This large contemporary Tx cohort shows that patients after Tx can be classified at very high risk for CVD events (>10% risk over 10 years by definition). The development of CVD prediction models considering the type of transplanted organ is needed to tailor cardio-preventive therapies.

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Table 1

SOT recipients	N[1]	Overall (n = 4254)	Heart (n = 354)	Lung (n = 449)	Kidney (n = 2429)	Liver (n = 1022)
Baseline characteristics						
Age, years	4254	53.2 (13.2)	49.9 (13.0)	49.7 (13.8)	53.7 (13.6)	54.9 (11.2)
Women, no. (%)	4254	1483 (34.9)	84 (23.7)	215 (47.9)	873 (35.9)	311 (30.4)
Previous CVD, no. (%)	4218	1141 (27.1)	179 (51.3)	73 (16.4)	724 (30.0)	165 (16.4)
BMI, kg/m^2	4126	25.7 (4.8)	25.4 (4.4)	22.3 (4.6)	26.2 (4.7)	26.4 (4.9)
Systolic BP, mmHg	3986	132.4 (23.3)	103.6 (16.4)	127.6 (19.1)	140.9 (20.7)	123.4 (21.4)
Diastolic BP, mmHg	3984	77.4 (14.6)	67.5 (11.7)	79.4 (13.1)	81.2 (13.4)	70.6 (14.7)
Fasting glucose[2], mmol/L	1725	6.3 (2.7)	6.4 (2.4)	6.0 (1.6)	6.1 (2.9)	6.8 (2.7)
HbA1c[2], %	1917	5.5 (1.2)	5.7 (0.7)	5.9 (1.2)	5.4 (0.9)	5.3 (1.1)
Total cholesterol, mmol/L	3812	4.2 (1.4)	4.3 (1.3)	4.5 (1.5)	4.4 (1.2)	3.4 (1.7)
LDL cholesterol, mmol/L	3631	2.2 (1.1)	2.4 (1.0)	2.5 (1.2)	2.3 (1.0)	1.9 (1.2)
HDL cholesterol, mmol/L	3721	1.2 (0.6)	1.1 (0.4)	1.5 (0.7)	1.3 (0.5)	1.0 (0.7)
eGFR[3], mL/min/1.73m^2		41.8 (42.4)	66.9 (26.8)	103.4 (21.6)	9.9 (9.6)	81.7 (30.0)
Smoking status, no. (%)	3547					
Never smoked		1560 (44.0)	88 (32.7)	177 (46.0)	1016 (48.0)	279 (35.9)
Stopped > 1 year		1255 (35.4)	129 (48.0)	189 (49.1)	661 (31.2)	276 (35.5)
Current smokers[4]		732 (20.6)	52 (19.3)	19 (4.9)	439 (20.8)	222 (28.6)
Transplant-related data						
Main etiology leading to the transplant, no. (%)	4254		Ischemic heart disease: 125 (35.3)	COPD: 160 (35.6)	Glomerulo-nephritis: 603 (24.8)	Alcohol-related liver diseases: 337 (33.0)
Duration of follow-up		n = 4232	n = 350	n = 447	n = 2420	n = 1015
Median (IQR), years		4.24 (1.88–7.46)	3.93 (1.52–7.38)	3.75 (1.65–6.40)	4.63 (2.16–7.92)	3.62 (1.42–6.86)
Min – max range, years		0 – 11.66	0 – 11.61	0 – 11.52	0 – 11.66	0 – 11.62
CVD-related deaths		188 (4.4)	34 (9.7)	33 (7.4)	73 (3.0)	48 (4.7)
CVD events		650 (15.4)	75 (21.4)	77 (17.2)	366 (15.1)	132 (13.0)
Coronary artery disease		313 (7.4)	33 (9.4)	29 (6.5)	181 (7.5)	70 (6.9)
Cerebrovascular disease		172 (4.1)	25 (7.1)	25 (5.6)	88 (3.6)	34 (3.4)
Peripheral artery disease		283 (6.7)	29 (8.3)	37 (8.3)	174 (7.2)	43 (4.2)
Composite CVD primary outcome		776 (18.3)	101 (28.9)	101 (22.6)	404 (16.7)	170 (16.8)
Person-years		17,906	1338	1656	10,929	3983
Incidence rate, per 1000 person-years (95%CI)		43.3 (40.4–46.5)	75.5 (62.1–91.8)	61.0 (50.2–74.1)	37.0 (33.5–40.8)	42.7 (36.7–49.6)
At specific time intervals						
0–2.5 years		57.8 (52.8–63.2)	131 (105–163)	75.0 (58.6–96.0)	47.3 (41.6–53.8)	53.5 (44.0–65.0)
2.5–5 years		31.5 (27.0–36.8)	35.1 (20.4–60.4)	55.8 (38.3–81.4)	25.6 (20.5–31.8)	36.5 (26.9–49.6)
5–7.5 years		33.0 (27.1–40.3)	25.5 (11.5–56.8)	33.3 (16.7–66.6)	35.7 (28.0–45.4)	28.1 (17.7–44.6)
7.5–10 years		27.2 (19.8–37.4)	18.4 (4.6–73.5)	35.9 (11.6–111)	27.3 (18.4–40.3)	28.0 (14.0–55.9)

Footnotes: Numbers are presented as means (SD), unless stated otherwise. [1]Available data across all organs. [2]Systematic data collection of glucose levels and HbA1c started in 2012. [3]Calculated with the CKD-EPI 2021 formula. [4]Those who had stopped less than 1 year before inclusion (n = 228, 6.4%) were grouped with those reporting active smoking at inclusion (n = 504, 14.2%).

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SOT, solid-organ transplant.

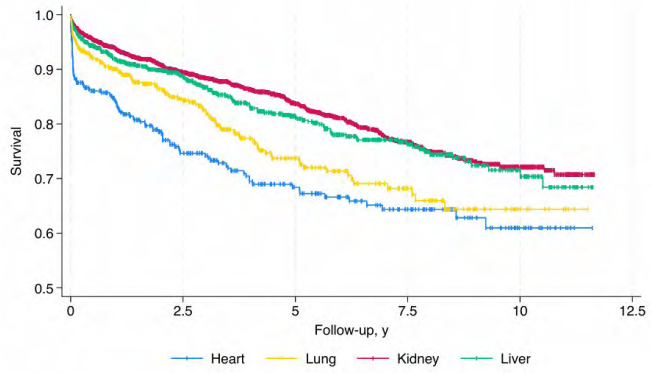

Figure 1. Kaplan-Meier curves of cardiovascular event-free survival of solid-organ transplant recipients by organ

FOS_03_7

RP1 IN SOLID ORGAN TRANSPLANT (SOT) RECIPIENTS WITH ADVANCED CUTANEOUS MALIGNANCIES (ARTACUS)

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Background: Skin cancers are the most common post-transplant malignancies in SOT recipients. While immune checkpoint inhibitors have improved outcomes in patients (pts) with advanced skin cancers, their use in SOT recipients is associated with high risk of allograft rejection. RP1 (vusolimogene oderparepvec) is an HSV-1–based oncolytic immunotherapy expressing a fusogenic glycoprotein (GALV-GP-R−) and GM-CSF. This study is assessing the safety and efficacy of single-agent RP1 in SOT recipients with skin cancer.

Methods: The study (NCT04349436) will enroll ≤65 SOT recipients with histologically confirmed advanced cutaneous squamous cell carcinoma (CSCC) and ≤10 with advanced non-CSCC skin cancer in 2 parts. Part A (completed) enrolled kidney and liver transplant recipients until safety was established, and Part B is enrolling kidney, liver, heart, and lung transplant recipients. Pts must have stable allograft function and ECOG performance status ≤1. Eligible pts have locally advanced or metastatic disease to the skin, soft tissue, or lymph nodes; pts with visceral metastases are excluded. Pts receive an initial intratumoral RP1 dose at 1 x 10^6 PFU/mL, followed by 1 x 10^7 PFU/mL every 2 weeks for up to 52 weeks or until confirmed disease progression or unacceptable toxicity. Tumor biopsies are collected for biomarker analyses and HSV-1 serostatus is monitored.

Results: At the time of analysis, 27 SOT recipients were enrolled (kidney, n=22; liver, n=4; lung, n=1) with a median (range) age of 68 (48–86) years; 24 pts had CSCC and 3 had Merkel cell carcinoma. At study baseline, 56% of pts had locally advanced disease and 44% had metastatic disease. The investigator-assessed objective response rate for efficacy-evaluable pts was 35% (8/23 [locally advanced, n=6; metastatic, n=2]); 22% of pts (5/23) had complete response. The most common (>20%) treatment-emergent adverse events were fatigue (33%), chills (26%), and pyrexia (26%). There was no evidence of allograft rejection.

Conclusions: This is the first trial assessing single-agent RP1 activity in SOT recipients with advanced cutaneous malignancies. RP1 monotherapy showed compelling anti-tumor activity in evaluable pts and was well tolerated, with a safety profile similar to that reported in non-immunocompromised pts with advanced skin cancers (IGNYTE study).

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FOS_03_8 ADJUVANT IMMUNOTHERAPY WITH CIK CELLS IN BEYOND MILAN HCC PATIENTS AFTER LT

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Background: Immunotherapy is now widely used for hepatocellular carcinoma (HCC). Immune checkpoint inhibitors (ICIs) are known to be highly effective but are often avoided after liver transplantation due to the risk of rejection. Cytokine-Induced Killer (CIK) cells have also shown promise as a cancer treatment, but their use following liver transplantation remains understudied due to concerns about acute rejection and the immunosuppressive environment. This study aimed to evaluate the safety and clinical efficacy of adjuvant CIK cell immunotherapy after liver transplantation in patients with advanced HCC.

Methods: This study assessed the safety and effectiveness of CIK therapy in 16 patients with HCC beyond the Milan criteria who underwent liver transplantation at two Korean hospitals between 2019 and 2021. CIK cells were administered in six escalating doses, either three or six times over weeks 4, 5, 6, 8, 10, and 12 post-transplantation. Clinical outcomes were compared with 44 propensity score-matched controls who did not receive CIK therapy. Subgroup analysis was performed using the Retreat score, R3-AFP score, and UCSF criteria.

Results: CIK therapy was well-tolerated without significant treatment-related adverse events. The maximum tolerated dose was 10×10^9 cells administered six times. The CIK group showed significantly higher recurrence-free survival (87.5% vs. 62.9%, P=0.027) and overall survival (100% vs. 81.5%, P=0.002) compared to the control group, with no significant differences in rejection-free survival (92.9% vs. 95.0%, P=0.926). Subgroup analysis revealed that patients with high Retreat scores (81.8% vs. 47.8%, P=0.034), elevated R3-AFP scores (77.8% vs. 33.3%, P=0.012), and those beyond UCSF criteria (81.8% vs. 44.4%, P=0.015) experienced improved recurrence-free survival.

Conclusions: Adjuvant CIK cell therapy after liver transplantation appears to be a safe and effective treatment for HCC beyond the Milan criteria, demonstrating improved recurrence-free survival and overall survival without increasing the risk of rejection. Further trials are warranted to confirm these promising results.

FOS_03_9 DE NOVO CANCER INCIDENCE AFTER SOLID ORGAN TRANSPLANTATION IN ENGLAND: THE EPCOT STUDY

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Background: Cancer post-transplantation is common and ranks as one of the biggest worries for transplant recipients. The incidence, however, remains poorly understood with published literature providing inconsistent rates. Our aim was to analyse post-transplant de novo cancer incidence using national record-linked transplant registry data.

Methods: Epidemiology of Cancer after solid Organ Transplantation (EpCOT) linked UK Transplant Registry data (held by NHS Blood & Transplant), cancer data (previously held by Public Health England), and administration and mortality data (held by NHS England) between 1985-2015 with outcomes to 2023. In this analysis, cancer incidence was assessed using standardised incidence ratios (SIR) and confident intervals (CI) against the general population.

Results: After excluding patients with a history of cancer pre-transplantation, our cohort included 62,691 solid-organ transplant recipients (68% kidney, 16.9% liver, 6.9% heart, 3.7% lung), accounting for 729,405 person-years (median years follow-up 9.79, interquartile range 4.55-17.55). There were 5,341 recorded cancers (8,931 including non-melanoma skin cancer [NMSC]), with an SIR of 1.31 (95% CI: 1.25-1.37) for women and 1.20 (95% CI 1.16-1.24) for men excluding NMSC. Incidence rates weren't uniform across cancer types. High rates were seen with lymphoma (SIR of 6.12, 95% CI: 5.43-8.64 for women and 5.25, 95% CI: 4.81-5.71 for men), and liver cancer (SIR of 6.90, 95% CI: 5.44-8.64 for women and 5.27, 95% CI: 4.56-6.06 for men), whilst low incidence rates were seen with prostate cancer (SIR 0.38, 95% CI: 0.33-0.43) and breast cancer (SIR 0.56, 95% CI: 0.49-0.63).

Conclusions: While transplant recipients in England have an increased risk of developing post-transplant cancer overall, risk for some cancers like prostate and breast are lower than the general population. Further planned analyses from EpCOT will improve our understanding of post-transplant cancer and inform clinical practice.

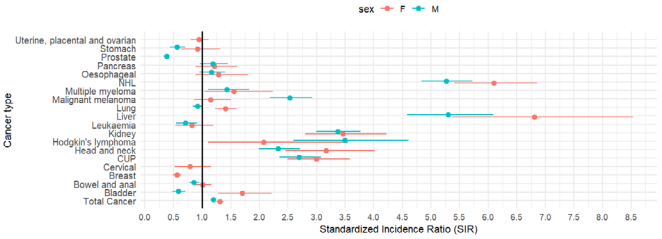
Table 1 - Characteristics of solid organ transplant recipients in England 1985-2015 (first transplants only)

Characteristics	Heart N (%)	Kidney N (%)	Liver N (%)	Lung N (%)	Pancreas N (%)	SPK N (%)	Total* N (%)
Total	4,563 (7.3)	42,051 (67.1)	10,642 (17.0)	2,500 (4.0)	209 (0.3)	1,721 (2.7)	62,691 (100.0)
Sex							
F	1,062 (23.3)	15,955 (37.9)	4,673 (43.9)	1,073 (42.9)	139 (66.5)	706 (41.0)	24,117 (38.5)
M	3,501 (76.7)	26,094 (62.1)	5,969 (56.1)	1,426 (57.1)	70 (33.5)	1,015 (59.0)	38,571 (61.5)
Age at transplant							
0-17	693 (15.2)	2,746 (6.5)	1,443 (13.6)	101 (4.0)	0 (0.0)	4 (0.2)	5,237 (8.4)
18-35	598 (13.1)	9,586 (22.8)	1,378 (12.9)	470 (18.8)	40 (19.1)	447 (26.0)	12,843 (20.5)
36-50	1,363 (29.9)	13,422 (31.9)	3,001 (28.2)	658 (26.3)	108 (51.7)	1,003 (58.3)	19,817 (31.6)
51-65	1,877 (41.1)	12,943 (30.8)	4,256 (40.0)	1,239 (49.6)	57 (27.3)	264 (15.3)	20,799 (33.2)
>65	32 (0.7)	3,354 (8.0)	564 (5.3)	32 (1.3)	4 (1.9)	3 (0.2)	3,995 (6.4)
Ethnicity							
Asian	237 (5.2)	4,061 (9.7)	947 (8.9)	51 (2.0)	3 (1.4)	98 (5.7)	5,455 (8.7)
Black	70 (1.5)	2,051 (4.9)	333 (3.1)	23 (0.9)	3 (1.4)	60 (3.5)	2,552 (4.1)
Chinese/Oriental	10 (0.2)	276 (0.7)	66 (0.6)	2 (0.1)	0 (0.0)	5 (0.3)	360 (0.6)
Mixed	14 (0.3)	104 (0.2)	16 (0.2)	1 (0.0)	0 (0.0)	3 (0.2)	139 (0.2)
Other	30 (0.7)	387 (0.9)	123 (1.2)	5 (0.2)	2 (1.0)	13 (0.8)	567 (0.9)
Unknown	1,287 (28.2)	8,883 (21.1)	955 (9.0)	277 (11.1)	2 (1.0)	59 (3.4)	11,693 (18.7)
White	2,915 (63.9)	26,289 (62.5)	8,202 (77.1)	2,141 (85.6)	199 (95.2)	1,483 (86.2)	41,925 (66.9)
Year of transplant							
1985-1995	1,742 (38.2)	11,880 (28.3)	1,803 (16.9)	366 (14.6)	1 (0.5)	59 (3.4)	16,181 (25.8)
1996-2005	1,622 (35.5)	12,006 (28.6)	4,085 (38.4)	848 (33.9)	15 (7.2)	335 (19.5)	19,317 (30.8)
2006-2015	1,199 (26.3)	18,165 (43.2)	4,754 (44.7)	1,286 (51.4)	193 (92.3)	1,327 (77.1)	27,193 (43.4)

Abbreviation: SPK, Simultaneous pancreas and kidney transplant

* Includes other solid organ transplants including heart & lung transplants and multi-visceral.

Figure 1 - Forest plot of standard incidence ratios for de novo cancer post solid-organ transplant



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FOS_04_1 ENVIRONMENTAL IMPACT OF TELEMONITORING IN KIDNEY TRANSPLANTATION: AN ANCILLARY STUDY OF THE AP'TX CLINICAL TRIAL

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Background: The Ap'Tx RCT(NCT03750331) aims at comparing tele-monitoring of stable kidney transplant recipients (KTR) using Ap'Telecare? with conventional monitoring. A total of 700 KTR have been enrolled and are being followed for 2 years. We sought to compare the environmental impact of those two types of post-transplant monitoring.

Methods: Carbon footprint of the first year post-tx monitoring was evaluated according to the GreenHouse Gas (GHG) protocol standard on 4 Ap'Tx trial patients who were or were not tele-monitored and who did or did not experience complications (rejection or recurrent infectious episodes). Along with emission related to outpatient care, hospitalization/ consultation and digital data storage, a cradle-to-grave inventory including production, freight, use and end of life of all medical devices and medicines was carried out.

Results: The first-year post-transplant carbon footprint varied from 915 to 3641 kgs eq CO^2/pt/year according to patients' characteristics with emissions related to complications, on-site consultations and medication being the most important categories. 76% of GHG emissions were due to complications-related hospitalisation. Telemonitoring was associated with a reduction of carbon footprint of 28% ($p<0.01$). Digital footprint represented 0.014 kgs eq CO^2/pt/year. Had the entire study population been switched to Ap'Telecare®-based monitoring, the carbon footprint would have been reduced by 1,500 tonnes eq CO^2/year.

Conclusions: Our results suggest that post-transplant telemonitoring has reduced environmental impact as compare to conventional follow-up. This is mainly driven by a decreased number of on-site consultations. Importantly, the digital carbon footprint of telemonitoring is negligible.

FOS_04_2 FIVE YEARS FOLLOW UP OF IMLIFIDASE DESENSITIZED KIDNEY TRANSPLANT RECIPIENTS

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Background: In four phase 2 clinical trials, patients received imlifidase-enabled kidney transplantation, turning a positive crossmatch (+XM) to negative. We here present data from 5 years follow up extension trial (n=39 patients). Patient survival, graft survival, renal function, antibody mediated rejection (ABMR) frequency, and presence of donor specific antibodies (DSAs) are presented.

Methods: Data from study (17-HMedIdeS-14; NCT 03611621) at 1, 2, 3, and 5 years after imlifidase were pooled with 6-month phase 2 data. Survival analysis was performed with Kaplan-Meier (censored at last known visit or death), renal function was estimated by eGFR (MDRD and KRS). ABMR was biopsy proven according to Banff 2017 criteria. DSAs were analyzed by LABScreen (One Lambda).

Results: Patient survival was 90% (CI: 80%-100%) with 3 deaths occurring between 6 months - 1 year, and no deaths occurring between 1-5 years. Death censored graft survival was 82% (CI: 70%-96%) with 3 graft losses in the feeder studies (1 IgM hyperacute rejection, 2 primary nonfunction), and 3 graft losses between 2-5 years (reduction of IS, medication nonadherence, and poor graft function). Mean eGFR was 50.1 mL/min/m^2 (MDRD) and 52.5 mL/min/m^2 (KRS) (Figure 1). Median MFI for immunodominant DSA pre-imlifidase was 6552 (IQR: 4225, 15944), rebounded to ~80% of pre-treatment levels with levels progressively decreasing over time. No late ABMR occurred between 3-5 years.

Conclusions: At 5 years, XM+ imlifidase kidney transplant recipients continue to demonstrate good patient and graft survival, despite the high-risk immunological profile. Kidney allograft function remains stable, indicating imlifidase as a viable and worthwhile treatment option for highly sensitized patients.

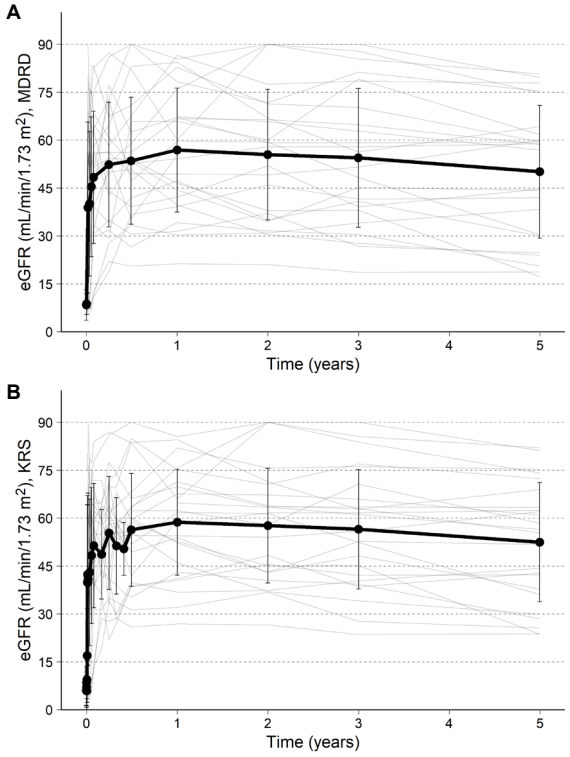

Figure 1. eGFR up to 5 years calculated with both MDRD (**A**) and KRS (**B**). Black lines and points are the mean and the error bars are the standard deviation. The thin grey lines represent the individual subject values.

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FOS_04_3 THREE DECADES OF RETRANSPLANTATION FOR CHRONIC LUNG ALLOGRAFT DYSFUNCTION: A RETROSPECTIVE ANALYSIS

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Background: Lung transplantation represents a final treatment option for carefully selected patients with end-stage lung diseases, and lung retransplantation may be considered in patients suffering from chronic lung allograft dysfunction (CLAD) after the primary transplant. In 2024, our center successfully completed 1,500 lung transplants, which led us to analyze the outcomes of this specific patient cohort.

Methods: All consecutive lung transplant recipients between 1991 and 2024 at our center were included in this study. Patients were categorized based on era: 1991–2000, 2001–2010, 2011–2020, and 2021–2024. For survival assessment of retransplanted patients, primary transplants were used as controls. Graft survival was analyzed using log-rank analysis and visualised by Kaplan-Meier survival curves. Demographic characteristics were assessed with Kruskal-Wallis, Fisher's and Chi-square test.

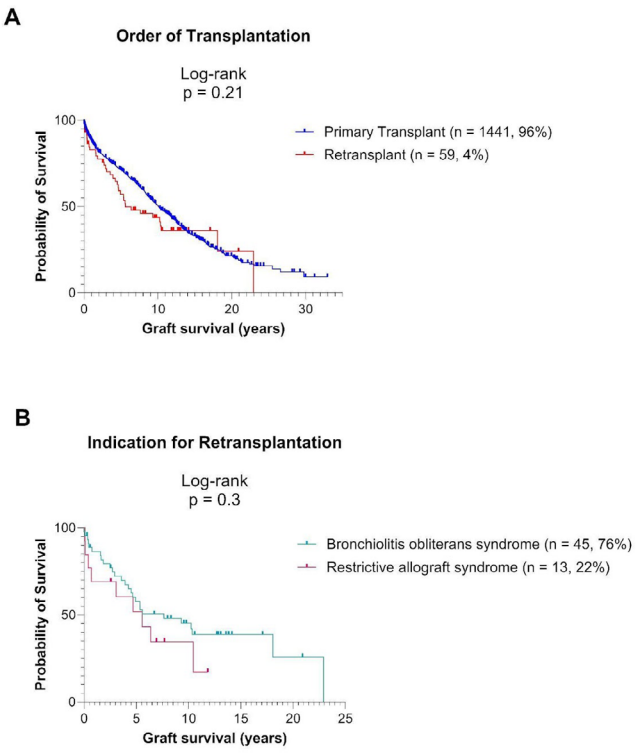
Results: A total of 59 (4%) retransplants were performed: 45 (76%) for bronchiolitis obliterans syndrome (BOS), 13 (22%) for restrictive allograft syndrome (RAS), and 1 (2%) due to pulmonary venous occlusion. A rise in RAS as a retransplant-indication was observed over time: 6% in 2001-2010, 29% in 2011-2020, and 40% in 2021-2024 (p<0.001; Table). No significant differences in graft survival were seen between primary transplants and retransplantations, nor between BOS and RAS (both p=ns; Figure).

Conclusions: In our cohort, patients after lung retransplantation demonstrated favourable outcomes with no statistical difference in survival between BOS and RAS as a retransplant-indication. These results contrast with those of previous studies [1,2] and may be attributed to the stringent selection criteria applied. The increasing proportion of retransplantation for RAS over time likely reflects improved recognition of this clinical phenotype, first described in 2011 [3]. Ongoing, careful evaluation of retransplant candidates is essential to assure good long-term post-transplant outcomes.

Table: Demographic data of patients who underwent lung retransplantation (reLuTx), grouped based on time periods.

	1991-2000	2001-2010	2011-2020	2021-2024	p
Number of reLuTx, n (%)	2 (4)	18 (31)	34 (58)	5 (5)	-
Type of procedure					
Unilateral, n (%)	2 (100)	2 (11)	2 (6)	0	**<0.0001**
Bilateral, n (%)	0	16 (89)	31 (91)	5 (100)	
Combined, n (%)	0	0	1 (3)	0	
Type of donation					
DBD, n (%)	2 (100)	15 (83)	26 (76)	4 (80)	**<0.0001**
DCD, n (%)	0	3 (17)	8 (24)	1 (20)	
Age of donor in years, median (IQR)	47 (N/A)	46 (35 - 52)	52 (40 - 58)	53 (30- 58)	0.41
Female gender, n (%)	2 (100)	13 (72)	14 (42)	3 (60)	**<0.0001**
Age at reLuTx in years, median (IQR)	48 (N/A)	36 (23 -54)	44 (31 - 52)	43 (31 - 52)	0.51
Indication diagnosis					
Obstructive, n (%)	2 (100)	17 (94)	23 (68)	3 (60)	**<0.0001**
Restrictive, n (%)	0	1 (6)	10 (29)	2 (40)	
Vascular, n (%)	0	0	1 (3)	0	
Graft survival					
30-days, n (%)	1 (50)	18 (100)	32 (94)	-	**<0.005**
1-year, n (%)	1 (50)	16 (89)	27 (79)	-	0.2
3-year, n (%)	1 (50)	12 (67)	18 (53)	-	0.46
5-year, n (%)	1 (50)	10 (56)	-	-	0.63

Figure:
A - Median graft survival for patients after primary transplantation and retransplantation.
B - Median graft survival after retransplantation for bronchiolitis obliterans syndrome and resitrictive allograft syndrome.



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FOS_04_4 OUTCOME OF SPLIT-LIVER TRANSPLANTATION WITH EXTENDED RIGHT GRAFTS WITHIN SCANDIATRANSPLANT

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Background: Split liver transplantation (SLT) addresses organ shortages by dividing one liver for two recipients, benefiting pediatric patients with size-matched grafts while preserving the adult donor pool. Since Scandiatransplant implemented a split liver policy and shared pediatric waiting list in 2015, pediatric waiting times have improved. However, extended right-lobe transplantation (ERLT) outcomes remain debated due to higher reported complication rates and inferior graft survival compared to whole liver transplantation (WLT). This study evaluates deceased donor ERLT outcomes in Scandiatransplant.

Methods: Adult liver transplant recipients from 2007 to 2022 across six countries and seven centers were retrospectively identified using the Nordic Liver Transplant Registry (NLTR). Multi-organ and re-transplantations were excluded. ERLT (n=139) was compared to WLT (n=4516) for patient and graft survival. Additionally, WLT cases eligible for SLT (sWLT, n=406) were matched with ERLT for further analysis. Propensity score matching, Kaplan-Meier survival estimates, and multivariable Cox regression were applied to assess donor and recipient factors influencing outcomes.

Results: ERLT recipients were more likely to be women (49.6% vs. 39.7%, p=0.05) and have malignancy as an indication (37.2% vs. 25.1%, p=0.003). While waiting times and MELD scores were similar, ERLT had longer cold ischemia times (p<0.001). ERLT was associated with higher rates of hepatic artery thrombosis (7.9% vs. 3.0%, p=0.033), biliary leakage (25.2% vs. 5.9%, p<0.001), and non-anastomotic biliary strictures (5.8% vs. 0.7%, p=0.002) compared to sWLT. Severe complications (Clavien-Dindo ≥3b) were also more frequent in ERLT (56.7% vs. 39.9%, p<0.002). Patient survival at 1, 3, and 5 years was similar (ERLT 90.6/86.3/80.9 vs. sWLT 94.6/90.0/86.9, p=0.49). However, ERLT graft survival was lower (ERLT 82.0/76.2/70.2 vs. sWLT 93.3/88.5/85.4, p=0.005). In-situ splitting had better graft survival than ex-situ (p=0.05).

Conclusions: SLT in Scandiatransplant has expanded the donor pool and maintained excellent patient survival. However, ERLT is linked to higher complication rates and lower graft survival, particularly with ex-situ techniques. Improving modifiable factors may enhance outcomes.

FOS_04_5 PANCREAS RETRANSPLANTATION, A TREACHEROUS YET FEASIBLE OPERATION: A SINGLE-CENTER EXPERIENCE

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Background: Recent improvements in the outcomes of pancreas transplantation have led to an increase in potential candidates for retrasplantation (PRT) following graft failure due to technical complications (TC) or chronic immunological rejection (IR).The objective of this study is to assess the results of a 24-year study of pancreas retransplantations in terms of patient and graft survival, based on the cause of primary graft failure.

Methods: A retrospective study was implemented to analyze the PRT performed in a single center between January 2000 and November 2024. Pancreatic graft loss was defined by the return to insulin dependence.

Results: A total of 507 pancreas transplantations were performed in our institution, of which 47 were retransplantations. The retransplantation group had a median age of 43 (IQR 37-48) years, and 53.2% were male. The median time between the first and second transplant was 58.6 (IQR 25.3-101.6) months.The primary graft failure was due to: immunological causes (n=27, 57.4%), technical complications (n=19, 40.4%) and a graft lymphoma requiring transplantectomy (n=1, 2.1%). A simultaneous pancreas-kidney (SPK) retransplantation was performed in 4 patients whereas pancreas alone retransplantation was carried out in 43 patients with a previously functioning kidney graft. The most common surgically related complication following PRT was vascular thrombosis, with no significant variation related to the cause of primary graft failure. After a median follow-up of 118 months (63.3 – 176.2), pancreas graft survival at 1,3, and 5 years was 82.1%, 72.7%, and 69.9% respectively, without differences between the two groups (p<0.05). No differences were found in terms of patient survival either at 1,3, and 5 years which were 100%, 95.5%, and 92.9%, respectively (p<0.05).

Conclusions: Pancreas retransplantation could be considered as a safe and effective second option in patients with previous graft failure, independently of the primary graft failure cause.

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FOS_04_6 INCIDENCE AND HIGH-RISK GROUPS OF HEPATIC ARTERY COMPLICATIONS AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: Hepatic artery complications (HACs) such as thrombosis (HAT) and stenosis (HAS) cause significant morbidity and mortality after pediatric liver transplantation (pLT); however, their incidence and risk factors remain poorly defined. This study aimed to investigate the incidence of HACs after pLT and identify high-risk groups.

Methods: We performed a retrospective, multicentric study from the HEPatic Artery stenosis and Thrombosis after liver transplantation In Children registry, which includes pLTs from 24 centers across 20 countries and six continents over a 20-year period. We examined the onset of HACs after pLT and analyzed the incidence of HACs across subgroups defined by pLT indication, age at pLT, donor type, transplant era, and annual center volume.

Results: A total of 8,469 pLTs were identified with 406 HACs, yielding an overall incidence of 4.8% (HAT: 3.4%; HAS: 1.4%). HACs occurred predominantly within the first month post-pLT (85.3%), with HAT peaking in the first week and HAS evenly distributed throughout the month. HAC incidence was higher after re-transplantation (6.5%) compared to primary pLTs (4.7%, $p = 0.04$) and after deceased donor liver transplantation (DDLT) compared to living donor liver transplantation (LDLT) (6.2% vs. 3.4%, $p < 0.01$). Among biliary atresia (BA) patients under 1 year, HAC rates were higher following DDLT than LDLT (7.6% vs. 3.2%, $p < 0.01$) and higher with whole grafts compared to partial grafts in DDLT (12.2% vs. 5.9%, $p < 0.01$). HAC rates significantly increased over time, from 3.6% (2002–2012) to 5.5% (2012–2022), and were highest in low-volume centers (11%, $p < 0.01$).

Conclusions: The overall incidence of HACs was 4.8%. Higher HAC incidence was observed in re-transplantations, DDLT (particularly with whole grafts in BA patients under 1 year), recent decade (2012–2022), and low-volume centers. Identifying these high-risk groups can help guide improvements in the prevention, detection, and management of HACs after pLT.

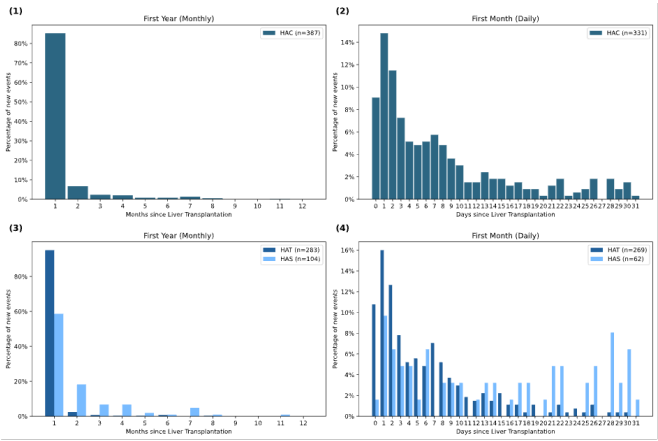

Figure 1. Temporal distribution of HAT and HAS. (1) Monthly distribution of HACs during the first year (2) Daily distribution of HACs during the first month (3) Monthly distribution of HAT and HAS during the first year, and (4) Daily distribution of HAT and HAS during the first month.

FOS_04_7 MESENCHYMAL STROMAL CELL THERAPY UNDER NORMOTHERMIC MACHINE PERFUSION: A PLACEBO-CONTROLLED STUDY IN A PIG MODEL

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Background: Kidneys from DCD or ECD are increasingly used in transplantation, although of suboptimal quality. Advanced preservation strategies, such as normothermic machine perfusion (NMP), may mitigate ischemic injury. Additionally, mesenchymal stromal cells (MSCs), known for their immunomodulatory and tissue-repair properties, offer a potential therapeutic approach. However, concerns regarding the toxicity of MSC injection directly into the renal artery persist. We assess the safety and efficacy of MSC administration during NMP in a paired placebo-controlled blinded study in pigs.

Methods: Pig kidneys (n=10) underwent 30 minutes of warm ischemia and 3 hours of cold ischemia before 6 hours of NMP at 37°C. After 45 minutes of NMP, 10 million human MSCs were injected into the renal artery of one kidney, while the contralateral kidney received a similar volume of placebo. Blinding was secured throughout the experimentation, including stats. Perfusion parameters were continuously monitored. Creatinine and iohexol clearances were assessed. Urine output and perfusate samples were collected hourly in order to quantify cytokine levels (e.g., IFN-γ, IL-2, IL-10, IL-1α, IL-6, TNF-α, IL-1β, IL-8).

Results: No significant differences were observed in perfusion parameters (flow, pressure, vascular resistance) between MSC-infused and placebo-treated kidneys, indicating the absence of perfusion disturbances caused by MSCs. Similarly, no significant differences were found in arterial blood gas metrics. The cytokine assay reveals that the majority of cytokines are undetectable at the onset of perfusion but exhibit an increase after three hours. Notably, TNF-alpha appears to decline further after six hours of perfusion but no significant difference was demonstrated between MSC-treated versus untreated grafts. Ongoing analyses aim to evaluate the clearance rates of creatinine and iohexol for further insights.

Conclusions: Our blinded, placebo-controlled, paired NMP pig model demonstrates that MSC administration into the renal artery is safe, without vascular toxicity or perfusion disturbances. The biological and histological assessment of MSC nephroprotection is ongoing.

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FOS_04_8

IMPACT PHARMACOLOGICAL GRAFT INFLOW MODULATION ON UTILIZING LEFT LOBE LIVING DONOR GRAFT IN ADULT LIVER TRANSPLANTATION

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Background: Right lobe grafts are favoured in LDLT due to size, despite higher donor risks. This study assesses whether pharmacologic graft inflow modulation (GIM) can increase the use of smaller left lobe grafts in adults

Methods: This was a single-cohort retrospective study, with data obtained from a prospectively maintained local registry, spanning Jan-2012 to Aug-2023.

Results: 202 left LDLT pairs were performed with a mean Graft-to-Recipient Weight Ration (GRWR) of 0.72 (SD 0.16). Octreotide was used perioperatively in 56% of cases and splenic artery ligation in 31%. Portal flow dynamics pre- and post-GIM are detailed in **Table 1**. The incidence of complications (Grade ≥1) was 48%, with major morbidity (Grade ≥3a) at 29% and Small-for-Size Syndrome (SFSS) occurring in 10% of cases. The median ICU and hospital stays were 5 and 28 days, respectively, with an in-hospital mortality rate of 8%. Following the 2019 introduction of pharmacologic GIM, the use of smaller left lobe grafts rose significantly (**Figures 1a, 1b**), representing a third of all adult LDLT cases. However, GRWR showed no correlation with SFSS (ILTS 2023 Consensus) or with short- or long-term outcomes (**Figures 1c, 1d**), even when GRWR was below 0.60% (Table 2).

Conclusions: With adequate graft inflow modulation and surgical expertise, adult left graft LDLT, down to a GRWR of 0.50%, can be a viable and safe option, with increased utilization of left lobe grafts in the adult liver transplant setting, while minimizing the risk of the donor.

Table 1. Adult left graft recipient characteristics and outcomes

Parameters	Values
	N=202
Adult left graft recipient	
Age, mean (SD), years	53 (16)
Female sex, n (%)	106 (52.5)
BMI, mean (SD) kg/m2	23.57 (4.17)
MELD-Na, mean (SD)	20.3 (6.4)
Growth to Recipient Weight Ratio (GRWR)	
GRWR, mean (SD)	0.72 (0.16)
Range (min, max)	(0.39, 1.48)
GRWR <0.50, n (%)	9 (5.0)
GRWR <0.60, n (%)	32 (17.6)
GRWR <0.70, n (%)	42 (23.1)
GRWR <0.80, n (%)	59 (32.4)
GRWR ≥0.80, n (%)	40 (22.0)
Indication for transplantation	
Metabolic & Genetic, n (%)	19 (9.9)
Viral hepatitis, n (%)	53 (27.7)
NASH, n (%)	40 (20.9)
Biliary, n (%)	17 (8.9)
Cryptogenic, n (%)	18 (9.4)
Autoimmune hepatitis, n (%)	27 (14.1)
Acute Liver Failure, n (%)	3 (1.6)
Alcoholic Liver Diseases, n (%)	5 (2.6)
Other, n (%)	9 (4.7)
Hepatocellular Carcinoma	29 (15.1)
Operative Characteristics	
Operation duration, median (IQR), min	416 (346-475)
Octreotide administration, n (%)	91 (56.2)
Octreotide dose, median (IQR), mcg/kg/h	1.0 (1.0-1.5)
Octreotide duration, median (IQR), days	7 (4-10)
Splenic artery ligation (SAL), n (%)	63 (31.2)
Both Octreotide and splenic artery ligation, n (%)	41 (20.3)
Either Octreotide or splenic artery ligation, n (%)	113 (55.9)
Hepatic portal hemodynamics	
Portal venous flow pre modulation, *mean (SD) ml/min*	1556 (758)
Portal venous flow post modulation, *mean (SD) ml/min*	1207 (574)
Portal venous flow delta, *mean (SD) ml/min*	-643 (660)
Hepatic artery flow pre modulation, *mean (SD) ml/min*	101 (80)
Hepatic artery flow post modulation, *mean (SD) ml/min*	150 (84)
Hepatic artery flow delta, *mean (SD) ml/min*	79 (69)
Short-term postoperative outcomes	
Acute kidney injury, n (%)	10 (5.2)
Ascites, n (%)	8 (4.2)
Biliary complications, n (%)	16 (8.3)
Bleeding, n (%),	14 (7.3)
Hepatic artery thrombosis, n (%)	14 (7.3)
Portal vein complications, n (%)	7 (3.6)
Hepatic vein complications, n (%)	0 (0.0)
Infection, n (%)	42 (22.9)
"Small for size syndrome" (ILTS Consensus 2023)	
None, n (%)	64 (35.8)
Grade A, n (%)	18 (10.1)
Grade B, n (%)	80 (44.7)
Grade C, n (%)	17 (9.5)
Overall morbidity (Grade ≥1), n (%)	92 (47.9)
GRWR <0.60% overall morbidity (Grade ≥1), n (%)	20 (48.8)
Major morbidity (Grade ≥3a), n (%)	56 (29.2)
GRWR <0.60% major morbidity (Grade ≥≥3a), n (%)	11 (26.8)
CCI™, median (IQR) points	20.9 (29.3)
ICU stay, median (IQR) days	5 (3-7)
Hospital stay, median (IQR) days	28 (19-36)
In-hospital mortality, n (%)	16 (8.3)

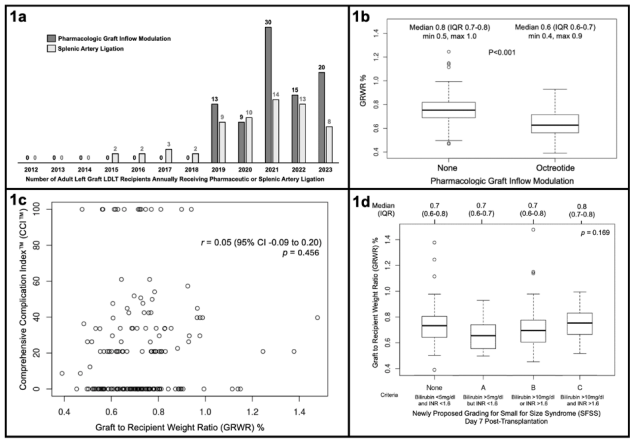

Figure 1. Comparative analysis of graft inflow modulation techniques and their impact on left graft LDLT outcomes. **Figure 1a**: Annual utilization of GIM techniques in LDLT (2012-2023). **Figure 1b**: Significantly lower GRWR in the Octreotide group. **Figure 1c**: Lack of correlation between GRWR and complications according to the Comprehensive Complication CCI™. **Figure 1d**: No significant difference in the GRWR distribution according to the SFSS Grading at day 7 post-transplantation (ILTS 2023 Consensus).

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Innovation in solid organ transplantation

FOS_04_9 APPLICATION OF A NOVEL SPATIAL TRANSCRIPTOMIC 6000-PLEX PANEL IN PIG-TO-HUMAN XENOTRANSPLANTATION

Valentin Goutaudier[1], Claire Williams[2], Erwan Morgand[3], Fariza Mezine[4], Jeffrey Stern[5], Aurélie Sannier[6], Adam Griesemer[5], Massimo Mangiola[7], Robert Montgomery[8], Alexandre Loupy[9]

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Background: Kidney xenotransplantation is a promising approach that has the potential to open new treatment avenues for patients currently on transplant waiting lists. Here we applied for the first time a 6000-plex gene panel to decipher the immune response after the transplantation of a genetically modified porcine kidney into a human recipient.

Methods: We performed in-depth multimodal phenotyping of tissue biopsies taken at 7 sequential follow-up times from Day 0 through Day 61. Initial bulk transcriptomic studies showed a molecular signature evocative of antibody-mediated rejection developing as early as day 10. In addition to a pre-transplant pig kidney control sample, we selected 4 post-transplantation time points to further explore and used the CosMx Spatial Molecular Imager to localize and profile the human immune cells infiltrating the xenograft in their spatial context. We designed a novel bioinformatic approach to accurately distinguish the approximately 3,000 human immune cells from the approximately 70,000 pig structural cells.

Results: Across all time points, macrophages were the most prevalent human cell type, in agreement with previous analyses. The human immune rejection response peaked at the D33 time point after which anti-rejection treatment was provided, leading to a successful decrease in the immune-molecular signs of xenoantibody-mediated rejection. We observed human myeloid cells present in every one of the post-transplant glomeruli in the sampled biopsies and characterized differential expression of pro- and anti-inflammatory myeloid genes over the course of treatment (**Figure**). We identified spatially-enriched human macrophage – pig structural ligand-receptor interactions present at early and late timepoints and catalogued spatially correlated modules of co-expressed genes.

Conclusions: Overall, our data suggest xenoantibody-mediated rejection, characterized by human innate immune cells infiltration in the porcine xenograft, localized within and outside of glomeruli. Discovery of these molecular mechanisms and the successful attenuation of the xenograft organ rejection with targeted treatment paves the way for potential new anti-rejection therapies to further enable human clinical trials.

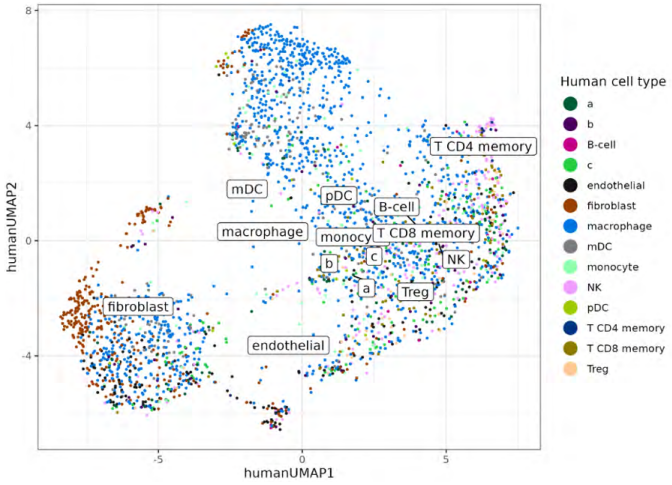

Figure. Clustering of putative human cells in the pig xenograft.

Histopathology and molecular signatures

FOS_05_1 MOLECULAR SIGNATURES OF REJECTION IN LIVER TRANSPLANT BIOPSIES USING THE BANFF HUMAN ORGAN TRANSPLANT GENE PANEL

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Background: Histologic assessment does not allow an accurate rejection diagnosis in liver transplantation (LT). The Banff Human Organ Transplant consensus gene panel (BHOT) offers reproductible molecular diagnosis in solid organ transplantation, but its application in LT biopsies remains unexplored. We aimed to identify specific molecular signatures and key functional pathways in liver allograft rejections using the BHOT panel.

Methods: We evaluated LT biopsies with circulating anti-HLA DSA testing from adult and pediatric recipients transplanted (2010-2020) in six French centers, excluding recurrence of liver disease, active HBV/HCV viremia. RNA was extracted from FFPE biopsies and sequenced using the BHOT panel (Nanostring® technology). Differential gene expression analysis was performed through 2-class comparisons based on histology, coupled with functional pathway analysis (PA).

Results: A total of 378 biopsies from 286 patients were assessed, with 226 (60%) performed for clinical indication. The median post-transplantation time was 1.29 years. DSA were positive for 181 (48%) biopsies. Among these, 99 (26%) were diagnosed as T-cell mediated rejection (TCMR); 22 (6%) as chronic rejection, 11 (3%) as antibody-mediated rejection, and 8 (2%) as plasma cell-rich rejection. TCMR-related transcripts were associated with IFNγ signaling (STAT1, CXCL9, CXCL10, CXCL11) and effector T cells (CTLA4, ICOS, BTLA). PA highlighted biological processes related to interleukins, IFNγ signaling, and immune cells interactions. Chronic rejection was associated with TGF-ß, MAPK (BMPR1B, TGFBR2, NR4A1), and NFKB (PLAU, BIRC3, BCL2A1) signaling. Plasma-cell type rejection was associated with IGHG 1-4 and IGKC transcripts.

Conclusions: Using the BHOT panel for the first time in LT biopsies, we identified meaningful molecular signatures for TCMR, chronic rejection, and plasma-cell type rejection, with functional analyses confirming their relevance. Ongoing analysis of larger cohorts will further validate these findings.

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FOS_05_2 BANFF HUMAN ORGAN TRANSPLANT PANEL FOR DETECTING ACUTE CELLULAR REJECTION IN LUNG TRANSPLANT BIOPSIES

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Background: Diagnosing the grade of acute cellular rejection (ACR) in lung transplant patients remains challenging yet crucial, given its association with long-term adverse graft outcomes. To gain insight into the pathophysiological mechanisms involved, we aim to identify the molecular profile among different severity grades of ACR using the Banff Human Organ Transplant (B-HOT) panel.

Methods: We analysed 212 transbronchial biopsies from 174 lung allograft recipients transplanted between 2010 and 2019 at Foch Hospital, France, and classified them as per ISHLT guidelines in the following clinical scenarios: subclinical biopsy-proven A1 ACR (n=42), biopsy-proven A1 with graft dysfunction or A2 ACR (n=46), antibody-mediated rejection (n=52), and non-rejection phenotypes (n=72). We sequenced all biopsies using the B-HOT panel and performed differential gene expression analysis comparing different severity grades of ACR vs. non-ACR biopsies. Significant differentially expressed genes (false discovery rate <0.05) were used for pathway analysis with ReactomePA.

Results: Subclinical biopsy-proven A1 ACR cases showed no differentially expressed genes compared to non-ACR cases. For biopsy-proven A1 with graft dysfunction and A2 ACR, we identified a molecular signature with significant upregulated transcripts associated with a T-cell mediated immune response, including T-cell activation and antigen recognition (CD3E, CD28, CTLA4, CD7, CD5, CD27, CD247, JAK3, IKZF1, ICOS, CD2, IL2RA, LILRB2), chemokine signalling (CXCL9, CXCL10), innate immunity responses (PTX3, CALHM6, GBP5, CD209) with macrophage activation (CD163, C1qB) as well as cell-related injury and repair. Pathway analysis showed that the top significant ACR-associated pathways included: TCR signalling (phosphorylation of CD3 and TCR zeta chains), lymphocyte interactions (specifically co-stimulation by CD28), and interferon and interleukin signalling (in particular IL-4 and IL-13).

Conclusions: Using the B-HOT panel, we identified a molecular signature and key functional pathways involved in clinical pulmonary ACR. We also show that subclinical minimal ACR cases do not demonstrate an immune-related molecular profile, aligning with prior evidence suggesting such cases can be monitored and may not require treatment.

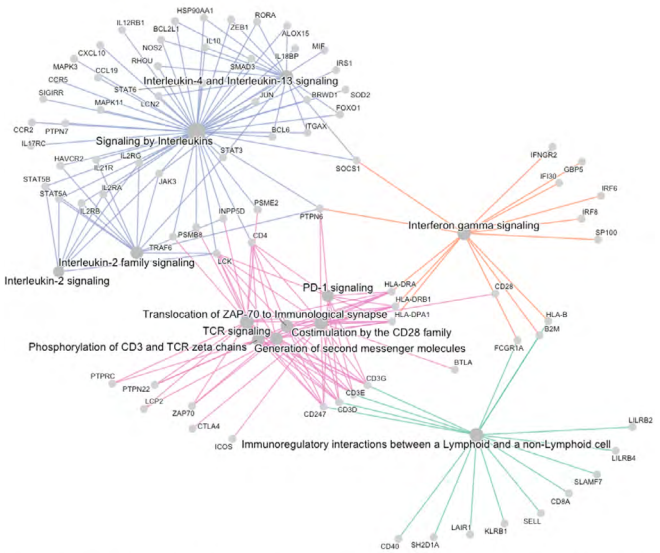

Figure. *The network diagram depicts the linkages between the significant differentially expressed genes and the biological concepts identified in the pathway analysis for clinical biopsy-proven acute cellular rejection.*

FOS_05_3 TRANSCRIPTOMIC SIGNATURES OF PANCREAS ACUTE REJECTION DECIPHERED BY RNA SEQUENCING OF PANCREAS GRAFT BIOPSIES

Maria Ramirez-Bajo[1], Jordi Rovira[2], Elisenda Bañón-Maneus[3], Ruben Lopez-Aladid[4], Enrique Montagud-Marrahi[5], Natalia Hierro-Garcia[6], Tim Swaab[7], Miriam Cuatrecases[8], Mª Angeles Garcia-Criado[9], Joana Ferrer-Fàbrega[10], Alejandro Álvaro-Meca[11], Fritz Diekmann[12], Josep M Campistol[13], Pedro Ventura-Aguiar[14]

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Background: Transcriptomic analyses in organ transplantation may improve histological diagnostic accuracy. Acute rejection (AR) presents common pathways between transplanted organs, but unique gene signatures associated with organ-specific cell types have been described to correlate with disease activity and outcomes.

Methods: We performed bulk RNA sequencing in 36 pancreas graft biopsies (No rejection n=11, T cell mediated rejection [TCMR] n=22; antibody mediated rejection [ABMR] n=3). Both for cause and surveillance biopsies were included. Non-coding genes were excluded from the analysis. Differential gene expression comparative analysis was conducted using an available dataset from kidney transplant (GSE36059).

Results: Of the 16,743 coding genes sequenced, 786 genes were differentially expressed between biopsies with and without AR, of which 507 were overexpressed and 279 were underexpressed. Following gene enrichment analysis, those associated with immune cell activation and cell-cell communication presented highest expression (i.e. CXCL13, CXCL9, CXCL10, IL7R, CD2, IKZF3). Principal component analysis clustered AR biopsies with high specificity. In AR biopsies DGE for pancreas-specific cell types was increased, such as those for ductal cells (SLC4A4, MUC5B), pancreatic stellate cells (ITGA1, ITGAD, DES) or Schwann cells (S100A9). When analysed separately, TCMR and ABMR biopsies presented an overlap of 201 DEGs, whereas TCMR presented 435 uniquely expressed genes, and ABMR 341. In a cell deconvolution analysis, both TCMR and ABMR presented an increase in M1 macrophages expression, but only for TCMR was an increase in CD8 T cell and NK cell observed. On a comparison to kidney transplant data, we observed an overlap of 275 genes in TCMR, but a unique differential expression in 496 genes for pancreas samples, whereas for ABMR we observed an overlap of only 24 genes and a unique expression in 189 for pancreas samples.

Conclusions: A transcriptomic analysis of pancreatic biopsies demonstrates similar pathways for TCMR and ABMR during pancreas acute rejection, but highlights the expression of unique genes associated with pancreas-specific cell types. These results warrant further investigation to the impact of these genes on graft outcomes.

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FOS_05_4 MOLECULAR CLASSIFICATION SYSTEM FOR CARDIAC ALLOGRAFT REJECTION POSITIVELY CORRELATES WITH REJECTION PATHOLOGY SEVERITY

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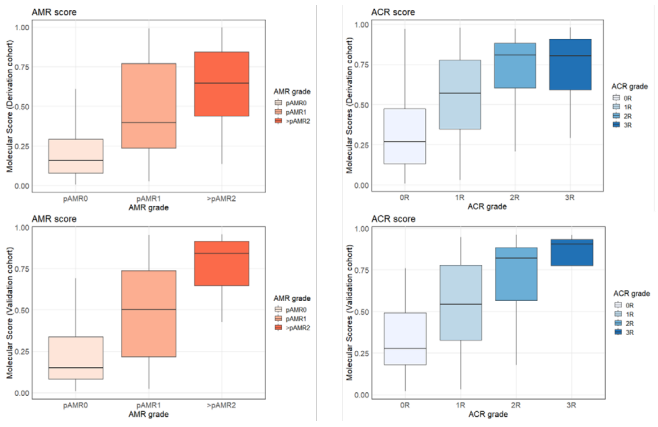
Background: Targeted molecular profiling combined with reproducible formalin-fixed paraffin-embedded (FFPE) EMB-based technology has the potential to support cardiac rejection diagnosis. We aimed to develop and validate targeted gene expression diagnostic models of cardiac rejection and show their association with ISHLT pathological grades.

Methods: We built a multicenter cohort of 591 FFPE-EMBs collected from four international centers between 2011 and 2021. Biopsies were graded according to the ISHLT working formulations, including 188 AMR cases, 289 ACR cases, and 114 non-rejection cases, randomly split in a derivation (n = 475) and a validation cohort (n = 116). Tissue gene expression was analyzed on FFPE-EMB using the Banff Human Organ Transplant gene set. Molecular classifiers for AMR and ACR were built using a supervised model. Association between molecular scores and pathology severity of rejection were analyzed in both derivation and validation set.

Results: The derivation included a total of 151 AMR (pAMR1H+: n = 46, pAMR1I+: n = 36, pAMR2-3: n = 69), 232 ACR (ACR 1R: n = 143, ACR 2-3R: n = 89) and 92 non-rejection cases. The validation set included a total of 37 AMR (pAMR1H+: n = 12, pAMR1I+: n = 15, pAMR2-3: n = 10), 57 ACR (ACR 1R: n = 31, ACR 2-3R: n = 26) and 22 non-rejection cases. Median AMR scores in AMR, ACR and non-rejection cases were 0.655 (IQR = 0.316), 0.217 (IQR = 0.254) and 0.140 (IQR = 0.209), respectively. Median ACR scores in ACR, AMR and non-rejection cases were 0.678 (IQR = 0.347), 0.263 (IQR = 0.364) and 0.302 (IQR = 270), respectively. AMR and ACR molecular scores were strongly associated with the pathology assessment of severity of rejection according to AMR and ACR international working formulations, respectively (derivation set: ACR: p for trend = 1.017E-46, AMR: p for trend = 2.911E-52; validation set: ACR: p for trend = 1.827E-13, AMR: p for trend = 5.174E-10, **Figure**). Molecular AMR score was not associated with ACR severity; neither was the ACR molecular score with AMR severity.

Conclusions: Tissue-based molecular diagnostic system developed closely aligned with histological grading of cardiac allograft rejection, enhancing diagnostic precision, and offering a reliable companion tool for routine practice.



FOS_05_5 MULTICENTER CLINICAL AND MOLECULAR INSIGHTS QUESTIONING THE ROLE OF INTIMAL ARTERITIS IN THE BANFF 2022 CLASSIFICATION

Karolien Wellekens[1], Angelica Pagliazzi[2], Priyanka Koshy[3], Thibaut Vaulet[4], Maarten Coemans[5], Maarten Naesens[3]

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Background: According to the Banff classification, intimal arteritis ("v") contributes to diagnosis of T cell-mediated (TCMR) and antibody-mediated rejection (AMR) and signifies more severe TCMR.

Methods: This multicenter cohort study analyzed 5144 kidney transplants and 14578 biopsies to assess the impact of v-lesions on biopsy classification and outcomes. Transcript-based validation using the Banff Human Organ Transplant (B-HOT) panel was conducted on 886 biopsies.

Results: Among 14578 biopsies, 707 (4.8%) exhibited v-lesions, originating from 534 transplants. Of these, 180 (25.5%) biopsies were classified as isolated v (t0-3i0 or t0i0-3), 123 (17.4%) as borderline changes with v (t1-3i1 or t1i1-3), 102 (14.4%) as TCMR-I with v (t2-3i2-3), 189 (26.7%) as AMR-MVI with v (Banff'22 AMR or DSAneg C4dneg MVI), and 71 (10.0%) as TCMR-I + AMR-MVI with v. Borderline changes with v showed no significant difference in 10-year graft failure rates compared to isolated v cases. In contrast, biopsies with TCMR-I, AMR-MVI with v, and TCMR-I + AMR-MVI with v demonstrated significantly higher graft failure rates (Table 1). Of the B-HOT-analyzed biopsies, 78 biopsies were v-positive (40 isolated v, 25 borderline changes, 13 TCMR-I) and 808 were v-negative (667 no rejection, 120 borderline changes, 21 TCMR-I). Differential gene expression in v-positive cases revealed significant upregulation of pro-inflammatory and TCMR-related pathways correlating with increasing tubulo-interstitial inflammation. However, no significant differences, including endothelial transcripts, were observed between v-positive and v-negative cases across no rejection/isolated v, borderline changes, and TCMR-I groups (Figure 1).

Conclusions: Additional TCMR and AMR-MVI criteria outperform isolated v-lesions in predicting graft prognosis. The lack of associated gene expression changes calls into question the validity of the current TCMR grading system, underscoring the need to reassess the role of v-lesions in the Banff classification.

Table 1: Univariable and multivariable 10-year outcome
Transplants were classified based on the first v lesion-positive biopsy.

N=534 "v" lesion-positive transplants (total)				
	Cox model			
Reference: Isolated v N=180	Univariable HR [95% CI]	p-value	Multivariable* HR [95% CI]	p-value
Borderline changes with v N=83	1.54 [0.81-2.94]	0.19	1.55 [0.81-2.96]	0.18
TCMR-I with v N=69	2.81 [1.55-5.07]	<0.001	2.79 [1.55-5.05]	<0.001
AMR-MVI with v N=138	2.34 [1.38-3.98]	0.002	1.93 [1.11-3.37]	0.02
TCMR-I + AMR-MVI with v N=64	3.26 [1.79-5.93]	<0.001	2.76 [1.49-5.11]	0.001

*Adjusted for HLA-DSA status at time of the biopsy (preformed and de novo HLA-DSA), biopsy timing post-transplantation (days after transplantation).

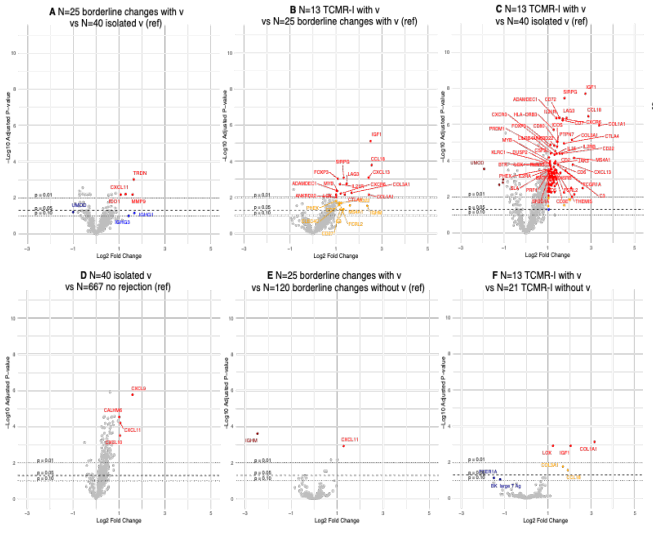

Figure 1: Differential gene expression in B-HOT-analyzed biopsies

Key genes and pathways are highlighted, with fold change (log2) on the x-axis and statistical significance (-log10 p-value) on the y-axis. All analyses were adjusted for concomitant (probable) AMR or microvascular inflammation, polyomavirus-associated nephropathy and timing post-transplantation.

Significance level
- highly significant p<0.01 upregulated
- highly significant p<0.01 downregulated
- significant p<0.05 upregulated
- moderately significant p<0.10 upregulated
- moderately significant p<0.10 downregulated
- not significant

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FOS_05_6 INTER-CENTER VARIABILITY OF BIOPSY-BASED TRANSCRIPT DIAGNOSTICS - COMPARISON OF BANFF LESIONS WITH MOLECULAR SCORES

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Background: Biopsy-based transcript diagnostics should objectively evaluate kidney allograft biopsies. The Banff 2022 Work Plan calls for validation of biopsy-based transcript assays in different centers to help define universally applicable molecular classifier thresholds.

Methods: 755 kidney allograft biopsies from 2 European centers were assessed by the Molecular Microscope Diagnostics system (MMDx®) at 2 laboratories in Portland, USA, and Prague, Czechia. We compared histological lesions to MMDx classifier and probability scores. The cohort encompassed 145 active/chronic-active antibody-mediated rejection (AMR); 117 probable AMR; 64 DSA-neg. C4d-neg. microvascular inflammation (MVI); and 93 T-cell mediated rejection (TCMR).

Results: Glomerulitis (g), peritubular capillaritis (ptc), interstitial inflammation (i), and tubulitis (t) drive the corresponding molecular lesion scores, rejection, AMR, and TCMR classifiers ($p<0.05$). Glomerular basement membrane double contours (cg) drive the molecular cg>0 probability only when MVI is present ($p<0.05$). While intimal arteritis (v) scores are more associated with molecular rejection and TCMR classifiers ($p<0.001$) compared to molecular AMR classifiers ($p=0.02$), isolated v lesions drive molecular rejection, TCMR, and AMR classifiers in individual cases only. Interestingly, C4d scores (by immunofluorescence staining) drive the molecular g>0 probability and AMR classifier even at a subthreshold level of C4d1 ($p<0.05$). A large inter-center variability is shown for all active histological lesion scores (g, ptc, i, t) and the corresponding molecular scores, rejection, TCMR, and AMR classifiers, that is most pronounced for MVI (g+ptc, $p<0.05$). In cases with AMR, probable AMR, DSA-neg. MVI, and TCMR, the molecular interpretation as molecular AMR or TCMR was 47% vs. 82%, 10% vs. 23%, 42% vs. 57%, and 20% vs. 24% between the centers, respectively.

Conclusions: Histological lesions drive the molecular probability and classifier scores across the 2 centers. The large inter-center variability may be attributed to different biopsy policies, time post-transplant, and the inter-observer variability of renal pathologists. Our data suggest that the added value of the MMDx must be assessed in the context of a center's individual characteristics.

FOS_05_7 ASSOCIATIONS OF REPEATED BIOPSY-BASED DIAGNOSES WITH KIDNEY TRANSPLANT SURVIVAL: AN OBSERVATIONAL COHORT STUDY

Arthur Vranken[1], Maarten Coemans[2], Maarten Naesens[3]

[1]University Hospitals Leuven; University Hospitals Leuven, [2]Ku Leuven; University Hospitals Leuven; Microbiology En Immunology, [3]Ku Leuven; Ku Leuven; Nephrology and Renal Transplantation

Background: The histology of kidney transplant biopsies, classified according to the Banff system, is an important determinant of post-transplant graft survival. While the underlying immune risk inherent to allotransplantation is not waning, the persistence of histological injury over multiple biopsies has not been investigated adequately.

Methods: In a large single-centre observational cohort study (N=1802 kidney transplant recipients with 5822 post-transplant biopsies), time-dependent covariates were constructed for T-cell mediated rejection (TCMR), antibody mediated rejection (AMR), microvascular inflammation in the absence of donor-specific antibodies (DSAneg MVI) and polyomavirus associated nephropathy (PyVAN), describing for each biopsy whether there had been zero, one, or at least two diagnoses. Associations with graft failure were assessed using multivariable cause-specific hazard models. To take into account potential informative sampling bias, sensitivity analyses were run in a protocol biopsy subset and an indication biopsy subset, adjusted for the number of biopsies.

Results: AMR had the highest proportion of repeatedness: in 49 % of recipients with an AMR diagnosis, a second AMR diagnosis followed at some point. Next followed TCMR with 32 %, DSAneg MVI with 29 % and PyVAN with 21 %. The hazard of graft failure was significantly and independently increased by the second diagnosis of TCMR (HR 2.55, 95% CI 1.58-4.12), AMR (HR 3.38, 95% CI 1.72-6.66), DSAneg MVI (HR 2.40, 95% CI 1.18-4.88) and PyVAN (HR 11.96, 95% CI 6.39-22.38). In the sensitivity analyses, results were confirmed for TCMR, AMR and PyVAN.

Conclusions: TCMR, AMR, DSAneg MVI and PyVAN often reappear or persist in multiple biopsies of kidney transplant recipients. A second diagnosis of TCMR, AMR or PyVAN more strongly increases the hazard of graft failure than a first diagnosis of TCMR, AMR or PyVAN, indicating that treatment of these conditions fails.

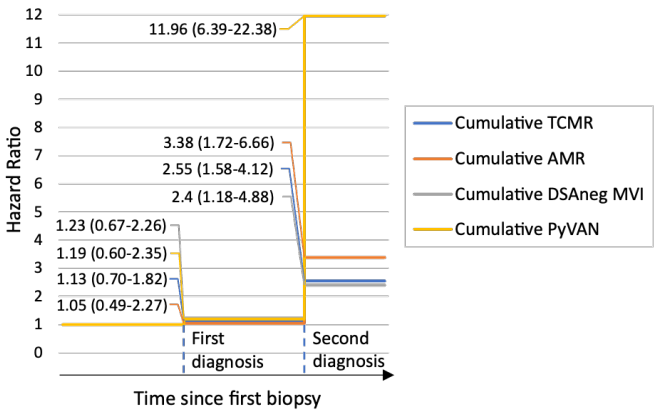

Figure 1. Adjusted hazard ratios with 95% confidence intervals describing associations of cumulative diagnoses with graft failure.

Abbreviations: TCMR, T-cell mediated rejection; AMR, antibody-mediated rejection; DSAneg,MVI; microvascular inflammation in the absence of donor-specific antibodies; PyVAN, polyomavirus associated nephropathy

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FOS_05_8 INTIMAL ARTERITIS WITHOUT SIGNIFICANT TUBULOINTERSTITIAL INFLAMMATION IN KIDNEY TRANSPLANT REJECTION

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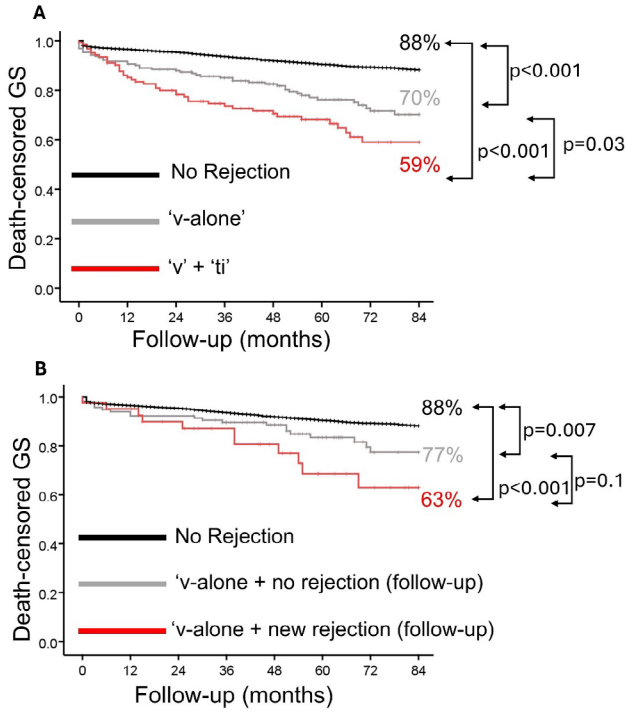
Background: Banff 'v' lesion (intimal arteritis) is traditionally considered to represent a severe form of rejection, termed vascular rejection. V lesions can be diagnosed in the absence of significant tubulointerstitial or microvascular inflammation (**v-alone**) and their clinical significance still remains unclear.

Methods: We conducted an observational cohort study of all adult patients who underwent kidney transplantation between Jan-13 & Dec-19 at 6 centers in the US and Europe. We examined the prevalence of the **v-alone** lesion in the first-year post-transplantation and assessed its histological response to treatment, and impact on 7yr-graft survival.

Results: We analyzed 5828 patients with 9780 bx in the 1st post-transplant year, of whom 315 (5.4%) had arteritis. Of these, 123 patients (39%) had concomitant ≥IA TCMR (**v+ti**), while 192 (61%) had **v-alone** lesions (with borderline TCMR, n=76; true isolated v lesions, n=116). Irrespective of whether v lesions were **v+ti** or **v-alone**, they completely resolved in a substantial proportion of patients when assessed on a follow-up bx (74% vs. 80%, p=NS). However, 40% of patients with **v+ti** lesions had persistent Banff ≥IA rejection on their follow-up bx, while 26% with **v-alone** lesions developed new Banff ≥IA rejection (p<0.001). Although patients with **v-alone** lesions had significantly better 7-yr death censored graft survival (DCGS, 70%) compared to those with **v+ti** lesions (59%, p=0.03), it was significantly inferior to patients without no rejection in the 1st year (NR, 88%, p<0.001, **Fig1a**).When compared to NR, **v-alone** lesions were associated with worse 7yr-DCGS independent of potential confounders. Finally, patients with v-alone lesions, who developed new Banff ≥IA rejection on follow-up bx (63%) had worse 7yr-DCGS compared to those who were rejection-free (77%, p=0.1) . Nonetheless, patients with v-alone lesions even with complete resolution of their rejection have inferior 7yr-DCGS compared to those with NR in the 1st year (88%, p=0.007, **Fig1b**).

Conclusions: Although Banff 'v' lesions when detected in the absence of significant ti inflammation respond better to treatment and carry better prognosis compared to patients with vasculitis and concomitant ti inflammation, they still are associated with a decline in graft survival compared to patients with no rejection.



FOS_05_9 BANFFNET: AUTOMATED AND EXPLAINABLE QUANTIFICATION OF BANFF LESION SCORES WITH DEEP LEARNING IMAGE ANALYSIS

Giorgio Buzzanca[1], Chiara Pala[2], Junling He[3], Rianne Hofstraat[4], Alessandra Tammaro[5], Dominique van Midden[6], Imke Bruns[7], Roman Bülow[8], Maximilian Koeller[9], Nicolas Kozakowski[10], Georg Böhmig[11], Philip F. Halloran[12], Soufian Meziyerh[13], Tri Nguyen[14], Eric Steenbergen[6], Luuk Hilbrands[15], Arjan D. van Zuilen[16], Frederike Bemelman[17], Giulia Callegaro[7], Bob van de Water[7], Garry Corthals[4], Marco Delsante[18], Francesca Testa[19], Francesco Fontana[20], Priyanka Koshy[21], Adeyemi Abiola[22], Hessel Peters Sengers[23], Sandrine Florquin[24], Peter Boor[8], Maarten Naesens[25], Aiko de Vries[26], Jesper Kers[27]

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Background: The Banff lesion scores comprise of a comprehensive set of histological parameters that represent active and chronic damage in the renal allograft. Due to the ordinal nature of the Banff scores and their arbitrary thresholds, accurate assessment and cross-cohort comparison is limited by high inter-observer disagreement across the spectrum of lesions. These observations indicate that we should strive towards quantitative and reproducible assessment of the kidney biopsy.

Methods: We introduce BanffNET, a weakly supervised deep learning framework integrating self-supervised learning with probabilistic modeling trained on >8000 digital biopsies from 3 medical centers (Amsterdam, Utrecht, Leiden). A low-capacity model predicts probabilities by generating patch-level estimates, followed by global aggregation using a Bayesian approach (**Fig 1A**). Validation was performed across 5 external cohorts (Leuven, Parma, Nijmegen, Aachen, Vienna).

Results: BanffNET consistently predicted the full spectrum of Banff lesion scores from digital biopsies, correlating strongly with local renal pathologists' assessments. BanffNET scores showed enhanced prognostic utility for graft outcome and aligned more closely with molecular data than pathologist assessment across multiple molecular modalities (MMDx, RNAseq and quantitative proteomics), stainings (H&E, PAS, silver), scanners (Philips, Hamamatsu, 3DHistech, Aperio), and cohorts (**Fig 1B-F**). For example, the top correlating transcripts associated with BanffNET's transplant glomerulopathy score include ABMR, NK cell and donor specific antibody gene sets whereas BanffNET's tubulitis score showed enrichment for TCMR gene sets. Local probability maps offer unprecedented interpretability, enabling instance-level insights into biopsy features, e.g. high attention for peritubular capillaritis (**Fig 1G**).

Conclusions: With BanffNET, we introduce the first deep learning image analysis pipeline for fully automated Banff lesion scoring with enhanced capabilities for quantitative and explainable kidney allograft biopsy assessment. Processing a dataset of 3.000 whole slide images to calculate BanffNET scores requires less than 24 hours of image processing, highlighting the potential value for high-throughput cohort enrichment.

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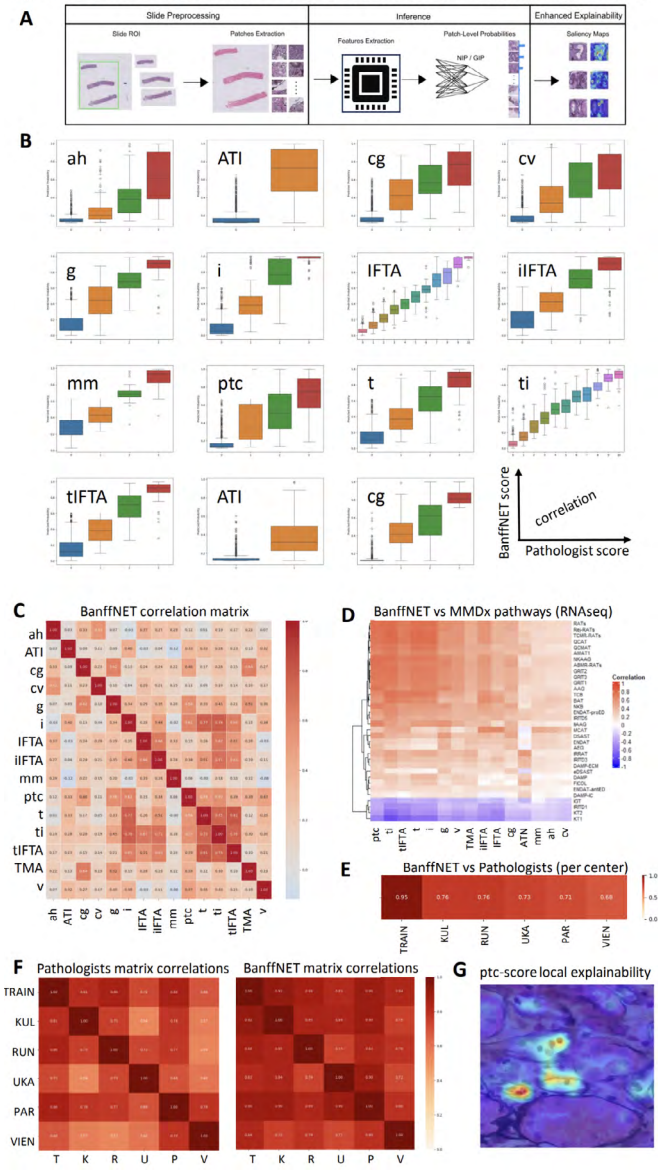
Histopathology and molecular signatures

Figure 1. Overview and performance of BanffNET to automate Banff lesion score quantification



Kidney transplantation: models, viruses, and immunity

FOS_06_1 EXTENDED VALIDATIONS OF THE IBOX SYSTEM IN REAL LIFE SETTINGS

Agathe Truchot[1], Marc Raynaud[2], Gillian Divard[3], Nassim Kamar[4], Sofia Naser[3], Yannis Lombardi[5], Christophe Legendre[6], Alexandre Hertig[6], Maarten Naesens[7], Elodie Bailly[8], Matthias Buchler[9], Marta Crespo[10], Kamilla Linhares[11], Brad Astor[12], Ivana Juric[13], Nikolina Basic-Jukic[14], Ilkka Helanterä[15], Enver Akalin[16], Mark Stegall[17], Andrew Bentall[18], Gaurav Gupta[19], Soler Pujol Gervacio[20], Dorry Segev[21], Helio Tedesco Silva Junior[11], Carmen Lefaucheur[22], Klemens Budde[23], Olivier Aubert[24], Alexandre Loupy[25]

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Background: The iBox prediction system for kidney allograft failure has recently received endorsement from EMA for use as a surrogate endpoint for clinical trials, and acceptance of its Qualification Plan by the FDA. Although validated in multiple settings, comprehensive validation is needed to extend its use in clinical trials and practice across diverse healthcare environments.

Methods: We included kidney recipients from 19 academic centers across Europe, North America, and South America. We developed flexible versions of the iBox for centers that don't routinely perform biopsies or anti-HLA DSA testing, and centers using various proteinuria measurement methods. We also assessed iBox's performance using the most recent CKD-EPI and KRS eGFR equations, in specific clinical contexts including initial nephropathy recurrence, PVAN, and type of immunosuppressive regimens used. Finally, we determined the performance of the iBox system up to 10 years post-evaluation. Predictive performances were assessed through discrimination, calibration, overall fit, and clinical utility.

Results: A total of 11,616 transplant recipients were included in the study (n=4,000 in the derivation cohort, n=7,616 in the validation cohorts). 1,483 (12.8%) patients lost their graft after a median follow-up post-risk evaluation of 5.26 years (IQR 3.11-7.00). The iBox system maintained good predictive performance across all scenarios (c-index 0.79-0.87, Brier Scores 0.08-0.11), including using different eGFR equations (MDRD, EKFC, CKD-EPI, and KRS; c-index 0.81), in patients with recurrent disease, in BK virus associated nephropathy (c-index range 0.79-0.87), and when extending the prediction horizon to 10 years post-risk evaluation (c-index 0.78). The iBox also demonstrated superior predictive capability compared to eGFR slope (c-index 0.81 vs 0.62, p<0.001) and circulating anti-HLA DSA (c-index 0.81 vs 0.57, p<0.001).

Conclusions: We confirmed in a large trial the consistency of the iBox predictive performance across diverse real-world settings and clinical scenarios, showing its versatility and reliability, thereby further supporting its use for patient risk stratification in clinical practice and as a surrogate endpoint for clinical trials.

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Kidney transplantation: models, viruses, and immunity

FOS_06_2 FIRST SEVERE INFECTIONS IN KIDNEY TRANSPLANT RECIPIENTS: A NATIONWIDE FRENCH COHORT STUDY

Léa Hoisnard[1], Tan-Lhernoud Laetitia[2], Sébastien Gallien[3], Philippe Grimbert[4], Giovanna Melica[5], Marie Matignon[6]

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Background: Infections remain the second leading cause of death after kidney transplantation (KT). We describe here the characteristics and 30-day mortality of first severe infections in kidney transplant recipients (KTR) across France.

Methods: We conducted a nationwide, population-based cohort study using the French national health data system including all KTR from January 2011 to December 2019. The primary outcome was the first severe infection requiring hospitalisation, identified by International Classification of Diseases, Tenth Revision (ICD-10) codes as the principal or associated diagnosis. Incidence rates were calculated, and cause-specific hazards of infection, death, or allograft loss were analyzed using the Kaplan-Meier method.

Results: A total of 23,676 KTRs were included (63.4% male, mean age 53.7 years, 80.7% with prior dialysis). We recorded 9,255 first severe infections, of which 58.5% (5,410) occured within the first-year after transplantation. The incidence rate was 151.1 per 1,000 person-years (95% CI: 146.5–155.6). The cumulative infection risk increased with age (Figure 1). Urinary tract infections (UTIs) were the most common, followed by lower respiratory infections (LRIs) and gastrointestinal infections (Figure 2), which were predominantly bacterial. The median time to first severe infection varied by site: 153 days (IQR: 58–516) for UTIs and 359 days (IQR: 139–840) for LRIs. Thirty-day mortality was highest for LRI with sepsis (30.5%), compared with 3.6% for non-septic LRI, 11.6% for UTI with sepsis, and 0.3% for non-septic UTI. Opportunistic infections, mainly herpes zoster and Pneumocystis pneumonia, accounted for 7.3% of severe infections (679/9,255)

Conclusions: First severe infections occurred mostly in the first year after KT and UTI predominated in this nationwide cohort study. First severe LRIs, but not UTIs, were associated with significant mortality in KTR. Bacteria were responsible for the majority of severe infections, but opportunistic pathogens, especially herpesviruses and Pneumocystis pneumonia, remained a significant burden.

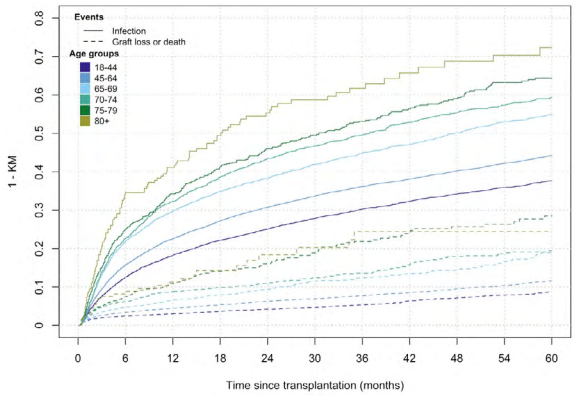

Figure 1 Cumulative cause-specific hazard of infection and death or graft-loss

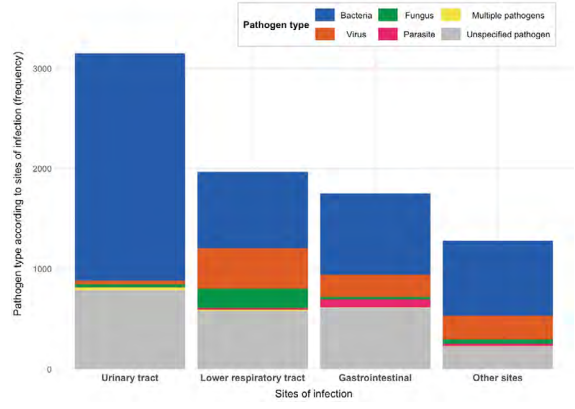

Figure 2: Description of first severe infections

FOS_06_3 LIVING WITH A TRANSPLANTED LIVER IS ASSOCIATED WITH AIRFLOW LIMITATION: A NATIONWIDE COHORT STUDY

Nicoline Arentoft[1], Shoaib Afzal[2], Hans-Christian Pommergaard[3], Safura-Luise Heidari[4], Rebekka Faber Thudium[4], Paul Suno Krohn[5], Jens-Ulrik Stæhr Jensen[6], Ask Bock[1], Jesper Rømhild Davidsen[7], Niels Kristian Muff Aagaard[8], Børge Grønne Nordestgaard[6], Michael Perch[9], Allan Rasmussen[10], Annette Dam Fialla[11], Susanne Dam Nielsen[12]

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Background: There is a close interaction between the liver and the lungs. However, the burden of pulmonary diseases with airflow limitation in liver transplant recipients is unknown as their assessment does not include routine pulmonary function tests. This study investigated lung function measured by spirometry in liver transplant recipients and in age- and sex matched controls from the general population. The study determined the association between living with a transplanted liver and airflow limitation as well as forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). Risk factors associated with airflow limitation was also investigated.

Methods: Spirometry was performed in 512 adult liver transplant recipients from The Danish Comorbidity in Liver Transplant Recipients (DACOLT) study and 2010 age and sex matched controls from The Copenhagen General Population Study (CGPS). Airflow limitation was defined as FEV_1/FVC <0.7 and predicted FEV_1 <80% as recommended by The Global Initiative for Chronic Obstructive Lung Disease.

Results: Liver transplant recipients had higher prevalence of airflow limitation than controls (10.7% vs. 7.1%, p=0.01). When adjusted for age, sex, ethnicity, cumulated smoking, and educational status, living with a transplanted liver was associated with airflow limitation with an adjusted odds ratio (aOR) of 2.06 (95% confidence interval (CI) 1.4-3.0 p<0.001). Liver transplant recipients had 363 mL (95% CI 297-430 mL, p<0.001) lower FEV_1 and 549 mL (95% CI 467-632 mL, p<0.001) lower FVC than controls. Previous pulmonary infection was associated with airflow limitation in liver transplant recipients (aOR 2.23 [95% CI 1.0-4.7], p=0.03).

Conclusions: Living with a transplanted liver is independently associated with airflow limitation, lower FEV_1 and FVC. Previous pulmonary infection increased the risk of airflow limitation. Increased awareness of pulmonary comorbidities in liver transplant recipients may be warranted.

Figure 1

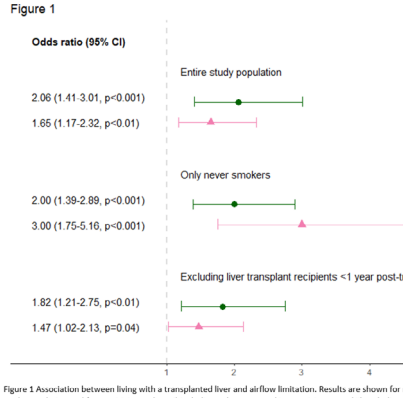

Figure 1 Association between living with a transplanted liver and airflow limitation. Results are shown for study population and for sensitivity analyses i) including only never smoking participants and ii) excluding post-transplantation. Adjusted odds ratios were adjusted for sex, age, ethnicity, cumulated smoking in pa

Figure 1
Odds ratio (95% CI)
Entire study population
2.06 (1.41-3.01, p<0.001)
1.65 (1.17-2.32, p<0.01)
Only never smokers
2.00 (1.39-2.89, p<0.001)
3.00 (1.75-5.16, p<0.001)
Excluding liver transplant recipients <1 year post-transplant
1.82 (1.21-2.75, p<0.01)
1.47 (1.02-2.13, p=0.04)
Adjusted
Crude
1
2
3
4
5
Figure 1 Association between living with a transplanted liver and airflow limitation. Results are shown for main analysis including the entire study population and for sensitivity analyses i) including only never smoking participants and ii) excluding liver transplant recipients <1 year post-transplantation. Adjusted odds ratios were adjusted for sex, age, ethnicity, cumulated smoking in pack years, and educational status.

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Kidney transplantation: models, viruses, and immunity

FOS_06_4 UK FAILING KIDNEY TRANSPLANT OUTCOMES REGISTRY ANALYSIS (FAKTOR)

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Background: Approximately 25% of kidney transplants fail within 10 years, with failing transplant management an international research priority. The FAKTOR study is investigating the management and outcomes of kidney transplant failure in the UK.

Methods: We used UK Renal Registry data on patients aged ≥18 with transplant failure (eGFR≤15ml/min/1.73m^2/new kidney replacement therapy (KRT) modality/death) from 01/2012 to 12/2021 from all centres in England, Wales and Northern Ireland. We followed patients for 5 years. Outcomes were assessed at each year post-failure as the first of: i) re-transplantation, ii) haemodialysis (HD), iii) peritoneal dialysis (PD), iv) death; those remaining alive without changing KRT modality were classed as v) managed conservatively if eGFR was <7.5ml/min/1.73m^2, or alternatively vi) being on the same transplant (failure defined as eGFR≤15ml/min/1.73m^2 allows potential period of survival on the same transplant). At 1 year post-failure, for each outcome we described patient characteristics: age, sex, ethnicity, socioeconomic deprivation level, primary renal disease, pre-dialysis eGFR (if applicable), centre and clinic type.

Results: 5553 patients with transplant failure were identified. Figure 1 shows the outcomes for up to five years post-failure. 13 were lost to follow up before 1 year, leaving 5540 in the analysis of 1-year outcomes (Table 1). HD was the most common outcome at 1 year (47.0%), followed by remaining alive on the same transplant (27.7%), PD (10.5%), dying (9.3%), pre-emptive re-transplantation (5.1%) and conservative management (0.5%). Age, sex, ethnicity, socioeconomic deprivation, primary renal disease and clinic type were all associated with 1-year outcome (p<0.0001), with those of white ethnicity and living in less deprived areas having a higher likelihood of re-transplantation. 6.6% in the least deprived areas had received a new transplant at 1 year, compared to 3.3% in the most deprived areas.

Conclusions: This is the first UK-wide description of outcomes following kidney transplant failure. We found variation in post-failure treatment modality associated with demographic factors, primary kidney disease and centre practice. Further FAKTOR analyses will aim to understand variation in care, re-listing, re-transplantation and causes of death.

Figure 1: Sankey chart showing outcomes up to 5 years post failure

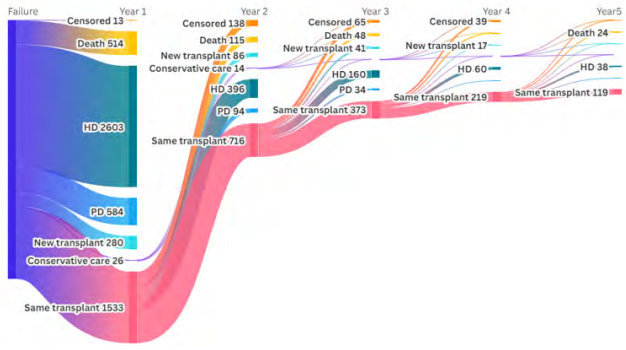

Table 1: Outcome at 1 year post transplant failure by patient characteristics

		All	Conservative care	Death	HD	New transplant	PD	Same transplant	p-value
All	N (%)	5540 (100)	26 (0.5)	514 (9.3)	2603 (47)	280 (5.1)	584 (10.5)	1533 (27.7)	
Age at failure	Median (IQR)	55.4 (45.2, 65.1)	54.4 (45.8, 68.4)	68 (58.2, 74.6)	53.1 (42.7, 62.9)	45.1 (37.3, 54.3)	51.2 (40.2, 61.5)	58.2 (49.4, 66.2)	<0.0001
Pre-dialysis eGFR	Median (IQR)	9.53 (7.58, 11.63)			9.64 (7.67, 11.72)		9.08 (7.31, 11.08)		0.0001
		N	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)	
Sex									
	Male	3075	10 (0.3)	257 (8.4)	1609 (52.3)	153 (5)	294 (9.6)	752 (24.5)	<0.0001
	Female	2465	16 (0.6)	257 (10.4)	994 (40.3)	127 (5.2)	290 (11.8)	781 (31.7)	
Ethnicity									
	Asian	628	1 (0.2)	54 (8.6)	353 (56.2)	19 (3)	55 (8.8)	146 (23.2)	<0.0001
	Black	533	3 (0.6)	25 (4.7)	277 (52)	8 (1.5)	31 (5.8)	189 (35.5)	
	Missing	13	0 (0)	4 (30.8)	4 (30.8)	0 (0)	0 (0)	5 (38.5)	
	Mixed	72	2 (2.8)	4 (5.6)	38 (52.8)	3 (4.2)	5 (6.9)	20 (27.8)	
	Other	75	1 (1.3)	3 (4)	48 (64)	3 (4)	7 (9.3)	13 (17.3)	
	White	4219	19 (0.5)	424 (10)	1883 (44.6)	247 (5.9)	486 (11.5)	1160 (27.5)	
IMD quintile									
	1 (most deprived)	1322	9 (0.7)	119 (9)	690 (52.2)	43 (3.3)	111 (8.4)	350 (26.5)	<0.0001
	2	1229	6 (0.5)	108 (8.8)	604 (49.1)	49 (4)	121 (9.8)	341 (27.7)	
	3	1065	4 (0.4)	94 (8.8)	494 (46.4)	58 (5.4)	120 (11.3)	295 (27.7)	
	4	1007	6 (0.6)	107 (10.6)	439 (43.6)	69 (6.9)	109 (10.8)	277 (27.5)	
	5 (least deprived)	915	1 (0.1)	86 (9.4)	376 (41.1)	60 (6.6)	123 (13.4)	269 (29.4)	
	Missing	2	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	1 (50)	

p-value from chi-squared tests for categorical variables, Kruskal-Wallis tests for continuous variables. 'Conservative care' and 'Same transplant' were grouped together for testing due to small numbers on conservative care.

FOS_06_5 IMMUNE MONITORING-GUIDED CMV SURVEILLANCE IN PREEMPTIVE THERAPY AFTER KIDNEY TRANSPLANTATION: RANDOMIZED CLINICAL STUDY

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Background: Preemptive therapy for cytomegalovirus (CMV) prevention requires weekly monitoring of CMV DNAemia. The use of CMV-specific cell-mediated immunity (CMV-CMI) may individualize CMV monitoring to guide preemptive therapy.

Methods: In open-label, single-center, randomized trial, kidney transplant recipients were enrolled if they were CMV-seronegative with seropositive donor (D+R-) or CMV-seropositive (R+) between May 2018 and October 2024. Patients were randomized in a 1:1 ratio to immune-guided monitoring based on CMV-CMI (QuantiFERON-CMV) assessed at 3 weeks after transplantation or to standard monitoring by weekly CMV PCR for 4 months. In immune-guided group, CMV PCR was performed every 4 weeks between 1 and 4 months if CMV-CMI assay was positive. Preemptive valganciclovir therapy was initiated after detection of CMV DNAemia (≥1000 IU/mL). The primary outcome was the incidence of significant CMV DNAemia (≥2000 IU/mL) at 12 months.

Results: Overall, 189 patients were randomized (97 in the immune-guided group and 92 in the standard group), of whom 60 immune-guided patients (62%; D+R-, 0%; R+, 74%) had positive CMV-CMI test and were scheduled to less frequent monitoring. The incidence of significant CMV DNAemia was comparable in both groups (49% vs 47%, P=0.838) including sub-analysis in R+ patients (44% vs 41%, P=0.766). Both regimens prevented CMV disease (3% vs 1%, P=0.350), however a numerically higher incidence of high-grade (≥10,000 IU/mL) CMV DNAemia was observed in immune-guided group (28% vs 19%, P=0.147). In immune-guided group, 9 patients received rescue valganciclovir for high-grade CMV DNAemia detected outside the specified monitoring. There were no differences in acute rejection and graft survival.

Conclusions: Compared to standard 4-month weekly monitoring, the use of CMV-CMI to guide CMV surveillance in preemptive therapy resulted in similar incidence of significant CMV DNAemia with very low CMV disease rates and enabled less frequent monitoring in majority of R+ patients.

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Kidney transplantation: models, viruses, and immunity

FOS_06_6 GAMMA DELTA T CELL THERAPY FOR CMV INFECTION: PRECLINICAL PROOF-OF-CONCEPT

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Background: The treatment of refractory cytomegalovirus (CMV) infections remains a major challenge for kidney transplant patients, despite recent advances brought by maribavir. There is currently growing interest in the development of adoptive cellular therapies targeting CMV, but given the limitations of αβ T-cell therapies in D+R- recipients, our aim was to explore a novel immunotherapy based on γδ T-cells, whose anti-CMV role has been previously demonstrated.

Methods: The amplification of human γδ T-cells was performed from PBMC in the presence of IL-4, interferon-gamma, IL-21, IL-1beta, IL-15, and an anti-CD3 antibody. Reactivity tests were conducted in the presence of fibroblasts, macrophages, and endothelial cells infected with CMV. To evaluate in vivo efficacy, we adapted the human protocol to derive a mouse γδ T-cell amplification protocol, recapitulating the phenotypic characteristics of human cells. Finally, amplification of CMV-reactive γδ T-cells was performed from 5 kidney transplant recipients with recurrent or refractory CMV infection, in order to test feasibility of an autologous cell therapy.

Results: We successfully amplified γδ T-cells from both CMV-seronegative and CMV-seropositive donors. Regardless of CMV serology, the amplified γδ T-cells exhibited a central memory cytotoxic phenotype. In response to CMV-infected cells, the amplified γδ T-cells degranulated, secreted IFNγ, and controlled viral dissemination in vitro. Mechanistically, CMV-induced reactivity was observed independently of γδTCR but required the LFA-1 costimulatory receptor. In an in vivo model, adoptive transfer of mouse ?? T cells recapitulating the features of the human cell product protected mice against lethal mouse CMV infection. Finally, we were able to amplify CMV-reactive γδ T-cells from kidney transplant recipients with refractory CMV, and these cells retained their viability and functionality in the presence of tacrolimus and everolimus.

Conclusions: These findings provide proof of concept for a future clinical trial of amplified γδ T-cells to treat refractory CMV disease in solid-organ transplant recipients, including high-risk CMV-naïve D+R- patients.

FOS_06_7 DEVELOPMENT AND VALIDATION OF A PREDICTION MODEL FOR RISK OF DEATH IN KIDNEY TRANSPLANT RECIPIENTS (MORTALITY BOX)

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Background: Accurate prediction of post-kidney transplant mortality is an unmet need, potentially improving organ allocation and patient monitoring. This study aimed to develop and validate an integrative system to predict short- and long-term mortality in kidney transplant recipients.

Methods: We included kidney transplant recipients from 14 academic centers across Europe and the US. The outcome of interest was all-cause mortality. To build a multivariable risk prediction model computable at the time of transplantation (mBox model), 121 clinical, biological, and imaging candidate prognostic factors were collected. To ensure model generalizability in the validation cohorts, abbreviated mBox models were also developed. Predictive performances were assessed through discrimination and calibration from 1 to 10 years post-transplantation.

Results: A total of 12,517 kidney recipients were included in this study, comprising 1,566 patients in the French derivation cohort, and 10,951 patients in the external validation cohorts. 2,486 (19.9%) patients died after a median follow-up of 5.08 years (IQR 2.97-7.00). The mBox model integrated 14 independent predictors including recipient's age, duration of dialysis, medical history, presence of anti-HCV antibodies, 5 biological variables (glycated haemoglobin, albumin, troponin, C-reactive protein, and γ-GT), and 2 imaging parameters (left ventricular mass and kidney allograft length). The mBox demonstrated strong discrimination and calibration in the derivation cohort (c-index 0.82 [95% CI 0.77-0.87] at 1-year and 0.80 [0.78-0.82] at 10 years post-transplant). Performances of the abbreviated mBox models were confirmed in the external validation cohorts from France (c-index 0.76 [0.73-0.78]), Europe (c-index 0.74 [0.70-0.79]), and the US (c-index 0.74 [0.70-0.79]). The mBox maintained good and stable performance across various subpopulations and clinical scenarios.

Conclusions: The mBox model, the first multimodal and widely validated kidney recipient mortality prediction system, computable at the time of transplantation, provides robust prediction performances and may help stratify patient risk, improving organ allocation and post-transplant decision-making.

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Kidney transplantation: models, viruses, and immunity

FOS_06_8 PREDICTION MODEL FOR LONG-TERM KIDNEY GRAFT SURVIVAL: THE KIDMO DEVELOPMENT STUDY

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Background: Numerous prognostic factors for kidney transplantation outcomes have been identified, yet Switzerland lacks a widely accepted clinical prediction model. Therefore, this study aimed to develop a model for predicting deceased-donor kidney graft survival.

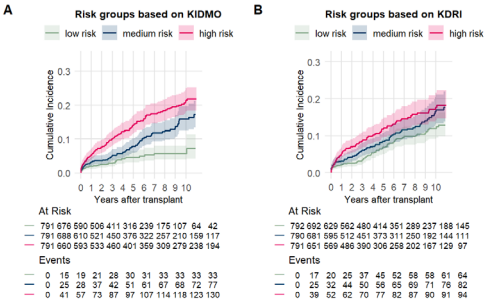
Methods: The kidney prediction model (KIDMO) study is a retrospective multi-center cohort study of all deceased-donor kidney transplant recipients in Switzerland between May 2008 and December 2021. Sixteen predictors were preselected based on literature and expert knowledge. The primary outcome was time to graft loss, with death as a competing risk. A Fine-Gray model with AIC-based backward selection via bootstrapping was used with internal-external validation across centers. The study protocol has been published (http://dx.doi.org/10.1186/s41512-022-00139-5).

Results: There were 2,720 eligible kidney recipients, 276 (10.1%) lacked consent, and 71 (2.9%) were excluded due to missing data. The analysis was performed with 2,373 recipients; among these, 254 (10.7%) experienced graft loss, 369 (15.5%) died, and 1,750 were censored, with a median follow-up of 6.1 years. The final model identified six prognostic variables: donor age, donor cause of death, donor diabetes, retransplantation, year of transplantation, and recipient age (Table 1). The model's C-statistic was 0.65 (95% CI 0.61–0.68), corrected to 0.63 for optimism. KIDMO demonstrated superior discrimination compared to the Kidney Donor Risk Index (KDRI) in the Swiss cohort (KDRI C-statistic 0.58, 95% CI 0.54–0.61); see Figure 1.

Conclusions: KIDMO offers clinicians a superior assessment of graft loss risk compared to existing tools. Unlike many current models that neglect calibration, KIDMO provides absolute risks rather than relative risks, significantly enhancing its clinical utility. The online risk calculator is accessible online (https://data.swisstransplant.org/kidmo/).

	Interquartile difference	Hazard ratio (95%-CI)	Chi-Square	d.f.	p-value
D age	23.00 (42.00–65.00)	1.88 (from 1.49 to 2.37)	29.1	2	< 0.001 ***
D age nonlinear	–	–	5.68	1	0.017 *
D deathcause	–	–	6.35	2	0.042 *
D deathcause anoxia	–	1.64 (from 1.12 to 2.40)	–	–	–
D deathcause cerebral hemorrhage	–	1.24 (from 0.89 to 1.73)	–	–	–
D diabetes	1.00 (0.00–1.00)	1.51 (from 0.91 to 2.50)	2.58	1	0.11
R age	19.00 (46.00–65.00)	0.82 (from 0.68 to 0.99)	4.3	1	0.038 *
T retpx	1.00 (0.00–1.00)	1.34 (from 0.98 to 1.82)	3.37	1	0.067 .
T tpxyear	6.00 (2012.00–2018.00)	0.81 (from 0.59 to 1.10)	11.9	2	0.003 **
T tpxyear nonlinear	–	–	3.01	1	0.083 .
TOTAL NONLINEAR	–	–	9.21	2	0.010 **
TOTAL	–	–	57	9	< 0.001 ***

Table 1: Results from the Fine-Gray regression model.



D: donor variable; R: recipient variable; T: transplant variable.

Figure 1: Risk-stratified cumulative incidence plots with 95% confidence bands showing graft loss probabilities (Aalen-Johansen estimator) for A) KIDMO and B) KDRI.

FOS_06_9 TORQUE TENO VIRUS IS ASSOCIATED WITH AN INCREASED RISK FOR MALIGNANCIES AFTER KIDNEY TRANSPLANTATION

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Background: The risk for malignancies is increased after kidney transplantation due to immunosuppression. Torque Teno virus (TTV) is a ubiquitous and non-pathogenic virus which reflects the immunocompetence of its host. TTV load has been shown to be associated with complications of under- and over-immunosuppression such as graft rejection and infection. No data are available on the association between TTV load and malignancies after kidney transplantation.

Methods: All 604 consecutive recipients of a kidney graft transplanted at Vienna General Hospital between 2016 and 2019 were screened. Main inclusion criteria were a follow-up more than one year post transplant and more than two available TTV measurements in year one post-transplant. TTV was quantified in the plasma using an in-house PCR as described by Maggi and colleagues. Follow-up data were collected for up to five years after transplantation.

Results: A total of 422 kidney transplant recipients (median age 55 years, 32.5% female) were included in this cohort analysis with a total of 52 incident malignancies occurring more than one year after transplantation (52% skin cancer). Mean TTV from month 4 to 12 post-transplant (TTV_{mean}) was associated with an increased risk for the development of a malignoma (HR 1.38, 95% CI 1.21-1.70, p=0.002). The highest risk for the development of a malignoma was calculated for TTV_{mean} above a cut-off of 7.5 log copies/mL (HR 2.19, 95% CI 1.24-3.89, p=0.007) adjusted for recipient age, sex, history of smoking, and BMI.

Conclusions: A high Torque Teno virus load - suggesting over-immunosuppression - is associated with the development of malignancies in kidney transplant recipients. TTV-guided immunosuppression might provide a useful tool to reduce post-transplant malignancies by avoiding over-immunosuppression.

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FOS_07_1 SEQUENTIAL HYPO- AND NORMOTHERMIC PERFUSED EXTENDED CRITERIA LIVERS: TWO-CENTER RESULTS OF 206 CASES

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Background: With the current organ shortage, liver machine perfusion is increasingly used to test and select extended criteria donor (ECD)-livers in an attempt to counter decreasing quality of available organs. Combining sequential oxygenated hypothermic and normothermic machine perfusion, linked by one hour of controlled oxygenated rewarming (DHOPE-COR-NMP) can be used to resuscitate donor livers and subsequently perform viability assessment. We aimed to analyze follow-up data from DHOPE-COR-NMP procedures for ECD-livers performed in two centers.

Methods: All ECD-livers treated with DHOPE-COR-NMP in the Erasmus Medical Center in Rotterdam and the University Medical Center Groningen between March 2019 and October 2024 were included, safeguarding a minimum follow-up period of 6 months. Livers were classified as ECD based on factors such as elevated laboratory values, or age above 61 years in the case of donation after circulatory death (DCD). The main outcome measure was death-censored graft survival. Secondary outcomes included overall patient- and graft survival, as well as post-transplant complications, such as non-anastomotic biliary strictures (NAS) and anastomotic strictures (AS). Outcome measures were reported at one year and any time post-transplant.

Results: Of the 206 DHOPE-COR-NMP procedures that were performed, 144 resulted in a liver transplant (utilization rate 70%) with a majority of ECD-DCD grafts (n=138, 96%). Death-censored graft survival and patient survival at 1 year were 90% and 91%, respectively. Primary non function did not occur in this cohort. Portal vein thrombosis occurred 3 times (2.1%) and hepatic artery thrombosis occurred 5 times (3.5%). The 1-year cumulative incidence of NAS was 6%. Of all NAS cases, 2 patients were successfully re-transplanted and one other case resulted in patient death. At one year, AS occurred in 26% of transplanted livers.

Conclusions: This study illustrates that graft resuscitation and subsequent viability assessment through DHOPE-COR-NMP allows for safe transplantation of ECD-livers with excellent outcomes. The incidence of NAS is low, especially considering the fact that this cohort mainly consisted of high-risk ECD-DCD livers.

FOS_07_2 SOLUBLE CD46 AS A MARKER OF HEPATIC STEATOSIS IN PROSPECTIVE LIVING LIVER DONORS

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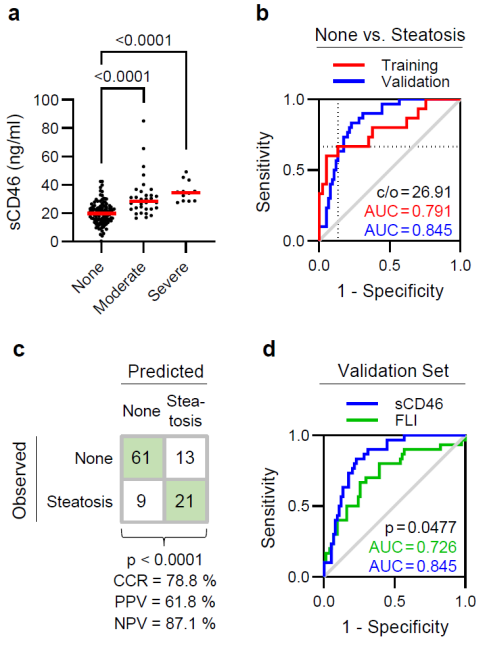
Background: We recently discovered that interleukin-4-secreting (IL-4$^+$) iNKT cells are over-represented in steatotic liver. This was attributed to stress-induction of matrix metalloproteases (MMP) in hepatocytes, which led to indiscriminate cleavage of immune receptors. Loss of cell-surface CD46 resulted in unrepressed differentiation of IL-4$^+$ iNKT cells. Soluble CD46 (sCD46) levels accurately classified oncological patients undergoing liver resection according to histological steatosis grade. Here, we asked whether sCD46 levels predict steatosis in prospective living liver donors.

Methods: sCD46 was measured in stored plasma from 156 prospective living liver donors. Steatosis was assessed by upper abdominal ultrasonography using the ratio of echogenicity in liver and kidney. Clinical data were collected from hospital records. Waist circumference was measured from abdominal CT images. Significance tests and receiver operating characteristic (ROC) curve analyses were performed in R (4.3.3). ROC curves were compared with the DeLong test.

Results: Prospective living liver transplant donors with moderate or severe steatosis had higher sCD46 levels than those without (Figure A). After stratified random assignment of cases to a training (n=52) or validation (n=104) set, we found that sCD46 performed well in classifying steatotic donors (Figure B). Training data were used to fix a cut-off for sCD46 of 26.91 ng/ml. In the validation set, the correct classification rate (CCR) was 78.8 %, positive predictive value (PPV) was 61.8 % and negative predictive value (NPV) was 87.1 % (Figure C). We further demonstrated sCD46 was superior to Fatty Liver Index (FLI) in classifying steatotic donors (Figure D).

Conclusions: sCD46 is a reliable diagnostic marker of hepatic steatosis, which can be conveniently and non-invasively measured in plasma samples. Our work raises the possibility of using sCD46 as a biochemical screening tool for evaluating prospective living liver donors.



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FOS_07_3 HYPOTHERMIC VERSUS NORMOTHERMIC EX-SITU PERFUSION IN DCD LIVER TRANSPLANTATION. A RANDOMIZED CONTROLLED TRIAL (DCDNET)

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Background: Despite prolonged warm ischemia time, the Italian experience has demonstrated good outcomes after liver transplantation (LT) from DCD donors combining normothermic regional perfusion (NRP) and end-ischemic machine perfusion (MP), nevertheless, there is no consensus on which technique should be used between dual-hypothermic oxygenated machine perfusion (D-HOPE) or normothermic machine perfusion (NMP) in this setting.

Methods: From December 2020 to August 2024, all LT performed from DCD donors were included in the study. Graft viability was assessed on NRP parameters. Once accepted a liver graft was randomized to NMP or DHOPE. The primary end point was to compare the incidence of serious adverse events (SAE: vascular and biliary complications and graft loss or patient death) between the two groups.

Results: In the study period 50 LT have been performed (44 from controlled DCD and 6 from uncontrolled DCD): 25 randomized to D-HOPE and 25 to NMP group. Median donor age was 68 (Q1-Q3=53-80) and 63 (Q1-Q3=55-80) years (p=0.74) in D-HOPE and NMP group, respectively. At a median follow up of 19 months, no difference in terms of SAE (24% versus 24%, p=1.0), post-reperfusion syndrome rate (36% versus 28%, p=0.37) and hospital stay (12 (9-20) vs 13 (10-16) days, p=0.16) were noted in the D-HOPE and NMP group, respectively. No one developed any vascular complication. There were 3 cases (8%) of biliary complications in D-HOPE group (2 anastomotic stenosis and 1 stones treated with ERCP) versus 6 cases (24%) in NMP group (1 anastomotic stenosis, 3 leakages and 2 ischemic cholangiopathy) (p=0.30). One patient in the D-HOPE group was re-transplanted due to delayed non function and two died for sepsis and neurological complications. One year graft survival were 100 and 85% in the NMP and DHOPE group respectively (p=0.29).

Conclusions: Our results showed no differences in terms of SAE between DHOPE and NMP when DCD graft are considered. The sequential use of NRP and end-ischemic MP allows the safe use of DCD grafts in liver transplantation despite the longer warm ischemia time.

FOS_07_4 ROUTINE USE OF PROLONG HYPOTHERMIC MACHINE PERFUSION TO ENABLE DAYTIME LIVER TRANSPLANTATION

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Background: Liver transplantation is often performed urgently due to unpredictable donor availability and the need to minimize cold ischemic time. As a result, many procedures occur at night, potentially compromising team performance, hospital logistics, patient outcomes, and cost effectiveness. We evaluated the clinical impact of implementing prolonged hypothermic oxygenated machine perfusion (DHOPE-PRO) in January 2023, standardizing its use for donor livers arriving late in the day to enable daytime transplants at our center.

Methods: This interim-analysis is part of a single-center clinical trial (DHOPE-PRO-LONG; NCT05680246). All liver transplantations performed between January 1, 2023, and October 1, 2024, were included. Outcomes were compared with a consecutive historical cohort from 2021- 2022. The primary outcome was the proportion of daytime liver transplantations, defined as (1) reperfusion occurring between 08:00 and 20:00, and (2) surgery start and end between 08:00 and 00:00. Actuarial graft and patient survival were also assessed.

Results: The 2021-2022 cohort included 155 liver transplantations (14% DHOPE-PRO), compared to 147 (52% DHOPE-PRO; p<0.001) in 2023-2024. In machine perfused livers, median DHOPE duration increased from 1.9h in 2021-2022 to 10h in 2023-2024 (p<0.001). Routine implementation of DHOPE-PRO in 2023 significantly increased the proportion of daytime surgeries, with 88% of reperfusions occurring before 20:00, compared to 50% in 2021-2022 (p<0.001; Figure 1). Additionally, 94% of surgeries concluded before 00:00, compared to 66% in 2021-2022 (p<0.001; Figure 1). Actuarial 1-year graft survival rates (98% vs 97%, p=0.152) and patient survival rates (98% vs 95% p=0.136) were comparable between cohorts.

Conclusions: The routine implementation of DHOPE-PRO enabled nearly all liver transplantations to be performed as daytime surgeries, without compromising graft or patient survival.

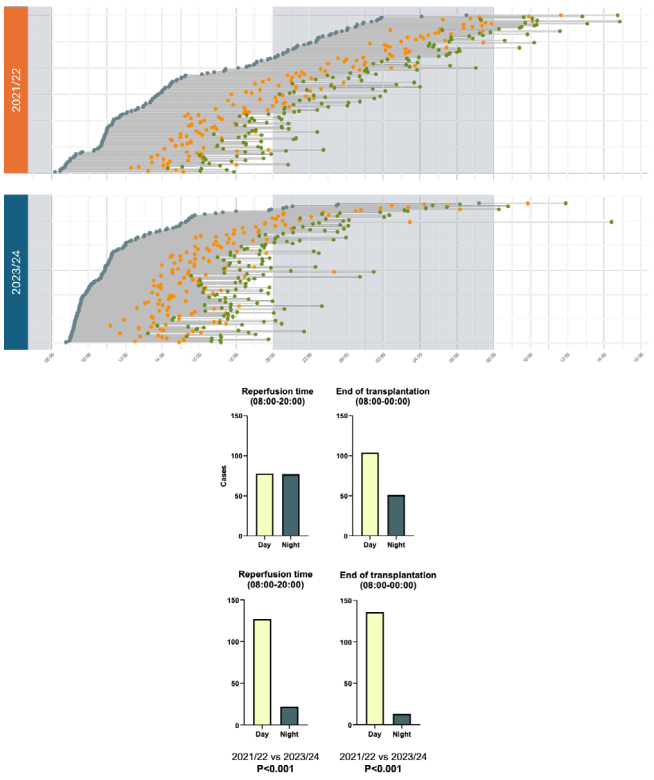

Figure 1 Distribution of liver transplantation time comparing 2021-2022 and 2023-2024

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FOS_07_5 PRESERVATION OF HUMAN LIVERS FOR 7 DAYS USING A FULLY AUTOMATED NMP DEVICE AND THE INNSBRUCK PERFUSION PROTOCOL

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Background: Prolonged *ex situ* normothermic machine perfusion (NMP) may serve as a platform to recover marginal livers. Long-term liver perfusion was previously achieved using open systems, custom-made or modified machines. We herein test a novel perfusion protocol introducing a bile volume-based perfusate replacement recipe using a commercially available, fully automated NMP device without modifications in non-transplanted human livers.

Methods: Non-transplanted human livers (N=22) were exposed to NMP (OrganOx Metra®, without adjustments) for up to 7 days. Livers were perfused either without perfusate modifications (control group,N=6) or with a previously established perfusion protocol (Innsbruck protocol,IP;N=16). The protocol includes red blood cell-based perfusate addition (300mL/24h) equaling bile volume loss. Serial perfusate samples and biopsies were analyzed for organ assessment.

Results: Applying the IP perfusion protocol enabled 7-day long-term NMP in four non-transplanted human livers, while control livers failed and deteriorated after 66[48–84] hours perfusion. Liver viability was characterized by continuous bile production, low perfusate bilirubin and low methemoglobin, and low inflammatory cytokines. Confocal microscopy and H&E histopathology confirmed excellent tissue viability and integrity after 7 days of perfusion. The bioenergetic function was stable indicated by adequate ATP production efficiency and outer mitochondrial membrane integrity. Clearance of mechanically induced free hemoglobin release seems crucial for a successful 7-day perfusion. Hemoglobin and hematocrit levels were maintained in physiological ranges in IP livers, but decreased significantly in control group.

Conclusions: 7-day preservation of non-transplantable human livers using the Innsbruck perfusion protocol in a fully automated commercial perfusion system is feasible. For this, preserved bile production and limited inflammation during perfusion, and bioenergetic competence at the start of NMP are a prerequisite.

FOS_07_6 MOLECULAR PROFILING OF THE EFFECTS OF NORMOTHERMIC REGIONAL PERFUSION ON DONOR LIVERS

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Background: Liver allograft transplantation is the only definitive treatment for end-stage liver disease. However, donor organ demand outstrips supply and many procured organs do not progress to transplantation due to concerns about organ quality. Normothermic regional perfusion (NRP) has emerged as a promising intervention to mitigate poorer outcomes associated with donation after circulatory death (DCD) donor livers, which experience warm ischemia, unlike donation after brain death (DBD) organs. However, the molecular differences between DCD and DBD organs, and the effects of NRP remain incompletely understood.

Methods: Bulk RNA-sequencing was performed on retrieval liver biopsies obtained from the Quality in Organ Donation (QUOD) biobank from n=72 DBD and DCD donors (table 1). Differential expression and gene set enrichment analyses (GSEA) compared groups of interest. Weighted gene co-expression network analysis (WGCNA) was applied to identify gene modules associated with NRP.

Results: DCD livers showed distinct inflammatory profiles compared to DBD livers. Specifically, gene sets related to Interferon Alpha Response and Interferon Gamma Response were enriched in DCD livers, while TNFα signaling via NFκB was the predominant enriched pathway in DBD livers. NRP induced a robust transcriptional response characterized by the upregulation of heat shock proteins, including HSPA1A/B, chaperones that are required for liver regeneration in mouse models. We also observed a change in gene set enrichment in DCDNRP livers towards a more DBD-like profile (figure 1) and gene ontology (GO) analysis revealed enrichment in terms such as 'unfolded protein binding' and 'heat shock protein binding' within modules correlated with DCDNRP livers. Similar potentially protective gene expression changes were noted when comparing NRP to ex-situ normothermic perfusion.

Conclusions: NRP enhances recovery in DCD livers by stimulating cellular stress responses and aligning their profiles more closely to DBD livers, supporting its clinical utility in improving organ outcomes.

Donor type	Number of patients
DBD	48
DCD	24
Perfusion	
DCD with NRP	8
DCD without NRP	16
Primary non-function	
Graft survival	64
Graft failure	8
Donor sex	
Female	41
Male	31

Table 1: Patient characteristics

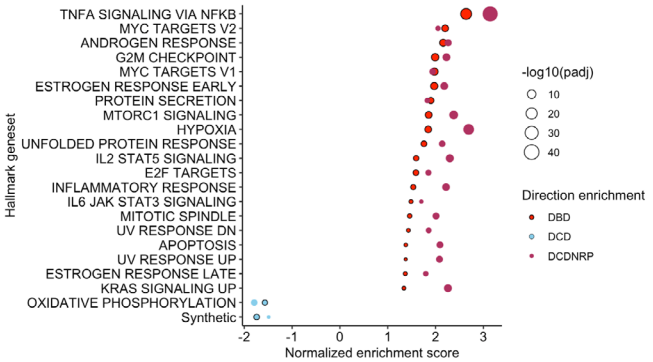

Figure 1: Dot plot showing common Hallmark pathways found in DCDNRP vs. DCD and DBD vs. DCD comparison

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FOS_07_7 EFFECT OF A DEFATTING COCKTAIL DURING COLD-TO-WARM EX-SITU PERFUSION OF HUMAN LIVERS

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Background: Normothermic ex-situ perfusion allow graft viability evaluation and metabolic modifications, such as drugs injection to modify lipid content with the aim of fatty livers rehabilitation. In a previous study, we demonstrated that a pharmacological defatting cocktail (DFAT) significantly reduced the triglyceride (TG) content of steatotic hepatocytes *in vitro*. The objective of the present study was to test the DFAT cocktail in discarded human livers during ex-situ perfusion.

Methods: Discarded livers were perfused according to an uninterrupted cold-to-warm protocol. The DFAT cocktail was injected after 30min under normothermic conditions (37°C), whereas no DFAT was administered to controls. Perfusate and liver tissue were collected throughout perfusion to assess functional parameters, lipid metabolism, and inflammation. Liver viability was evaluated using UK criteria.

Results: Twelve discarded highly marginal livers (median DRI 2.02 [1.6-3.47], including 10 steatotic livers (median macrosteatosis 55% [10-90%]) underwent cold-to-warm perfusion for 7,5 to 22 hours. DFAT injection was performed in 9 livers, triggering a marked increase in triglyceride (TG) into the perfusate (+165% at 90min), a reduction of TG content in liver tissue with a peak effect at 30 min (-47%, p=0.034) an increase in the hepatic expressions of genes related to lipid export, β-oxidation and autophagy, and a decrease in that of lipogenesis-related genes. Five livers (41.6%) reached viability criteria, including 3 (33%) in the DFAT group and 2 (67%) in the control group. A 10% reduction of histological macrosteatosis was observed in the DFAT group.

Conclusions: Continuous cold-to-warm ex-situ perfusion combined with DFAT injection triggers the release of triglycerides and the activation of lipid export, β-oxidation and autophagy pathways, together with a trend towards steatosis reduction. Prolonged normothermic ex-situ perfusion may allow effective defatting and improve graft viablity.

FOS_07_8 TISSUE PROTEOMIC ANALYSIS OF DIFFERENT DONOR AGES IN LIVER TRANSPLANTATION WITH NORMOTHERMIC MACHINE PERFUSION

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Background: Mean donor age for liver transplantation is increasing each year. Normothermic machine perfusion (NMP) has been associated with a decrease in graft injury and increased organ utilisation, when compared to static cold storage (SCS), in a randomised controlled trial by the Consortium for Organ Preservation in Europe (COPE). This study aims to compare the tissue proteomics profiles of liver donors according to their age and to evaluate the effect of NMP and changes in proteome over time at retrieval, post-preservation and 1-hour post-reperfusion.

Methods: Liver biopsy samples, at 3 timepoints, were obtained from 220 deceased donors and provided by COPE and were divided in 3 groups: young donors (<55 years), old donors (65-74 years) and very old donors (>75 years). Quantitative label-free mass spectrometry was used for the proteomic analysis (LFQ LC-MS/MS). Perseus, SPSS, String and Panther were used for bioinformatic and pathway analysis.

Results: Overall, 330 samples were analysed. The expression of 196 proteins, regulating detoxification of reactive oxygen species, glutathione conjugation, and synthesis of bile acids, salts, and glycogen is significantly affected by age and type of preservation at all timepoints. Post-reperfusion the expression of 39 proteins was significantly affected by the interaction of age and type of preservation with most changes observed in cellular oxidant detoxification and hydrogen peroxide catabolic processes. Comparing the 3 age groups with NMP post-reperfusion, proteins related to tissue response to stress (proteasome), protein synthesis and cell proliferation in livers from very old donors (> 75 years) were upregulated compared to both the other age groups (p< 0.05, FDR 1%) (Figure 1).

Conclusions: This proteomics analysis describes the significant changes in protein expression over the course of preservation and reperfusion, depending on the donor age and type of preservation applied. NMP supports increased expression of proteins involved in stress response, protein synthesis, and cell proliferation after reperfusion in livers from very old donors, suggesting that this technology could offer greater benefits for this specific subgroup.

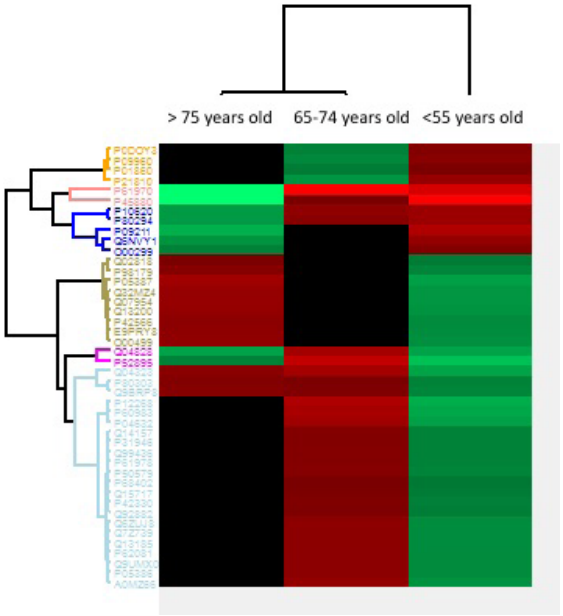

Figure 1. Supervised hierarchical clustering of significantly different proteins in NMP samples according to donor age.

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Better livers, better outcomes

FOS_07_9 OUTCOMES OF DONATION AFTER CIRCULATORY DEATH LIVER TRANSPLANT FOR PRIMARY SCLEROSING CHOLANGITIS

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Background: Normothermic regional perfusion (NRP) may mitigate the risks of using donations after circulatory death (DCD) grafts in patients with primary sclerosing cholangitis (PSC). This study aimed to compare the liver transplantation outcomes using DCD and donations after brain death (DBD) grafts.

Methods: This retrospective, multicenter cohort study was conducted between 2016 and 2022. The primary endpoints were graft and patient survival rates. The secondary endpoints were incidences of early allograft dysfunction (EAD), primary nonfunction (PNF), biliary and vascular complications, and recurrence.

Results: The DCD-NRP and DBD groups comprised 32 and 123 grafts, respectively. No significant differences were observed between the groups regarding donor and recipient characteristics. The 1- and 3-year graft survival rates in the DCD-NRP group were 94% and 86%, respectively (DBD group: 87% and 86%, respectively; p = 0.89). The patient survival rates at 1- and 3-years in the DCD-NRP group were 94% and 86%, respectively (DBD: 89% and 87%, respectively; p = 0.67). No differences were observed between the groups regarding the incidence of anastomotic biliary strictures, ischemic-type biliary lesions, PNF, EAD, hepatic artery thrombosis, or disease recurrence.

Conclusions: The safety and outcomes of NRP-DCD and DBD grafts are comparable in patients with PSC; therefore, their use can improve their access to transplantation.

Lessons from the registries

FOS_08_1 MACHINE LEARNING IN PREDICTING 3-MONTH MORTALITY FOR LIVER TRANSPLANT CANDIDATES WITH HCC

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Background: Predicting waitlist mortality in liver transplant (LT) candidates with hepatocellular carcinoma (HCC) is complex, as it involves risks of death from liver failure and dropout due to tumor progression. Traditional scoring systems assess liver disease severity but fail to account for tumor-related risks, while HCC-specific models overlook liver failure. This study addresses these limitations by using machine learning (ML) to predict 3-month mortality in LT candidates with HCC.

Methods: Data from the OPTN/UNOS registry were analyzed, including adult LT candidates who (i) died or were delisted due to clinical deterioration within 3 months or (ii) survived beyond 3 months. The dataset included 25 clinical and laboratory variables, plus 6 dynamic variables derived from changes in laboratory values, yielding 31 total features. Logistic Regression and Random Forest (RF) models were evaluated using both feature sets. To address class imbalance, down-sampling was applied.

Results: Among 11,641 patients (mean age 60; MELD 22), 448 died or were delisted within 3 months. Traditional scores showed mixed results: ALBI outperformed Child-Pugh (AUC: 0.710 vs. 0.699), and MELD-based scores demonstrated the highest overall performance, but all exhibited imbalanced sensitivity and specificity. ML models trained on 25 variables surpassed traditional scores, with RF achieving an AUC of 0.800 and a better sensitivity-specificity balance. Incorporating dynamic variables further improved performance; RF achieved an AUC of 0.825 with balanced sensitivity (76.06%) and specificity (76.21%). Gini feature importance revealed novel predictors, including largest tumor size, alpha-fetoprotein levels and dynamics, functional state, BMI, and ascites.

Conclusions: ML models, particularly Random Forest, outperform traditional scores in predicting 3-month mortality for LT candidates with HCC. By integrating predictors such as alpha-fetoprotein dynamics and tumor size, ML offers a more comprehensive assessment of both liver dysfunction and tumor-related risks.

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FOS_08_2 KIDNEY PAIRED DONATION: A 12-YEAR SWISS NATIONAL PERSPECTIVE

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Background: Kidney transplantation is the most effective treatment for End-stage kidney disease (ESKD) but is limited by organ shortages and donor-recipient incompatibilities. Kidney paired donation (KPD) programs have emerged as an innovative solution to expand access to living donor transplants. This study aims to describe the implementation of this program in Switzerland and the characteristics of this population as well as patient and graft survival.

Methods: This retrospective, multicenter study analyzed 51 KPD transplants performed in Switzerland between 2011 and 2023. Data from the Swiss Transplantation Cohort Study were used to evaluate donor and recipient characteristics, HLA mismatches, and transplant outcomes. Descriptive statistics, including medians, means, and standard deviations, were calculated. Patient and graft survival rates were assessed using Kaplan-Meier survival analyses.

Results: Over 12 years, 51 KPD transplants were performed across five out of six Swiss transplant centers, with Geneva and Zurich centers performing 82% (n=42), of procedures. The program reached its peak activity in 2014, followed by a subsequent decline. The median waiting time was 426 days (mean 582.67 ± 502.05 days), with a median dialysis duration of 785 days (mean 1406.50 ± 2497.64 days). ABO compatibility was achieved in 88.2% (n=45/51) of cases. HLA mismatches were frequent, 49%.02 (n=25/51) had two mismatches for HLA-A, 72.5% (n=37/51) for HLA-B, and 49%.02 (n=25/51) for HLA-DRB1. Outcomes were excellent, with 100% (n=46/46) graft and patient survival at one year, and 97.8% (n=45/46) at five years.

Conclusions: The KPDS program has greatly expanded access to living donor transplants in Switzerland for highly sensitized patients, who have shown favorable transplant outcomes. However, its limited growth and logistical challenges highlight the need for further optimization and expansion to enhance donor-recipient compatibility and improve long-term outcomes. Collaborative efforts across transplant centers could help maximize its impact.

FOS_08_3 DEVELOPMENT A DISCRETE EVENT SIMULATION ENGINE TO ASSESS THE DIFFERENT ALLOCATION POLICIES IN UK LUNG TRANSPLANTATION

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Background: Lung allocation policies vary internationally from score-based to centre-based prioritisation with criteria determined by national urgency. The impact of implementing new allocation policies can be difficult to predict, with competing interests in waiting lists and the presence of post-transplant outcomes.

Methods: We worked with the UK transplant registry to design an allocation simulation engine combining an analytical hierarchical process, discrete event simulation, Kaplan-Meier survival curves, and operational research queueing that removes hard boundaries to assess the impact of different policies. Our approach uses net benefit, the delta between the waiting list and post-transplant survival, as our success metric. This enabled statistical comparison of policies per simulation run.

Results: Lung allocation prioritising waiting list survival resulted in fewer waiting list deaths at the cost of lower net benefit, lower post-transplant survival and increased waiting times. Allocation prioritising post-transplant survival resulted in an increased survival rate and net benefit, with lower waiting times yet increased waiting list mortality. Our work showed statistically significant differences in waiting list deaths between policies ($p<0.000001$). Fig. 1 shows each simulated policy's predicted waiting list deaths distribution yearly. Results are explained by mathematically defined assumptions and statistical models, not machine learning.

Conclusions: Our simulation engine allows the effect of different lung allocation policies on waiting list survival, post-transplant survival and net benefit to be compared statistically. The data will help inform stakeholder preferences on new allocation policies before implementation. The automation of the process allows 20 years of allocation to be assessed in 5 mins processing time and could be applied to different organs or allocation policies.

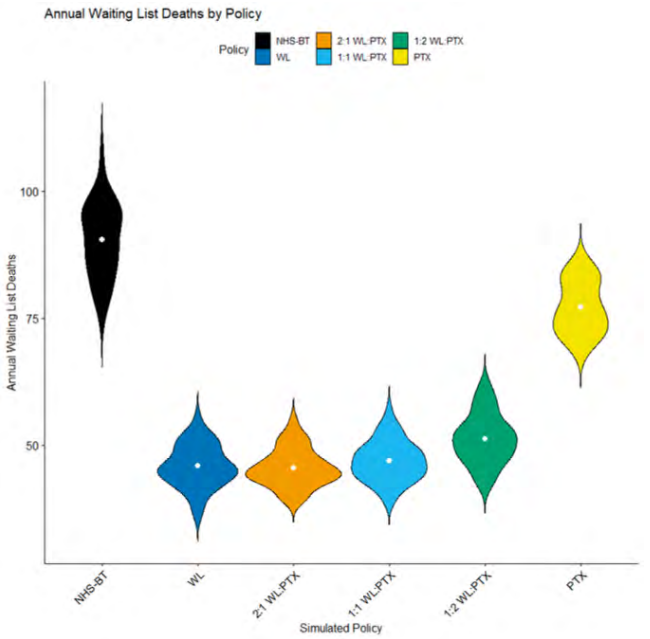

Fig 1. Number of annual waiting list (WL) deaths. Policies vary on waiting list and post-transplant (PTX) survival. X:Y is the ratio between the waiting list and post-transplant survival. Policies are compared against the UK's transplant urgent schemes.

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FOS_08_4 HOSPITAL-BASED AND INDIVIDUAL DISPARITIES IN LIVER TRANSPLANTATION ACCESS: A NATIONAL HEALTH DATA SYSTEM ANALYSIS

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Background: Several studies have shown that non-medical factors can determine access to liver transplantation (LT). Most of this data comes from North America, where the healthcare system has specific features that are difficult to transpose to Europe. We aimed to investigate the factors associated with access to LT in patients admitted to hospital for a first episode of decompensated cirrhosis in France and to determine whether there are treatment gaps in certain centres due to the aetiology of the underlying liver disease.

Methods: In this analytical retrospective cohort, we used data from the French national health data system to extract patients between 18-70 years hospitalized for a first decompensation of cirrhosis between 2015 and 2022, followed until December 2023. We built a frailty model to search for factors associated with access to LT and to quantify inter-centre variability. Then, using a method derived from indirect standardization, we described the differences between the expected and observed incidence of transplantation in patients with an alcohol-related background, between hospital centres.

Results: We identified 65,771 patients, with a mean follow-up time of 36 months and 195,270 person-year. Of these patients, 73.5% were men and 82.3% had an alcohol-related cirrhosis. By December 31st, 2023, 3,596 (5.5%) had been transplanted and 35,660 (54.2%) had died. Patients with an alcohol-related liver disease (ALD) were less likely to be transplanted (HR= 0.75, CI95% = [0.69 – 0.81]), as were women (HR=0.75, CI95% = [0.69 – 0.81]), patients with solidarity-based complementary health insurance (HR= 0.82, CI95% = [0.74 – 0.90]) and more socially deprived patients (HR= 0.97, CI95% = [0.94 - 0.99]). The poorer access to LT for ALD patients was evenly distributed between centres.

Conclusions: Our study highlights several factors contributing to unequal access to LT in France. The lower access for ALD patients suggests the presence of structural stigma. Modification of national-based policies could lead to a more equitable access to LT

FOS_08_5 THE IMPACT OF DONOR AND RECIPIENT DIABETES ON GRAFT AND PATIENT SURVIVAL IN KIDNEY TRANSPLANTATION

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Background: Kidney donors with comorbidities including diabetes can be considered to increase available organs for transplantation. There is potential that these donors have subclinical diabetic nephropathy which progresses post transplantation. We aimed to investigate the safety of diabetic kidney donors by assessing graft and patient survival when a donor, recipient or both have diabetes.

Methods: Data from the Australia and New Zealand Dialysis and Transplant Registry were used to analyse first-time recipients of deceased-donor kidneys between 2003-2022. A Cox proportional hazards model compared the primary outcomes of death censored graft survival (DCGS) and overall patient survival across four combinations of donor/recipient diabetic status. Secondary outcomes of rejection and estimated glomerular filtration rate (eGFR) over time were analysed with logistic regression and linear mixed models, respectively.

Results: We identified 11, 343 recipients with a mean age of 51 years (SD 12.6). Most donors were via the brain-death pathway (79.4%). The four groups included n=7381 donor/recipient both non-diabetic, n=3249 recipient only diabetic, n=524 donor only diabetic and n=189 donor/recipient both diabetic. Unadjusted DCGS was worse only if both donor and recipient were diabetic (figure 1); with the difference maintained after adjustment (aHR 1.70; 95% CI 1.15-2.51; p =0.008). For this group, patient survival was the poorest compared to the reference group of neither diabetic (aHR 1.77; 95% CI 1.33-2.37; p <0.001), followed by diabetic recipients of non-diabetic kidneys (aHR 1.38; 95% CI 1.18-1.61; p <0.001). Non-diabetic recipients of diabetic donor kidneys did not have reduced patient survival (aHR 1.00; 95% CI 0.83-1.22; p=0.977). There was no difference in rejection between the groups. Diabetic donor kidneys had only a minor reduction in eGFR in the first five years post-transplant.

Conclusions: Diabetic donor kidneys can safely be used to increase opportunities for transplantation in non-diabetic recipients. Though patient and graft survival are comparably reduced in a diabetic donor/recipient combination, for some patients this may remain an acceptable alternative to remaining wait-listed, particularly for those approaching the limits of eligibility for transplant.

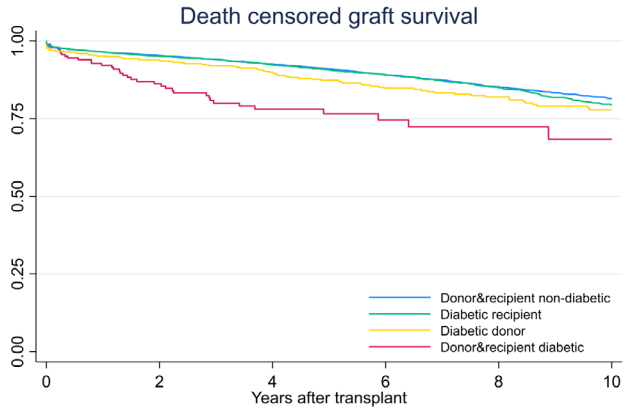

Figure 1. Kaplan Meier Survival curves for deceased donor kidney transplant recipients from the ANZDATA Registry 2003-2022

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FOS_08_6 TESTING THE EAP AT PREDICTING CLINICAL DECISION-MAKING FOR HIGH RISK OFFERS

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Background: Globally, the gap between the need for kidney transplants and available organs remains vast, with SRTR reporting 41,765 additions to the U.S. deceased-donor kidney waitlist in 2021 but only 19,762 transplants performed. The nonuse rate climbed to 24.6%, driven by high KDPI offers, potentially wasting valuable resources and increasing the environmental impact of prolonged dialysis. Sustainable transplantation systems require careful policy design, but pre-rollout testing in selected centers is fraught with risks. Hypothetical environments offer a promising alternative, yet their ability to replicate real-world clinician decision-making, especially for high KDPI offers, remains unproven.

Methods: We integrate data from two sources. The first is SimUNet, a simulation tool developed by UNOS Labs that mirrors the DonorNet interface, where 80% of hypothetical offers have a KDPI > 0.70 to reflect higher-risk decisions. The second links surgeon on-call logs from participating centers to retrospective OPTN kidney offer data over four years. This unique approach allows us to compare clinicians' choices across hypothetical and real-world settings to assess alignment.

Results: Analysis reveals limited correlation between risk preferences in SimUNet and DonorNet, with significant variability among clinicians. To investigate this heterogeneity, we stratify clinicians based on how well the Expected Acceptance Probability (EAP) model explains their retrospective behavior. Among those with high EAP alignment, we observe a positive correlation between hypothetical and real-world decisions. This pattern is absent for clinicians with low EAP alignment.

Conclusions: The EAP model offers insights into decision-making consistency across contexts, particularly for clinicians who rely heavily on available information. These findings underscore the complexity of clinical decision-making and the need for further exploration to design effective, sustainable policies. Reducing organ nonuse is critical to improving global transplantation equity and addressing the environmental costs of inefficient resource use, aligning with broader international goals for sustainable healthcare systems.

FOS_08_7 FIXING THE SCORE: GEMA-NA VERSUS MELD-NA FOR LIVER ALLOCATION IN AOTEAROA NEW ZEALAND

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Background: Gender inequity exists within organ allocation for liver transplantation (LT). Females and patients with ascites or sarcopaenia are disadvantaged by prioritisation methods that rely on MELD and MELD-Na scores. The Gender-Equity Model for Liver Allocation (GEMA) score has been shown to better predict waitlist mortality and delisting than MELD-Na. We aimed to assess the discriminatory and reclassification abilities of the GEMA score within the New Zealand (NZ) context.

Methods: A prospectively-held database of all LTs ever performed in NZ was analysed. Data from 1581 adult LT patients with cirrhosis was analysed. Each patient had a MELD-Na and GEMA-Na score calculated for the time of listing. The ability of the GEMA-Na score to predict waitlist dropout due to death or clinical deterioration was compared to the MELD-Na score and evaluated using Harrell's concordance statistic method. The change in waitlist prioritisation based on GEMA-Na score, compared to MELD-Na score, was also analysed to determine which patients were positively reclassified.

Results: There were 517 eligible LT recipients with cirrhosis included, of which 138 (26.7%) were female. The average listing MELD-Na and GEMA-Na scores were 15 and 16, respectively. There was a 10.23% rate of delisting due to deterioration and a 5.4% waitlist mortality rate. The GEMA-Na score demonstrated superior ability to predict waitlist delisting or death compared with MELD-Na (concordance = 0.669 versus 0.638). Female-only analysis showed improved discrimination for the GEMA-Na score versus MELD-Na (concordance = 0.883 versus 0.772). Excluding HCC patients improved the discriminatory ability of both scores (concordance = 0.792 for GEMA-Na versus 0.765 for MELD-Na). GEMA-Na based allocation led to a positive reclassification in 47% of patients. Overall, 42% of female patients were upgraded on waitlist prioritisation using GEMA-Na.

Conclusions: GEMA-Na score demonstrated a superior discriminatory ability to predict death or deterioration on the waitlist compared to MELD-Na when HCC patients were excluded. This superiority was enhanced in female recipients. Female patients were more likely to be positively reclassified on the waiting list with GEMA-Na scoring. Implementation of GEMA-Na allocation may address inequitable LT waitlist outcomes.

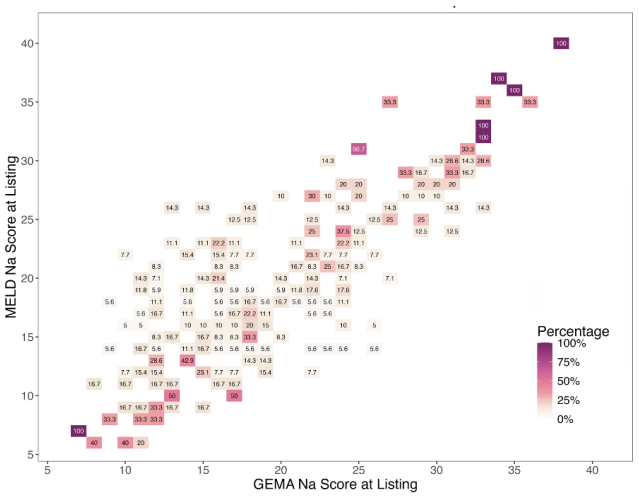

Figure 1: **Re-classification plot showing the concordance rate of GEMA-Na versus MELD-Na in the non-HCC cirrhotic population.** Patients deviating to the left indicate lower GEMA-Na scores compared with MELD-Na and deviations to the right indicate higher GEMA-Na scores compared with MELD-Na. Numbers indicate percentages of GEMA-Na for a fixed value of MELD-Na.

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FOS_08_8 IDENTICAL VERSUS COMPATIBLE BLOOD TYPING: INVESTIGATING BEST PRACTICES IN LUNG TRANSPLANTATION

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Background: Lung transplantation offers hope for patients with chronic lung disease, yet organ scarcity remains a significant challenge. While ABO-identical matches are traditionally preferred, changes in lung allocation policies and research on ABO typing have increased ABO-compatible transplants.

Methods: This retrospective cohort study investigates lung transplant recipients from the United Network for Organ Sharing database between June 2005 and June 2023. Adult patients with acute rejection documentation, ischemic time, and BMI information were included (n= 32,761). Univariate analysis compared characteristics between ABO-identical and ABO-compatible groups. Logistic regression incorporating confounders investigated the primary outcome of acute rejection. Kaplan-Meier survival and Cox proportional hazards models assessed the role of ABO compatibility on 5-year survival.

Results: There was no significant difference in acute rejection between ABO-identical and ABO-compatible groups (univariate, p= 0.990) and (multivariate, OR=1.025 CI= 0.86-1.21). However, ABO-identical transplants show a significantly better 5-year survival rate than ABO-compatible (p= 0.019) and are associated with a decreased risk of death (HR= 0.9116, CI= 0.8516-0.9759). Yet, when stratified by disease category and Lung Allocation Scores (LAS) only patients receiving transplants for obstructive lung disease and top quartile LAS scores show significant differences of (p= 0.043) and (p= 0.014) respectively with higher survival rates in identical ABO typing compared to ABO-compatible. All other LAS quartiles and lung disease categories show no significant survival outcome differences.

Conclusions: This study enables us to increase the donor population and improve outcomes in a disease and LAS-specific manner. These findings bring insight into the role of ABO compatibility in optimizing lung transplant outcomes and inform clinical decision-making to enhance donor organ utilization.

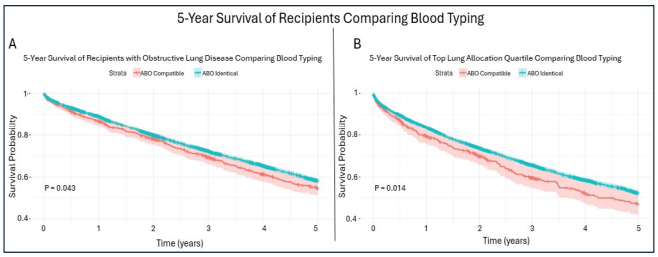

Figure 1: Kaplan-Meier 5-year survival of lung transplant comparing blood typing in A) obstructive disease category and B) top lung allocation score quartile.

FOS_08_9 PERFORMANCE INDICATORS FOR COMPARATIVE ANALYSIS OF ORGAN DONATION AND TRANSPLANTATION PROGRAMMES IN EUROPE

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Background: Assessing the performance of healthcare systems across countries helps to identify areas of improvement and guides national policy initiatives. However, there is currently a shortage of specific indicators tailored to evaluate national organ donation and transplantation programmes.

Methods: To develop a comprehensive scorecard, we took a three-step approach: First, we conducted a targeted literature review of key regulatory documents, national transplant organisation reports (NTO), and existing databases to identify potential indicators. We then classified these indicators using an established framework for transplant system analysis and refined them through preliminary expert consultations. Finally, we validated the resulting 158 potential indicators through a systematic Delphi consensus process. The Delphi panel comprised 32 participants selected for their expertise in health policy, organ donation, transplantation, and patient representation. Participants anonymously rated indicators presented in random order using a 5-point Likert scale across two rounds (first round: n=24, second round: n=22). We set 80% agreement as the threshold for consensus.

Results: Of the 158 indicators evaluated, 87 (55%) achieved the predetermined consensus threshold. The final indicator set incorporates established quantitative metrics such as waiting list statistics (total no. of patients, new registrations, deaths), donation rates (per million population, per number of deaths and in relation to mortality related to brain death), and complication rates. The set is distinguished by its inclusion of novel system-level indicators addressing infrastructure adequacy (e.g., presence of dedicated donor coordinators), resource utilisation efficiency (e.g., organ discard rates), and equity in care delivery (through mandated reporting of sociodemographic factors and patient-reported outcomes).

Conclusions: This validated set of performance indicators provides a standardised tool for assessing transplant system performance across European countries. The indicators can support performance benchmarking of national organ donation and transplantation systems, evidence-informed policy development and improvement initiatives in organ donation and transplantation programmes.

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From preservation to transformation in renal transplantation

FOS_09_1 DELIVERY OF MRNA THERAPEUTICS DURING MACHINE PERFUSION OF DONOR KIDNEYS

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Background: Development of post-transplant kidney fibrosis significantly reduces graft function. Preventing fibrosis can impact the quality of life of transplanted patients. Normothermic machine perfusion (NMP) of donor organs before transplantation enables targeted delivery of therapeutics, minimizing systemic effects. Synthetic messenger RNA (mRNA) encoding therapeutic proteins is promising due to its cost-effectiveness, favorable safety profile and capacity for controllable and transient expression of therapeutic proteins. This study assesses the feasibility of mRNA therapy during kidney-NMP.

Methods: mRNAs encoding a secretive protein (human erythropoietin, hEPO) and an intracellular protein (mCherry) were used as proof-of-concept. Porcine kidneys (n=15) were perfused on NMP using an erythrocyte or acellular-based perfusate for 6-12 hours at 37°C. After 30 minutes of NMP, kidneys were infused with either DSPE (1,2-Distearoyl-sn-glycero-3-phosphoethanolamine) or TPGS (D-alpha-tocopheryl polyethylene glycol 1000 succinate) based lipid nanoparticles (LNPs) carrying 150 µg mRNA into the renal artery. Perfusate, urine and tissue samples were obtained during NMP. The same protocol was used in human donor kidneys (n=7). Initial safety and pharmacokinetics were tested through porcine auto-transplantation with one week follow-up (n=3).

Results: mRNA treatment did not alter perfusion characteristics or post-transplant kidney function. Porcine kidneys exhibited elevated hEPO protein levels in perfusate and urine 1 hour after hEPO mRNA delivery, with levels increasing through NMP. mCherry protein was detected in cortex and medulla tissue in both human and porcine kidneys during and at the end of NMP. Notably, mCherry was observed in the glomeruli and tubules alike. mRNA delivery was successful using both erythrocyte and acellular-based perfusates. mRNA delivery by TPGS-LNPs resulted in higher protein expression compared to DSPE-LNPs.

Conclusions: Expression of therapeutic proteins was achieved during NMP paving the way for ex-vivo mRNA therapy of kidney grafts, in which production of therapeutic proteins in the kidney will persist after transplantation. Ongoing studies are testing the delivery of mRNAs encoding tissue-regenerating proteins to limit post-transplant fibrosis.

FOS_09_2 DEVELOPMENT AND VALIDATION OF A NOVEL RISK PREDICTION MODEL FOR KIDNEY TRANSPLANT OUTCOMES IN THE EUROPEAN POPULATION

Stijn C. van de Laar[1], Matthew Robb[2], Hidde de Heus[3], Robert Porte[4], Robert C. Minnee[5], Frank J.M.F. Dor[6]

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Background: Living and deceased donor kidney transplantation (LDKT and DDKT) require clinicians to select the optimal donor for recipients. When no compatible living donor is available, alternatives such as kidney exchange programs or ABO/HLA-incompatible LDKT may be considered. Tools like the KDPI and LKDPI donor risk index are essential for predicting transplant outcomes and have been widely used to support decision-making. However, these models were developed based on US transplant populations, and their applicability in Europe may be influenced by differences in donor demographics, transplantation practices, and recipient characteristics. This study aimed to develop the (Living donor) European Kidney Transplant Risk Assessment ((L) EKTRA) models tailored to European populations.

Methods: All adult-to-adult LDKT and DDKT performed in the UK (2007–2023) were analyzed. EKTRA and LEKTRA scores were developed using Cox proportional hazards models with pre-transplant variables, excluding incomplete cases. LEKTRA coefficients were scaled relative to EKTRA. Validation was conducted using bootstrap resampling and an external Dutch cohort. Predictive performance was assessed with time-dependent ROC analysis up to 10 years.

Results: This study analyzed 38,940 transplants (14,508 LDKT, 24,432 DDKT). The KDPI demonstrated an AUC of 0.59 at 10 years, while EKTRA achieved 0.66. LEKTRA showed strong predictive performance, with a C-index of 0.69 and AUCs of 0.74, 0.71, and 0.70 at 1, 5, and 10 years, outperforming LKDPI (C-index = 0.59). Kaplan-Meier curves demonstrated significant graft survival stratification by LEKTRA risk groups ($p < 0.001$).

Conclusions: This study validates the utility of the KDPI and LKDPI in European populations and introduces EKTRA and LEKTRA, which are tailored to European DDKT and LDKT contexts. By addressing population-specific differences and optimizing predictive variables, EKTRA and LEKTRA provide robust tools to complement existing models. These models enhance donor risk quantification, graft survival predictions, and donor selection in kidney exchange programs. Integrating them into European transplant registries and guidelines could further standardize decision-making, improve donor matching, and optimize transplant outcomes.

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From preservation to transformation in renal transplantation

FOS_09_3 ONE-YEAR OUTCOME OF HMP(O2)-PERFUSED KIDNEYS AFTER THE IMPLEMENTATION OF A NATIONAL MACHINE PERFUSION SERVICE

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Background: In October 2022, a national hypothermic machine perfusion (HMP) service was implemented for all kidneys from expanded criteria donors (ECD) and kidneys donated after circulatory death (DCD) procured and transplanted in Belgium. The aim of this study is to evaluate the functional one-year outcome of these kidneys continuously perfused with HMP.

Methods: A retrospective analysis was performed on 242 HMP-perfused kidney transplantations (DBD+DCD) performed between 1/10/2022 and 30/09/2023 of which 49 from ECD (defined as a DBD donor between 50-60yrs old with 2/3 following criteria (arterial hypertension, serum creatinine>1.5mg/dl and death due to cerebrovascular accident) or a donor> 60yrs) and 193 from DCD donors. The LifePort Kidney Transporter (?Organ Recovery Systems) was used for all MP procedures. Active oxygenation realized by preceding bubble O_2 of the perfusate and continuous surface O_2 during HMP was applied to all DCD>50yrs and in study context in 14 DCD≤50yrs[5]. Donor demographics and functional outcome were analyzed.

Results: The 1-year functional outcome according to donor type is illustrated in Table 1.

Donor type	All (ECD +DCD)	DBD ECD	DCD	DCD≤50y	DCD>50yrs
Type of kidney preservation (HMP, $HMPO_2$)	HMP(O2) (n=242)	HMP (n=49)	HMP (n=193)	HMP(O2)[5] (n=77)	$HMP(O_2)$ (n=116)
Delayed graft function, %	14.35	9.14	16.67	9.46	19.64
Mean eGFR @1y, ml/ min/1.73m²	54.25	52.03	54.69	61.10	49.73
Organ rejection @1y, %	10.05	2.33	12.82	8.96	14.00
Death-censored graft survival @1y, %	96.28	100	94.34	97.40	93.97
Patient survival @1y, %	98.34	95.91	98.96	100	98.28

The reasons for graft loss (13/242) were primary nonfunction (n=1), rejection (n=1), donor-transmitted infection (n=1), graft infection (n=1), arterial thrombosis (n=1), venous thrombosis (n=2), unknown (n=2) and patient's death (n=4).

Conclusions: Functional outcome of HMP-preserved kidneys after the introduction of a national HMP program for all ECD and DCD kidneys is excellent and reassures transplant teams in their decision-making process when such higher-risk kidneys are offered for transplantation.

FOS_09_4 RESCUING DONOR KIDNEYS FOR TRANSPLANTATION AT A DEDICATED NORMOTHERMIC PERFUSION CENTER

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Background: In 2024, 31,677 deceased donor kidneys were recovered in the US with the intent to transplant, however 9,266 (29%) were discarded. Rescue of these organs may be facilitated using normothermic machine perfusion (NMP), which can prolong out of body time and provide additional viability assessment. While NMP has been increasingly used internationally, barriers to adoption of NMP in the US include limited availability, staffing and facility resource limitations, geographic distances between donor and recipient hospitals, blood shortage, and nationwide reliance on hypothermic machine perfusion (HMP).

Methods: To overcome obstacles to US-based NMP, the first regional NMP center for discarded kidneys was established in West Lafayette, Indiana. Organized as an independent public benefit company, this center was constructed to provide NMP as a regional hub-and-spoke service to transplant centers and Organ Procurement Organizations (OPOs), offering functional assessment of unused donor kidneys (Table 1). An acellular, human serum albumin- based perfusate was chosen and validated pre-clinically to avoid the need for blood. Additionally, an extended second cold ischemic time was validated during the pre-clinical testing to mimic transportation from the central NMP center to the accepting transplant hospital. Central IRB approval was granted in March 2024, and the first kidney was transplanted after NMP on April 20th, 2024 (clinicaltrials.gov: NCT06263023).

Results: To date, 68 unused kidneys were transported to the central NMP center. 59 (87%) of these kidneys were transplanted successfully after NMP by 9 transplant centers. Median initial cold ischemic time (CIT) prior to NMP was 20.3 hours (range 11.5- 30 hrs). Median transport CIT (after NMP and prior to transplant) was 15 hours (range 9- 33 hrs) with median total out of body time (donor cross clamp to recipient reperfusion) of 38.5 hours (range 27.2- 60 hrs). Characteristics of donor kidneys transplanted after NMP can be found in Table 2.

Conclusions: Acellular NMP is feasible when performed by a centralized hub and reduces kidney discard by providing objective viability assessment. Moreover, NMP allows for extended preservation times up to 60 hours, enabling improved logistical planning and broader sharing of deceased donor kidneys.

Table 1. COMPARISON BETWEEN KIDNEY ASSESSMENT METHODS

Renal Biomarker	Ice (4°C)	HMP (4°C)	NMP (35°C)
Renal Flow Rate		✓	✓
Renal Pressure		✓	✓
Renal Resistance		✓	✓
Perfusate pO_2/ pCO_2/ pH			✓
Urine pO_2			✓
TCO_2/ HCO_3^-/ Base Excess			✓
Perfusate Na^+/ K^+/ Cl^-			✓
Urine Na^+/ K^+/ Cl^-			✓
Lactate/ Glucose			✓
AST (marker of mitochondrial death)			✓
Oxygen Consumption			✓
Hosgood Transplant Suitability Score			✓

Table 2. CHARACTERISTICS OF 59 HTP KIDNEYS RESCUED BY NMP

Donor Age (years)	Median: 53	Range: 15- 69
# DCD Donors	36 (57%)	With NRP: 8 (14%)
# Donors with HTN	35 (59%)	
Glomerular Sclerosis %	Median: 4	Range: 0- 71
Peak sCr (mg/dL)	Median: 1.61	Range: 0.7- 11.09
KDPI %	Median: 64	Range: 24- 98
1st CIT pre-NMP	Median: 20.2 hrs	Range: 11.5- 30 hrs
2nd CIT post-NMP	Median: 15 hrs	Range: 9- 33 hrs
Total Out Of Body Time	Median: 38.5 hrs	Range: 27.2- 60 hrs
Renal Resistance pre-NMP	Median: 0.24	Range: 0.08- 1.03
Renal Resistance post-NMP	Median: 0.14	Range: 0.05- 0.30

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From preservation to transformation in renal transplantation

FOS_09_5 A NOVEL KIDNEY NORMOTHERMIC MACHINE PRESERVATION TECHNOLOGY ENABLES KIDNEY PRESERVATION UP TO 5 DAYS

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Background: Normothermic machine perfusion (NMP) technologies for heart, liver, and lung preservation and assessment are a clinical reality. However, NMP technologies enabling kidney NMP are still emerging. Here we present a preclinical study of a novel kidney NMP technology which allows kidney NMP for up to 5 days.

Methods: NMP device functions and perfusion recipe details were developed and assessed following a systematic, stepwise preclinical testing strategy. Following the development phase, use case validation testing and preclinical assessment in 24-118 h perfusions of non-utilized human kidneys were performed. Testing involved 215 porcine and 142 non-utilized human kidneys and a total of over 13,300 h of NMP.

Results: The novel perfusion device features a low-hemolysis pneumatic pump, closed-loop control of perfusion parameters, kidney moisture management, live video display and recording, cloud connectivity, real-time data logging and display as well as machine learning capabilities. Integrated sensors include system and perfusion pressure, flow, pH, temperature, glucose, and urine generation. The developed RBC and albumin-based perfusion protocol facilitated stable renal perfusion with unaltered viability and preserved histology except for some degree of proximal tubular cell vacuolization at 24 hours. In a head-to-head comparison with 24-hour SCS, NMP showed better hemodynamic function, reduced injury, and an improved coagulation profile during simulated reperfusion. Next, 49 non-utilized human kidneys (median age 58 years, KDPI 81%) were perfused for 24–118 hours after prolonged CIT (median 38 hours). Perfusions were generally stable with a median renal blood flow of 277 mL/min, pH of 7.3, and median free hemoglobin levels of 126 mg/dL. Injury markers, including LDH and NGAL, remained low. Histopathological analysis confirmed preserved renal architecture with minimal tubular cell changes at 24-118 hours of NMP.

Conclusions: This novel device and protocol provide a next-generation solution for kidney preservation. Its automated design enables high-quality prolonged NMP with minimal injury. This technology closes a critical gap in organ preservation and offers transformative potential for kidney transplantation.

FOS_09_6 UNSUPERVISED ANALYSIS USING IMAGING MASS CYTOMETRY REVEALS SPATIAL IMMUNE DIVERSITY IN ISCHEMIA REPERFUSION INJURIES

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Background: The main consequence of ischaemia-reperfusion injury (IRI) is delayed graft function (DGF), but IRI also favours the development of interstitial fibrosis and has a negative impact on long-term graft outcome. Renal ischaemia leads to tissue inflammation, but the composition, kinetics and origin of cellular infiltrates are not well described.

Methods: Immune cell distributions in transplant biopsies from kidney transplant recipients with different durations of DGF were assessed by imaging mass cytometry (IMC) using a validated panel of 24 metal conjugated markers investigating hypoxia (HIF1a marker) and immune responses. Unsupervised clustering was applied to the overall immune cell composition and compared with early post-transplant clinical events. Cellular neighborhood analyses were performed based on the spatial proximity of cells.

Results: Unsupervised analysis characterised 12 clusters. Five were immune clusters, one was composed of B and T cells, and the others were composed of different patterns of macrophages: proinflammatory, anti-inflammatory, myofibroblastic and repair macrophages. Unsupervised analysis revealed 2 groups in our cohort that could be distinguished by the intensity of the immune infiltrates. These two groups differed in the intensity of DGF ($p<0.05$). Notably, the four macrophage clusters, regardless of their phenotype, were significantly more represented in the group with longer DGF ($p<0.05$). Cellular neighborhood analysis revealed an immune niche. Indeed, complex immune aggregates of B cells, T cells and macrophages were found around the tubules. Importantly, a spatial coordination between repair macrophages (CD45low CD163+ CD68low Col4- Col1+), hypoxia induced macrophages (CD45low CD163+ CD68low HIF1a ++) and hypoxic tubules (Aquaporin1 + HIF1a+) highlighted the interaction between immune infiltration and areas of tubular stress.

Conclusions: Immune infiltrates, especially certain subtypes of macrophages, can partially differentiate between the phenotypes and severity levels of delayed graft function.

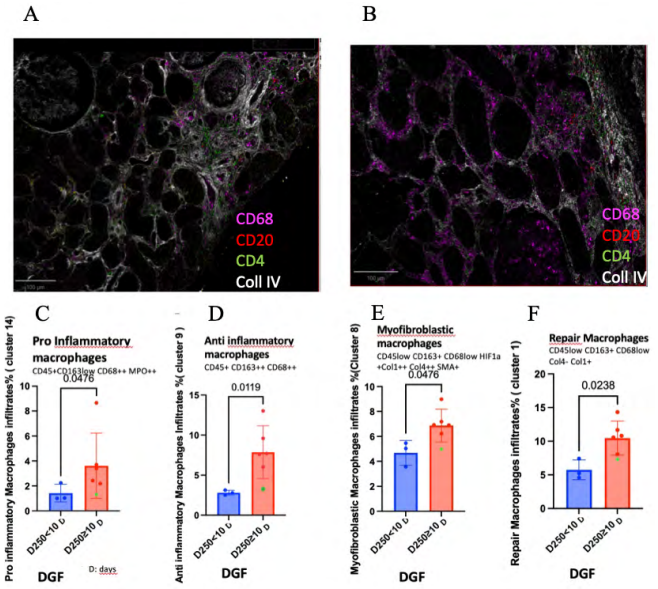

Figure 1. Comparison of immune infiltrates according to intensity of DGF kidney area.

Figure Legends:

A.B Representatives ROIs displaying tissular segmentation for glomeruli and tubulo-interstitial compartments. Gating strategy is applied to display the main immune cells (T cells are shown by CD4 in green ; B cells are shown by CD20 in red; M1 macrophages are shown by CD68 in purple .These ROIs come from a patient with a short duration of DGF(A) and with a longer DGF (B).

C. Proportion of Pro Inflammatory macrophages according to intensity of DGF

D. Proportion of Anti Inflammatory macrophages according to intensity of DGF

E. Proportion of Myofibroblastic macrophages according to intensity of DGF

F. Proportion of Repair macrophages according to intensity of DGF

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From preservation to transformation in renal transplantation

FOS_09_7 TARGETING HUMAN CYTOMEGALOVIRUS IN HUMAN KIDNEYS USING SYN002, A NOVEL FUSION TOXIN PROTEIN

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Background: Cytomegalovirus (CMV) causes minimal harm in its latent state. However, transplanting a kidney from a CMV seropositive donor puts an immunocompromised seronegative recipient at risk of severe CMV infection and graft failure. Fusion toxin proteins (FTP) have been used in vitro to kill CMV infected cells with greater efficiency than antivirals. We investigated the safety and feasibility of the administration of an FTP, SYN002, to human kidneys during normothermic machine perfusion (NMP).

Methods: Five pairs of human kidneys were recruited into the study. One of each pair was treated with SYN002 during NMP and compared to the paired control kidney. Prior to NMP, kidneys were flushed with Ringer's solution and the effluent from the renal vein collected. Perfusate was also collected after NMP. Cells were isolated then cultured and stained for the CMV specific immediate-early antigen expression. Perfusion parameters, perfusate, urine and tissue samples were collected for assessment of function and injury.

Results: There was no significant difference in renal perfusate flow [area under the curve (AUC) control 1196 vs treated 1250 ml/min/100g.h, P=0.791] or intrarenal resistance [AUC control 3.00 vs treated 2.4 mmHg/min/100g.h, P=0.366]. There was also no significant difference in injury markers between the treated and control kidneys (P>0.05). In cells collected from the perfusate, the mean foci of infection did not decrease in the control group but was reduced by 95% in the treated kidneys (P=0.01).

Conclusions: Treatment for CMV during NMP appeared safe and reduced the foci of infection in cells isolated from the perfusate.

FOS_09_8 OPTIMIZATION OF DONOR KIDNEYS WITH SEVOFLURANE DURING NORMOTHERMIC MACHINE PERFUSION

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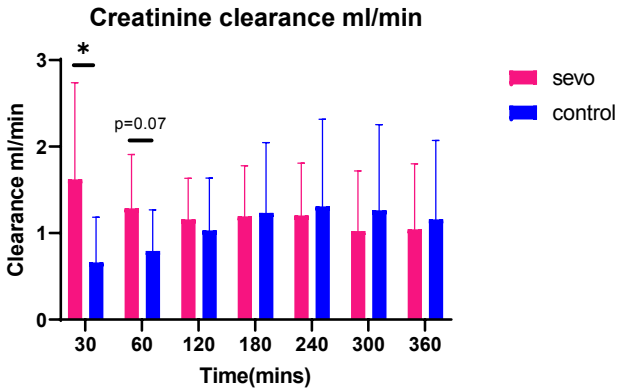
Background: Volatile anesthetics, like sevoflurane, have shown to reduce ischemia reperfusion injury in various studies. The potential mechanisms of protection involve inhibition of opening mitochondrial permeability transition pores, protection of the endothelial cells and glycocalyx, inhibition of cell death pathways, inhibition of inflammatory. Normothermic machine perfusion (NMP) of kidneys creates a therapeutic window of opportunity to add pharmacological substances with the aim to reduce injury, enhance repair and detect biomarkers to evaluate organ function before transplantation. We hypothesize that administration of sevoflurane during NMP reduces injury and improves kidney quality.

Methods: We set-up a slaughterhouse porcine model with administration of sevoflurane using a vaporizer during NMP and tested the feasibility and stability. Then executed 16 experiments (8 paired kidneys, n8/group), with or without sevoflurane. Kidneys were retrieved and subjected 30mins warm ischemia time then flushed with UW solution, preserved cold storage for 24h, after which 6h NMP was initiated. Sevo-NMP group (n=8) was treated with 4% sevoflurane for the first 1h during the 6h NMP while the Control-NMP group was treated without sevoflurane. Perfusate, urine, and tissue samples were collected and physiological measurements were recorded. Two groups data were analyzed with multiple paired t test.

Results: There are no differences in intrarenal resistance, perfusate flow rate, fractional sodium excretion, lactate, weight gain between two groups. The Sevo-NMP group showed higher urine production at 30mins (p=0.02) and higher oxygen consumption at 60mins (p=0.01). Total protein and cumulative protein in urine in Sevo-NMP group are markedly increased at multiple timepoints. Creatinine clearance in Sevo-NMP group is also higher than Control-NMP group within the first hour. Both AST and LDH in the perfusate of Sevo-NMP group showed significantly higher levels compared to the Control-NMP group at multiple timepoints. Sevo-NMP group 30 min fractional potassium excretion was reduced (p=0.01) while urea in the urine was increased statistically (p=0.05).

Conclusions: Vaporizer setting 4% of sevoflurane can promote glomerular filtration rate and kidney metabolism but may cause potential renal cell damage.



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From preservation to transformation in renal transplantation

FOS_09_9 PRESERVATION OF KIDNEYS AT SUBZERO TEMPERATURE USING NATURE-INSPIRED CRYOPROTECTANTS - AN INTERCONTINENTAL APPROACH

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Background: Limited supply and growing demand lead to a shortage of transplantable organs worldwide. Therefore, innovative preservation methods are explored. The combination of subzero organ preservation and normothermic machine perfusion (NMP) allows for exploration of intercontinental organ exchange, offering improved graft viability, monitoring, quality and better matching/transport logistics. In this study, we aimed at kidney preservation using a nature-inspired anti-icing agent at -5°C followed by resuscitation using extracorporeal NMP.

Methods: 7 porcine kidneys were retrieved using a living-donor procedure in Baltimore (USA). Upon flushing with a non-toxic peptoid-based cryopreservative (XT-ViVo®, X-Therma Inc., California) and storage in a -5°C environment (TimeSeal®, X-Therma Inc., California), they were transported using a passenger aircraft to Innsbruck (Europe). After 48 hrs -5°C±1°C storage, 6 hrs of NMP using Kidney Assist (Organ Assist, Groningen) were conducted. Before, during, and after NMP, biopsies were taken for histological, viability, and high-resolution respirometry (HRR). Perfusion was assessed using hyperspectral imaging (HSI) and biochemical parameters of perfusate and urine were analyzed.

Results: Hemodynamic flow remained stable (131 mL/min [119-137]; median [IQR]) throughout perfusion, with a renal resistance index around 0.6. All kidneys metabolized oxygen at all times, with a peak at 2 hrs of reperfusion (22 mLO_2/min/100g [12.4-28.6]; median [IQR]), followed by a reduction towards 6 hrs of NMP (15 mLO_2/min/100g [11.8-16.6]). Physiologic pH, moderate perfusate lactate (32 mg/dL [22-58]) and ion levels were detected. All kidneys produced urine upon reperfusion and during NMP (133 ml/h [88-140]). HRR revealed a preferred substrate pathway (succinate) without significant changes over the course of NMP. A more detailed analysis of the succinate-pathway revealed a significant decrease in OXPHOS capacity (p=0.0015) and ATP production efficiency (0.0002) with a concurrent increase in outer mitochondrial membrane damage (p=0.0073). HSI revealed stable micro-perfusion throughout 6 hrs of NMP.

Conclusions: We show that ice-free subzero preservation combined with NMP is a promising method for extended organ storage and global organ exchange in the future.

Novel approaches to immunosuppression in kidney transplantation

FOS_10_1 MONITORING ANTI-CD38 TREATMENT WITH FELZARTAMAB IN ANTIBODY-MEDIATED KIDNEY ALLOGRAFT REJECTION

Martina Schatzl[1], Katharina Mayer[2], Aylin Akifova[3], Susanne Haindl[4], Matthias Diebold[5], Uptal Patel[6], Donna Flesher[6], Ekkehard Schütz[7], Julia Beck[7], Eva Schrezenmeier[8], Philip F. Halloran[9], Patrick Gauthier[10], Nicolas Kozakowski[11], Bernd Jilma[12], Klemens Budde[13], Georg Böhmig[4]

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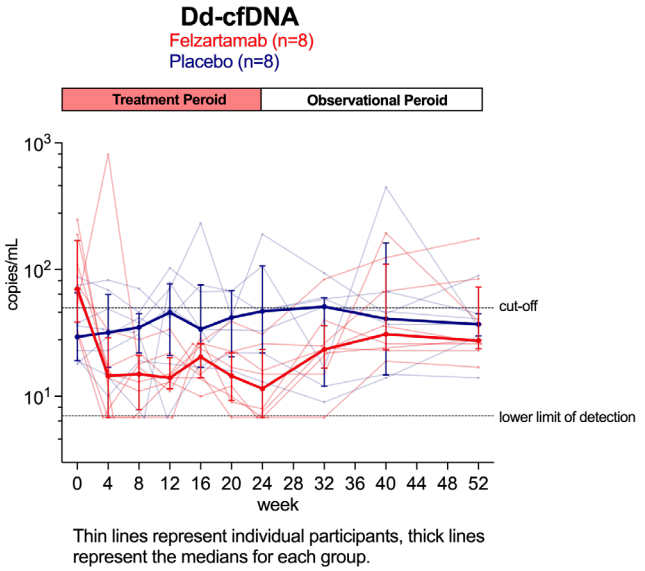
Background: In a recently published randomized, double-blind, bi-center (Vienna;Berlin), placebo-controlled phase 2 trial, felzartamab, a monoclonal CD38 antibody, reversed morphological and molecular antibody-mediated rejection (AMR) activity after kidney transplantation (Mayer et al.,NEJM 2024;391:122). The herein presented sub-study of this felzartamab trial aimed to investigate, whether noninvasive biomarkers reflecting plasma cell activity (donor-specific antibody [DSA] characteristics), graft injury (donor-derived cell-free DNA [dd-cfDNA]) and intragraft inflammation (C-X-C motif chemokine ligands [CXCL]9 and 10), could reflect the resolution of AMR activity and/or its recurrence after treatment cessation.

Methods: Twenty-two recipients were randomized 1:1 to receive 9 doses of felzartamab or placebo over a 6-month treatment period, followed by a 6-month observational period. Kidney biopsies were performed at 24 and 52 weeks. DSA mean fluorescence intensities (MFI), titers, and C1q-fixing capability, along with CXCL9/10 levels in serum and urine were measured using microbead assays. Dd-cfDNA was quantified at tight intervals using digital droplet PCR in a subset (16/22) of patients.

Results: Dd-cfDNA levels (Figure 1) decreased in all but one patient within the first four weeks of treatment (median decrease in absolute dd-cfDNA-levels from baseline: -79% [IQR -91% to -60%]). After treatment cessation, dd-cfDNA gradually increased. In contrast, DSA characteristics (MFI values, DSA titers, C1q-fixing), as well as CXCL9 and CXCL10 levels in serum and urine, showed no meaningful changes, with no significant differences between groups.

Conclusions: These results suggest that dd-cfDNA, may serve as a useful biomarker for monitoring early response to felzartamab treatment. More importantly, dd-cfDNA could indicate the recurrence of rejection after treatment cessation in a timely none-invasive manner, which is subject to ongoing investigations.



Thin lines represent individual participants, thick lines represent the medians for each group.

Figure 1

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Novel approaches to immunosuppression in kidney transplantation

FOS_10_2 CELLULAR BASIS OF ANTI-HLA ANTIBODY REBOUND AND REJECTION IN KIDNEY TRANSPLANT PATIENTS DESENSITIZED WITH IMLIFIDASE

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Background: The recently approved desensitization therapy for highly sensitized (HS) kidney transplant (KT) candidates Imlifidase has a unique mechanism of action cleaving all human IgG subclasses, which immediately, albeit temporarily depletes IgG antibodies. However, its impact on B-cell biology, allo-antibody rebound, and allograft rejection remains elusive.

Methods: In 22 HS KT candidates receiving Imlifidase as desensitization therapy and a step-wise induction therapy based on thymoglobulin, rituximab and IVIG starting at day 4 after KT, we analyzed the cellular basis driving anti-HLA antibody rebound and ABMR using multidimensional spectral flow cytometry and functional cell-based assays.

Results: During the first 6 months, 13 patients (59%) developed BPAR, 1/13 (8%) TCMR at day 5 and 12/13 (92%) ABMR at 35.3±48.9 days post-KT. 4/22 patients (18%) developed subclinical MVI/DSA neg and 1/22 (5%) borderline lesions. We confirmed immediate depletion of anti-HLA antibodies and cleavage of BCR on circulating memory B cells (mBc) within 4 hours post-therapy, and fast recovery by day 5. There was no association between pre-KT DSA characteristics and ABMR occurrence, while rapid and high immunodominant DSA rebound within the first 3 weeks strongly associated with subsequent ABMR (Table). Pre-KT antibodies with the highest MFI showed the highest rebound, particularly those matched with antigens from prior grafts. Interestingly, PLS-DA analysis revealed increased plasmacells and switched-mBcs in patients with rapid DSA rebound and ABMR, correlating with active HLA-specific IgG-producing mBc against previously recognized antigens. Notably, despite no significant changes in circulating cellular subsets after KT, including HLA-specific IgG-switched mBc, Imlifidase functionally inhibits these cells' ability to produce anti-HLA antibodies.

Conclusions: In HS KT recipients receiving Imlifidase for HLA-incompatible KT, DSA rebound facilitating ABMR is driven by high pre-transplant frequencies of alloreactive mBc, especially those against previously recognized HLA antigens.

	ABMR (n=12)	No ABMR (n=10)	p-value
BASELINE CARACTERISTICS			
Sex (male); n (%)	5 (42 %)	6 (60 %)	0.392
Age (mean + SD)	50 ± 11.1	50.43 ± 11.04	0.592
Time on dialysis (years)	12.3 ± 7.6	11.15 ± 6.8	**0.003**
Time on the waiting list (years)	7.58 ± 3.78	7.3 ± 3.17	0.888
Number of prior KT 0 1 2 3	 1 (8.3 %) 4 (33.3 %) 5 (41.2 %) 2 (16.6 %)	 1 (10 %) 7 (70 %) 2 (20 %) 0 (0 %)	0.266
Past pregnancy	4 (33.3 %)	3 (30 %)	0.457
Past Blood transfusion	10 (83.3%)	8 (80%)	0.279
Last cPRA (Mean + SD)	99 ± 2.03	99.37 ± 1.4	0.906
CDC cross-match (Positive)	1 (8.3%)	0 (0%)	0.350
FC cross-match (Positive)	12 (100 %)	10 (100 %)	0.906
Number of DSA (mean + SD) Class I Class II	4.19 ± 1.91 2.29 ± 0.96 1.91 ± 1.7	4.28 ± 1.95 2.29 ± 0.96 2 ± 1.7	0.130 0.709 0.122
Sum of DSA MF; median (IQR)	10425 (6949-25047)	15343 (7061-19400)	0.760
iDSA MFI; median (IQR)	8360 (4799-11935)	5651 (3370-7940)	0.177
iDSA HLA class **Class I** **Class II**	 5 (41.6%) 7 (58.39%)	 6 (60%) 4 (40%)	0.392
POST-KT IMMUNOLOGICAL DATA			
Time of highest iDSA MFI (days, mean + SD)	15.75 ± 3.03	13.6 ± 5.08	0.4510
Highest iDSA MFI; median (IQR)	15617 (1607-20240)	1438 (785-2436)	**0.0137**
Sum of DSA MFI; median (IQR)	28059 (3381-44938	3609 (1791-11856)	**0.0423**

Table. Demographical and immunological characteristics of KT patients presenting or not ABMR.ABMR Antibody-mediated rejection, CDC complement-dependent cytotoxicity, cPRA calculated panel-reactive antibodies, DSA donor-specific antibody, FC flow cytometry, IQR interquartile range, KT kidney transplantation, iDSA immunodominant DSA, SD standard deviation.

FOS_10_3 IMLIFIDASE IN KIDNEY TRANSPLANT RECIPIENTS WITH A POSITIVE CROSSSMATCH: RESULTS OF THE FRENCH COHORT

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Background: Imlifidase is authorized for desensitization of highly sensitized adult kidney transplant candidates with a positive crossmatch against a deceased donor. French consensus guidelines have determined the following eligibility criteria: Age <65 years-old, cPRA ? 98%, ? 3 years on the waiting list, immunodominant DSA with MFI > 6,000 (and < 5,000 at 1:10 dilution) and a negative post-imlifidase complement-dependent cytotoxic crossmatch (CDCXM).

Methods: The ISKIA registry was established to collect clinical, immunological and pathological data of all patients transplanted with imlifidase in France. Using this registry, we report here on the real-world outcomes of the first 30 kidney transplantations performed between November 2022 and August 2024.

Results: The mean age was 48?11 years-old. All 30 patients had been on dialysis for an average of 123?51 months. The mean number of DSA was 4.3?1.6. Before imlifidase, flow cytometry XMs were positive in 26 patients (96%) (3 missing data) while CDC XMs were positive in 4 patients (13%). Conversion of baseline positive crossmatch to negative after imlifidase occurred in 100% of patients. However, 24 patients (80%) exhibited a DSA rebound before day 15. Early clinical antibody-mediated rejection (ABMR) occurred in 10 patients (33.3%). All had a DSA rebound. Four additional patients (13.3%) exhibited subclinical ABMR on the day 10 protocol biopsy. One patient died at month 1 from a septic shock. On the month 3 protocol biopsy, 7 out of 24 patients (29%) were still found to have subclinical ABMR. No graft loss occurred. At the last follow-up (median 10.5 months), serum creatinine was 130?44 µmol/L. Nineteen patients (63%) developed at least 1 infection (BKPyV DNAemia>10,000 c/mL: 16.7%, CMV: 10%, UTI: 40%, Pneumonia: 10%).

Conclusions: These real-world data show that the use of imlifidase to desensitize patients has an acceptable medium-term efficacy and safety profile in selected patients, despite a high incidence of ABMR.

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FOS_10_4 ECULIZUMAB AND OBINUTUZUMAB INDUCTION IN KIDNEY TRANSPLANTATION: 2-YEAR RESULTS OF A SINGLE-CENTER EXPLORATORY TRIAL

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Background: The prevention of antibody-mediated rejection (AMR) after kidney transplantation (KT) remains an unmet clinical need. In sensitized deceased donor (DD) KT recipients, AMR rates as high as 50% have been reported, with poor graft survival. There is evidence that eculizumab can block complement-dependent antibody-mediated cytotoxicity. Also, recent reports suggest that obinutuzumab has more powerful B-depleting and DSA-inhibiting properties than rituximab. We describe a multimodality induction protocol with eculizumab and obinutuzumab.

Methods: In this exploratory study, we analyzed data from 12 high risk (Class I and/or Class II PRA >95% with C1q-fixing DSA >3000 MFI) DD KT recipients treated with the following induction: pre-op plasma exchange (PEX), eculizumab 900 mg before reperfusion, methylpred 1500 mg total-dose on days 0-2, thymoglobulin 5 mg/kg total-dose on days 0-4, PEX 3-to-5 sessions between day 5 and 14, polyclonal immunoglobulin (IVIg) 2 gr/kg total-dose (after PEX), and obinutuzumab 1000 mg 14 days after IVIg infusion. Patients also received LCP-tacrolimus, MMF, and prednisone. Outcomes were compared with those of 20 historical KT recipients treated with pre-op PEX, methylpred, thymoglobulin, post-op PEX, IVIg, and rituximab.

Results: After 2 years, the experimental group showed better patient survival (100% vs 90%; P=ns), graft survival (100% vs 75%; P=ns), and AMR (0% vs 35%; P=0.04) rates than the control group, with similar renal function (serum creatinine: 1.7, 1.3-2.8 mg/dL vs 1.5, 1-3.1 mg/dL; P=ns). Remarkably, 80% of the graft losses recorded in the control group were due to AMR. Despite complement inhibition, all patients treated with obinutuzumab showed rapid, complete, and sustained (up to 1 year) peripheral B-cell depletion, with a significant reduction (<3000 MFI) in preformed class I or class II DSA levels and no detectable de novo DSA. Infusion-related reactions, infections, and malignancies were similar in the two groups. Protocol histology and liquid biopsy obtained within 1 year of obinutuzumab infusion did not show active, chronic active, or chronic AMR.

Conclusions: Eculizumab and obinutuzumab can safely prevent the occurrence of early and rebound AMR in sensitized DD KT recipients. Obinutuzumab effects on peripheral B cells are complement independent.

FOS_10_5 THREE-YEAR FOLLOW-UP OF THE EVERCMV STUDY

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Background: The use of everolimus (EVR) combined with reduced-dose anti-calcineurins is an interesting immunosuppressive strategy for the prevention of cytomegalovirus (CMV) infections at the beginning of renal transplantation in CMV-positive patients. However, the long-term study of this strategy, particularly in terms of graft function, is necessary with currently few data.

Methods: This is a retrospective study with a 3-year follow-up of the population of a prospective study (EVERCMV) that randomized 186 non-high immunological risk, cytomegalovirus (CMV) positive patients to receive EVR with reduced-dose ciclosporin (Ciclo) or mycophenolate mofetil (MPA) with standard-dose Ciclo.

Results: A greater proportion of patients discontinued EVR (55.8% vs. 9.4%, p < 0,001). There was no difference in survival (88,2 % vs 93 %, p = 0,3866), graft function (41,56 vs 43,66 mL/min/1,73m², p = 0,2285), rejection (26,7 % vs 30,6 %, p = 0,1733) and de novo DSA (12,8 % vs 15,3 %, p = 0 ,3831).

Conclusions: In conclusion, reduced dose EVR + Ciclo has equivalent efficacy to Ciclo + MPA at 3 years of kidney transplantation in patients at non-high immunologic risk.

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FOS_10_6 ANTI-THYMOCYTE GLOBULINS PROVIDE NO BENEFIT OVER BASILIXIMAB FOR KIDNEY GRAFTS AFTER DONATION AFTER CARDIAC DEATH

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Background: The use of kidney transplants obtained from donation after cardiac death (DCD) began in France in 2015. Until 2019, we followed the French regulatory agency proposal for induction with anti-thymocyte globulins (ATG), supposed to limit the risk of delayed kidney graft function (DGF, defined herein as ≥1 dialysis before day 7). ATG was replaced by Basiliximab (BSX) at the start of Covid-19 pandemic to limit the risk of infection. In this monocentric retrospective study, we take advantage of this evolution to assess the impact of induction therapy on transplant outcomes after DCD.

Methods: Between 2015 and 2023, 163 patients received a kidney from a DCD donor: 64 (39%) received ATG (mean 4,9mg/kg), 94 (57%) BSX (20mg days 0 and 4). 5 patients who received another regimen were excluded.

Results: The groups were comparable in terms of age, sex and kidney disease. There was no difference in DGF (ATG vs BSX: 17.9% vs 17.0%, p>0.99). At one year post-transplant, biological parameters reflecting graft function were similar (ATG vs BSX: GFR: 60.2±20.4 vs 61.8±20.1 mL/min, p=0.66; proteinuria: 26.2 vs 33.9 mg/mmol, p=0.41), as was the prevalence of de novo DSA (ATG vs BSX: 1.9% vs 1.4%, p>0.99). Kidney biopsies were comparable in terms of inflammation or fibrosis (ATG vs BSX: Banff g+cpt: 0 [0; 1] vs 0 [0; 2], p=0.73; i+t: 0 [0; 2] vs 0 [0; 3], p=0.74; cg: 0 [0; 0] vs 0 [0; 1], p=0.46; IF/TA: 1 [0; 3] vs 1 [0; 3], p=0.40). During follow-up, incidence of CMV infection, BKV nephropathy, and EBV reactivation was comparable between the groups (Log-rank p=0.96, p=0.41 and p=0.70, respectively). Patients in the ATG group tended to have more cancer complications. Finally, ATG induction is on average 70% more expensive than BSX induction.

Conclusions: Induction with ATG is more expensive and provides no significant advantage over BSX in renal transplantation from a DCD donor. Thus, the choice of induction therapy should follow the same principles applied to brain-dead donor.

FOS_10_7 TOCILIZUMAB INDUCTION THERAPY IN KIDNEY TRANSPLANTATION

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Background: Antibody induction therapy is frequently used as an adjunct to the maintenance immunosuppression in adult kidney transplant recipients (KTRs). There are few comparisons of antibody induction therapy allowing early glucocorticoid withdrawal in KTRs. The purpose of the present study was to compare induction therapy involving tocilizumab with the most commonly used induction regimens in patient populations at either high immunologic risk or low immunologic risk.

Methods: We randomly assigned patients to receive tocilizumab or conventional induction therapy such as basiliximab. Patients were stratified according to acute rejection risk, with a high risk defined by a repeat transplant, a peak or current value of panel-reactive antibodies of 30% or more. The 102 high-risk patients received tocilizumab (one dose of 8 mg/kg, in 52 patients) or basiliximab (a total of 40 mg over 4 days, in 50 patients). The 113 low-riskpatients received tocilizumab (one dose of 8 mg/kg, in 62 patients) or basiliximab (a total of 40 mg over 4 days, in 51 patients). All patients received tacrolimus and mycophenolate mofetil and underwent a 10 -days glucocorticoid (prednisone) taper in a regimen of early steroid withdrawal. The primary end point was biopsy-confirmed acute rejection at 6 months and 12 months. Patients were followed for 2 years for safety and efficacy end points.

Results: The rate ofbiopsy-confirmed acute rejection was significantly lower in the tocilizumab group than in the basiliximab group at both 6 months (5.3% vs. 10.9%, P<0.01) and 12 months (7.9% vs. 12.9%, P<0.01). At 2 years, the rate of biopsy-confirmed acute rejection in low-risk patients was lower with tocilizumab than with basiliximab (9.7% vs. 17.7%, P< 0.05), but among high-risk patients, no significant difference was seen between tocilizumab and basiliximab (19.2% vs. 16.0%, P = 0.68). Adverse-event rates were similar among all four treatment groups.

Conclusions: By the first year after transplantation, biopsy-confirmed acute rejection was less frequent with tocilizumab than with conventional therapy. The apparent superiority of tocilizumab with respect to early biopsy-confirmed acute rejection was restricted to patients at low risk for transplant rejection; among high-risk patients, tocilizumab and basiliximab had similar efficacy.

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FOS_10_8 EFFECTIVENESS OF THE TREATMENT OF ANTIBODY MEDIATED REJECTION: A REAL WORLD EVIDENCE STUDY

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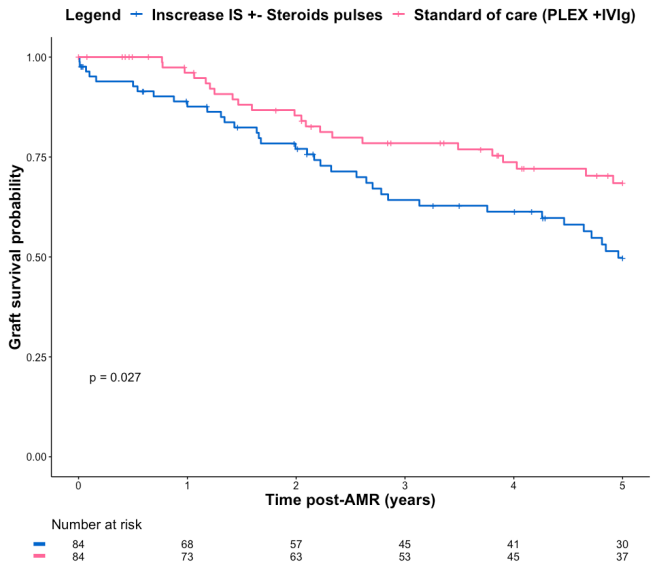
Background: Antibody-mediated rejection (AMR) is the leading cause of long-term graft failure in kidney transplant recipients (KTR). However, the current standard of care treatment is mainly based on small observational studies. The aim of this study was to provide real world evidence of the effectiveness of AMR treatment in kidney transplant recipients.

Methods: This multicenter prospective cohort study included all patients who presented a first clinical antibody-mediated rejection (active of chronic active) between 2007 and 2020 in five French, two European, two American and one Chinese centers. AMR cases were reassessed using the latest Banff 2019 classification. All demographic, clinical, biological, immunological, histological and AMR treatments were collected at time of rejection and during the follow-up up to death, graft loss or lost to follow-up. The patients were separated in two groups no specific AMR treatment versus standard of care (SOC) and then compared after a propensity score matching.

Results: A total of 881 patients were included, with mostly a diagnosis of active AMR (n=557, 63.2%). The AMR occurred in a median time of 16.1 [1.5-58.3] months post-transplantation, mean eGFR was 35.3 (21.9) ml/min/1.73m2, 627 (71.2%) had positive anti-HLA DSA. After matching, 84 patients treated with SOC were compared to 84 patients who didn't receive a specific AMR treatment. A 5 years post AMR, the allograft survival was significantly better for the matched patients treated with SOC with 68.5% 95% CI [56- 78] versus 49.8% 95% CI [0.37- 0.61], p=0.027 (figure).

Conclusions: This study reports the largest cohort of AMR with treated and untreated patients. Antibody-mediated rejection has a severe prognosis that frequently leads to graft failure. This study provides evidence that the standard of care treatment improved transplant outcomes after antibody mediated rejection.



FOS_10_9 IMMUNOLOGICAL AND HISTOLOGICAL REVERSAL OF REFRACTORY ABMR WITH DARATUMUMAB IN KIDNEY TRANSPLANT PATIENTS

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Background: Effective treatments for antibody-mediated rejection (ABMR) in kidney transplantation are still lacking. Anti-CD38 therapies, targeting plasma cells, some mature B-cell subsets, and NK cells, may have a beneficial therapeutic effect in ABMR, as recently shown with Felzartamab.

Methods: We designed a non-randomized pilot study assessing the safety and efficacy of daratumumab as rescue therapy for refractory ABMR to conventional therapy (PE, IVIG and/or rituximab). Patients received 8 doses of 1800mg subcutaneaously over 3 months. Changes on histological lesions, allograft function and DSA were assessed between baseline and end of treatment. Also, spectral flow cytometry analysis of distinct circulating B, T and NK cell subsets as well as donor(HLA)-specific memory B-cell function was assessed over the course of this therapy. Dd-cfDNA was used to non-invasively measure changes on histological graft injury

Results: All study patients are described in table 1. ABMR occurred at a mean time of 45.3±44.0 months after transplantation, being acute ABMR in 10/13 (77%), chronic active ABMR in 3/13 (23%). We report the outcomes of 8/13 (62%) patients that have achieved the last follow-up, full study data will be presented at ESOT, if abstract accepted. Histological assessment after daratumumab therapy revealed a significant improvement of microvascular inflammation (MVI), with a relevant reduction of mean glomerulitis (ag 2.00±0.89 to 0.83±0.75 (p=0.080)), peritubular capillaritis (ptc 2.17±0.41 to 1.17± 0.75 (p=0.046) and global MVI score (4.17±1.17 to 2.00±1.41 (p=0.030)) (Fig 1A). Immunodominant DSA MFI was significantly reduced after treatment (11657±7956 to 5215± 6113, p=0.008). Complete clearance of DSA was observed in 2/8 (25%) patients. No patient progressed to transplant glomerulopathy. Kidney function and proteinuria remained stable. 2 patients presented pneumonia and one recurrent pyelonephritis with a septic shock, no infusion-related adverse event was observed.

Conclusions: Our preliminary data strongly suggest that daratumumab treatment for refractory ABMR is associated with a significant recovery of active microvascular inflammatory lesions of ABMR and down-regulates circulating DSA. Mechanistic studies will bring deeper insight on the mechanisms of action of the drug.

Characteristics	N=13
Male, sex n (%)	8 (62)
Median recipient age (yr)	40 (22-59)
Type of donor:	
LRD. n (%)	2 (15)
BDD. n (%)	4 (29)
DCA. n (%)	7 (50)
Previous kidney transplantation, n (%)	9 (69)
Median cPRA at transplantation	76 ± 41
Preformed anti-HLA donor-specific antibody, n (%)	9 (69)
Positive crossmatch at transplantation, n (%)	5 (43)
Immunosuppression: Induction treatment:	
Thymoglobulin, n (%)	10 (77)
Basiliximab, n (%)	3 (23)
Immunosuppression: Maintenance treatment, n (%)	
Steroids + mycophenolic acid+ Tacrolimus	13 (100)
Type of ABMR, n (%)	
Active	10 (77)
Chronic active	3 (23)
Median eGFR at rejection (ml/m/1.73m²)	54 ± 21
Median protein:creatinine ratio at rejection (mg/gr Cr)	372 ± 313
Initial rejection treatment	
IVIG, n (%)	10 (77)
Rituximab, n (%)	8 (62)
Plasma exchang/IA n (%)	10 (77)
Eculizumab, n (%)	4 (31)
Esterase inhibitor C1	1 (8)
Median time from end of initial rescue therapy to initiation of Daratumumab (months)	5±4
Types of DSA, n (%)	
HLA class I only	2 (15)
HLA class II only	8 (62)
HLA class I and II	3 (23)
>10,000 MFI of immunodominant DSA at the peak level	6 (46)
Any adverse event, n (%)	
Bacterial pneumonia	3 (23)
Pyelonephritis	1 (8)
Urinary septic shock	1 (8)
Graft loss	0
Patient death	0

ABMR antibody-mediated rejection, CKD chronic kidney disease, LRD livingrelated donor, BOD brain-death donor, DCA donation after cardiac arrest, cPRA calculated Panel Reactive Antibodies, HIA human leukocyte antigen, eGFR estimated glomerular filtration rate, IVIG intravenous immunoglobulins , DSA donor specific antibody

Table 1. Patients characteristics.

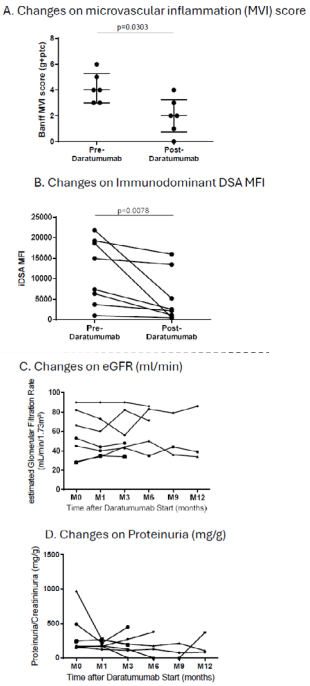

Figure 1. Biological and histological monitoring during and after Daratumumab treatment.

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BRIEF ORALS

Next generation immune regulation and rejection

BOS60_01_1 IMPACT OF TREGS AND B REGULATORY CELLS ON RENAL FUNCTION AND THEIR CROSSTALK EARLY POSSTRANSPLANT

Ariadni Fouza[1], Asimina Fylaktou[2], Anneta` Tagkouta[3], Maria Daoudaki[4], Maria Stangou[5], Lampros Vagiotas[6], Aliki Xochelli[7], Margarita Samali[8], Persefoni Talimtzi[9], Georgios Katsanos[10], Georgios Tsoulfas[11], Nikolaos Antoniadis[12]

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Background: Bregs and Tregs are involved in kidney transplantation. Prospective immunophenotyping performed in a renal transplant cohort before (T0), at 6 (T6) and 12 months (T12) after transplantation to investigate association between B cell subpopulations and graft function. Cross-talk between Tregs and tBregs, mBregs, plasmablasts and graft function was also assessed.

Methods: The frequency and absolute numbers of Tregs CD3+CD4+CD25+-FoxP3+, tBregs CD19+CD24++CD38++, mBregs CD19+CD24++CD27+ and plasmablasts CD19+CD38++ CD27++ IgD+/-, determined in 43 kidney recipients free of rejection. Kidney function was assessed by eGFR.

Results: At T6, the frequency of Tregs (5.2-4.7, p=0.04), tBregs (2.3-0.2%, p<0.01) and plasmablasts (0.45-0.07, p<0.01) as well as tBregs absolute no (1.5-0.1, p<0.01) decreased significantly compared to T0. The mBregs frequency and absolute remained unchanged. At T12 a similar pattern observed. At T6, plasmablast frequency (r=0.36 and p=0.008), tBregs frequency and absolute no, were positively and significantly correlated with eGFR r=0.47 p<0.001 for frequency and r=0.5 and p<0.001 for absolute numbers but not at T12(r=0.19, p=0.179 and r=0.12, p=0.29. A positive correlation observed between absolute no of Tregs and mBregs at T6(r=0.65, p=0.002) and T12(r=0.72, p=0.003), but not between Tregs and tBregs. No correlation observed for B cell populations at T0 or for any cell population at T12.

Conclusions: The data from our cohort showed a transient statistical correlation between the frequency and absolute number of tBregs and renal function at six months, which was not seen at 12 months post-transplant. Furthermore, the absolute numbers of Tregs and mBregs were associated with good renal function at both six- and 12-months post-transplant.

BOS60_01_2 INVESTIGATION OF LEUCOCYTE IMMUNOGLOBULIN LIKE RECEPTORS BINDING TO NON-SELF HLA IN HUMAN MACROPHAGE

Jovanne Palvair[1], Ludivine Dal Zuffo[2], Claire Tinel[3], Baptiste Lamarthée[4]

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Background: The investigation of monocytes/macrophages infiltrating the graft upon rejection is becoming more prevalent. The ability of those cells to recognise donor tissue has been highlighted in mice, independently of the adaptive immune system. This capacity is mainly attributed to the modulation of the expression of Leucocyte Immunoglobulin Like Receptors (LILRs) on their surface. LILR can interact with non-self HLA molecules on donor renal cells, activating recipient-derived monocytes/macrophages. Using single-cell RNA sequencing in blood and biopsies from kidney transplant recipients, our team has previously reported overexpression of LILRB1 in monocytes and macrophages, as well as LILRB2, B3, and A5 upon rejection. LILRB receptors are often described as inhibitory due to the presence of immunoreceptor tyrosine-based inhibition motifs (ITIMs) in their intracellular domain. In addition, a decrease in T cell proliferation has previously been described upon interaction with dendritic cells overexpressing LILRB2.

Methods: To investigate the role of these receptors in primary human macrophages, a lentiviral-based strategy was chosen. Transduction efficiency was evaluated by flow cytometry. The impact of LILRB overexpression in macrophages was assessed on the proliferation of autologous T cell. In addition, the ability of LILRs to bind HLA molecules was determined.

Results: After several optimization attempts, transduction efficiency was sufficient to investigate the interaction of cells overexpressing LILRB1, B2, and B3 with HLA-A2 and -B27 molecules. The ability of LILRB2 to interact preferentially with HLA-B27 molecules was observed. Furthermore, overexpression of this receptor did not seem to impair the proliferation of autologous T cells, contrary to previous reports (Fig 1).

Conclusions: Successful transduction of human macrophages was achieved. We have demonstrated the interaction of LILRB1 and B2 with HLA-B27 molecules. For functional testing, we co-cultured LILRB2 overexpressing macrophages with autologous T cells activated using CD3-CD28 beads. Further investigation of the impact of this interaction is underway, highlighting the controversial effect of those receptors on immune response and kidney rejection.

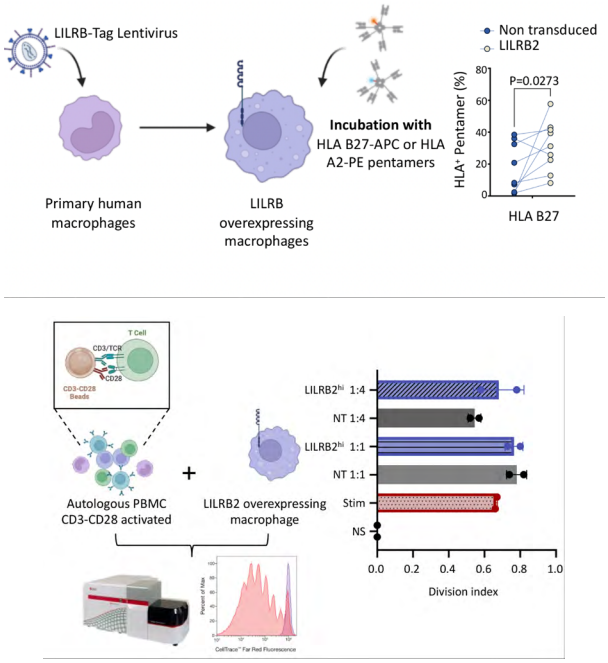

Fig 1: HLA LILRB2^{hi} macrophage binding and impact on T cell

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Next generation immune regulation and rejection

BOS60_01_3 MULTIMODAL SPATIAL PROFILING OF THE MICROVASCULAR INFLAMMATION IN KIDNEY ALLOGRAFTS

Erwan Morgand[1], Valentin Goutaudier[2], Marta Sablik[3], Fariza Mezine[4], Thibaut Thalamas[5], Anais Certain[6], Jessy Dagobert[7], Jerome Verine[8], Dany Anglicheau[9], Jean-Baptiste Gibier[10], Bertrand Chauveau[11], Mehdi Maanaoui[12], Audrey Beq[13], Robert Colvin[14], Elena Crespo[15], Eric Daugas[8], Arnaud Del Bello[16], Michelle Elias[17], Cécile Badoual[8], Viviane Gnemmi[18], Jean-Sébastien Hulot[19], Lionel Couzi[20], Nassim Kamar[21], Christophe Legendre[22], Arnaud Lionet[12], Michael Mengel[23], Christine Randoux-Lebrun[24], Oriol Bestard[25], Gillian Divard[26], Patrick Bruneval[27], Olivier Aubert[28], Carmen Lefaucheur[29], Aurélie Sannier[30], Alexandre Loupy[31]

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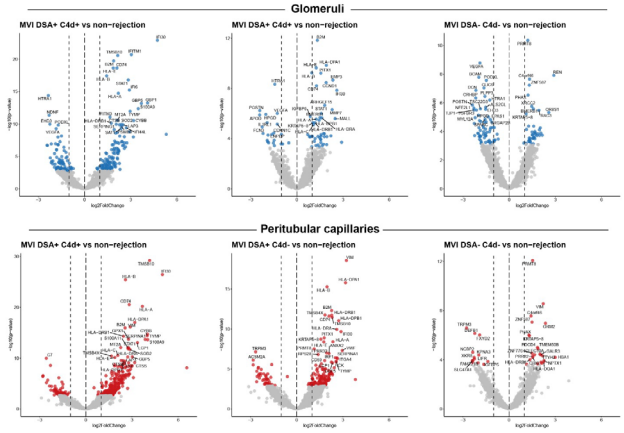
Background: Kidney allograft microvascular inflammation (MVI) DSA-negative C4d-negative is a new entity recognized by the Banff 2022 classification, however the mechanisms driving this inflammation remain poorly understood. In this context, we aimed to decipher its immuno-molecular landscape.

Methods: MVI cases were identified in a multicentric cohort of kidney transplant patients and compared to MVI-negative control cases (total n = 309). Biopsies were graded according to Banff 2022 classification and sequenced using the Banff Human Organ Transplant panel. Whole-transcriptome digital spatial profiling and cellular deconvolution were performed on each phenotype of interest using the Nanostring® GeoMx platform. Finally, microvascular infiltration was characterized using a multiplex immunofluorescence panel staining for CD34, CD68, CD3, NKp46, CD15 and CD20.

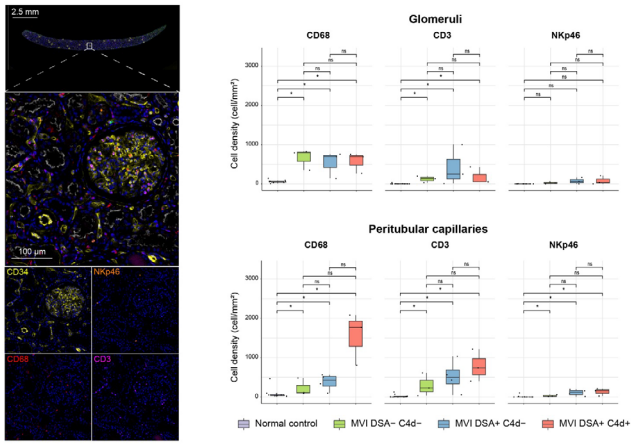
Results: Three MVI phenotypes were analyzed: 1) MVI DSA- C4d- (n = 49, 15,9%), 2) MVI DSA+ C4d- (n = 45, 14,6%), 3) MVI DSA+ C4d+ (n = 46, 14.9%), as well as a control group of non-MVI cases (n = 169, 54,6%). When compared to controls, all MVI cases shared a common molecular signature, characterized by an upregulation of genes associated with antibody-mediated injury, interferon-gamma response, and activation of macrophages, NK cells, and T cells. This common signature was less intense in MVI DSA- C4d- cases, particularly regarding the interferon-gamma response. Spatial profiling analysis revealed that this molecular signal was more prominent in peritubular capillaries than in the glomeruli (A). Cellular deconvolution further demonstrated that MVI DSA- C4d- cases were particularly associated with NK cells and conventional dendritic cells. Automated quantification of immunofluorescence staining revealed that microvascular infiltration was predominantly composed of CD68+ macrophages, CD3+ T cells, and NKp46+ NK cells (B).

Conclusions: We demonstrate that the immuno-molecular signature in kidney allograft MVI DSA- C4d- is moderate in intensity compared to MVI DSA+ C4d- and MVI DSA+ C4d+, and predominantly characterized by the presence of NK cells and conventional dendritic cells in the peritubular capillaries. Our findings open avenues for more mechanistically-driven therapeutic approaches for MVI.

A - Digital spatial profiling of MVI cases



B - Immunophenotyping of the intracapillary infiltration in MVI cases



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Next generation immune regulation and rejection

BOS60_01_4 PEPTIDE-SPECIFIC ALLOREACTIVE B CELLS ARE FOUND AT HIGH FREQUENCY DURING HEART GRAFT REJECTION

Martina Denkova[1], Moumita Paul-Heng[2], Shivanjali Ratnaseelan[3], Eric Taeyoung Son[3], Alexandra Hill[3], Chuanmin Wang[3], Tristan Le Ruyet[4], Katherine Jackson[4], Jake Henry[4], Anthony Purcell[5], Dene Littler[5], Jamie Rossjohn[5], Daniel Christ[4], Nicole Mifsud[6], Alexandra Sharland[7]

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Background: *In vitro* studies have demonstrated differential reactivity of human alloantibodies towards HLA-A2 expressed on cells of different tissue lineages, implying a role for tissue-specific peptides in B cell allorecognition. Here, we sought to determine whether abundant self-peptides presented by H-2K^b (K^b) on cells of C57BL/6 donor hearts would be recognized specifically by alloreactive B cells during heart graft rejection.

Methods: Hearts were transplanted from C57BL/6 donors to BALB/c recipients. B cells isolated from recipient spleen on d7 were stained with a panel of 12 barcoded K^b-peptide dextramers and a self-peptide/MHC (pMHC) control. Single cells were captured using BD Rhapsody; VDJ sequences, transcriptome and dextramer counts were determined. Immunoglobulin genes were aligned against a BALB/c germline reference (OGRdb). One pMHC-specific B cell receptor (BCR) was synthesized as a recombinant antibody, and affinity of binding to its putative ligand and control K^b-peptide monomer was measured using Bilayer Inferometry (BLI).

Results: B cells segregated into distinct clusters based on pMHC specificity (Fig 1A). More than 40% of alloreactive B cells bound a single specificity and not other pMHC within the 12-plex panel (Fig 1B). Typical dextramer-binding profile for a pMHC-specific BCR is shown in Fig 1C. Particular BALB/c immunoglobulin heavy chain variable (IgHV) genes were overrepresented among BCR recognising individual pMHC (Fig 1D), and many pMHC-specific B cells expressed the transcriptional profile of germinal centre cells or plasmablasts, indicating involvement in an active immune response. The BCR shown in 1C was synthesized as a recombinant antibody and bound its ligand Kb-RTYTYEKL with affinity (KD) of 32 nM, 10,000-fold stronger than a K^b-peptide control.

Conclusions: A sizeable proportion of alloreactive BCR detected *in vivo* during acute rejection recognize specific peptides complexed with allogeneic MHC.

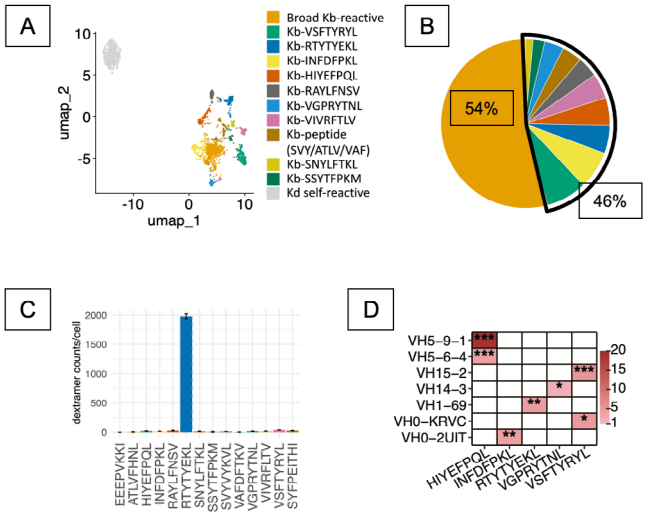

Figure 1.

BOS60_01_5 AUGMENTED GRAFTS TO FIGHT ANTIBODY-MEDIATED-REJECTION VIA GENETIC ENGINEERING OF THE ENDOTHELIUM

Eline Terrazzoni[1], Olivier Thaunat[2], Virginie Mathias[3], Valérie Dubois[4], Floriane Fusil[5]

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Background: Antibody-mediated rejection (AMR), a leading cause of graft failure, occurs when donor-specific antibodies (DSAs) bind to alloantigens expressed by graft endothelial cells (ECs), triggering microvascular inflammation. Preventing the generation of de novo DSAs currently relies on transplant recipients adhering to lifelong immunosuppression regimens. However, these regimens come with significant side effects, such as infections and cancers, and are only partially effective, with the prevalence of de novo DSA estimated at 10-20% after five years. In this study, we set out to test the original hypothesis that AMR could be prevented by making graft endothelium resistant to DSA-mediated damage.

Methods: Conditionally immortalized human glomerular endothelial cells (CiGEnC) were genetically modified using lentiviral vectors to express either a non-signaling truncated form of the high-affinity human IgG receptor (CD64tr) or the IgG-degrading enzyme from Streptococcus pyogenes (IdeStm) on their membranes. The IgG capture ability of CD64tr and the protease activity of IdeStm were confirmed by flow cytometry and FRET, respectively. In an in vitro AMR model, co-culturing purified human natural killer (NK) cells with DSA-coated CiGEnC led to NK cell activation, as indicated by CD107a and IFNγ expression (measured by flow cytometry), and resulted in CiGEnC death, monitored in real-time via impedance measurements using xCELLigence.

Results: IdeStm expression in ECs reduced CD107a and IFNγ expression in co-cultured NK cells to levels comparable to negative controls. In contrast, CD64tr expression only partially decreased these activation markers. Nonetheless, both strategies provided protection against NK cell-mediated cytotoxicity compared to unmodified ECs.

Conclusions: Based on the preliminary results exposed above, we propose that transferring immune escape mechanisms into graft endothelial cells could serve as a novel genetic engineering strategy to prevent AMR.

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BOS60_01_6 CD8 T CELLS FROM KIDNEY TRANSPLANT RECIPIENTS WITH HUMORAL REJECTION ARE RESISTANT TO GZMB BREG

Manuel Laslandes[1], Gaelle Tilly[2], Tess Van Meerhaeghe[3], Elina Deneele[4], Amandine Dupuy[5], Nabila Djouadi[6], Richard Danger[7], Hoa Mai[8], Sophie Brouard[9], Nicolas Degauque[10]

[1]Chu de Nantes; Chu de Nantes, [2]Inserm U643 Itert; Cr2ti-U1064, [3]Hôpital Erasme; Nephrology, [4]Nantes Université / Inserm / Chu de Nantes, [5]Cr2ti-Umr1064; Chu Hôtel Dieu Nantes, [6]Chu de Montpellier, [7]Crti -Inserm Umr1064 -Itun; Cr2ti-U1064; Chu Nantes, Inserm, Universite Nantes, [8]Universite DE Nantes; Agence Comptable - Service Facturier, [9]Cr2ti Inserm Umr1064; Cr2ti-U1064, [10]Cr2ti Inserm Umr1064; Cr2ti-U1064; Umr 1064

Background: Kidney transplant recipients (KTR) with operational tolerance display in the blood an expansion of a regulatory B lymphocyte subpopulation expressing Granzyme B (GZMB$^+$ Breg) and a lower level of Effector Memory expressing CD45RA (TEMRA) CD8 T cells. Recent data have highlighted the involvement of TEMRA CD8 in antibody-mediated rejection (ABMR). We hypothesized that a defect in the regulatory cross-talk between GZMB$^+$ Breg and TEMRA CD8 contributes to the pathophysiology of ABMR.

Methods: *In vitro*, autologous and heterologous co-culture models of TEMRA CD8 and GZMB$^+$ Breg induced from circulating B cells have been developed in healthy volunteers (HVs) and in KTR with stable graft function or with biopsy-proven ABMR. The kinetic of the immune-metabolic response of CD8 T cells (proliferation, cytokine secretion, production of pro-inflammatory cytokines and cytotoxic molecules, metabolism, cytotoxicity assay, signalization) was analyzed longitudinally by spectral flow cytometry. A mini-bulk transcriptomic analysis was performed on CD8 T cells that had been purified following a 3-day coculture with GZMB+ Breg.

Results: The effector functions of TEMRA CD8 from HV or KTR with stable graft function were impaired by GZMB$^+$ Breg, with a reduced proliferation, lower production of inflammatory cytokines and cytotoxic molecules, lower cytotoxicity function while preserving their survival. The functions of HVs' CD8 T cells were also efficiently suppressed by GZMB$^+$ Breg from KTR with ABMR. In contrast, total CD8s from KTR with ABMR were resistant to autologous GZMB$^+$ Breg's regulation. Finaly, the regulation of T CD8 by GZMB$^+$ Breg relies on the inhibition of metabolic program that integrates glycolysis with mROS production and mTOR pathway.

Conclusions: GZMB$^+$ Breg effectively regulate TEMRA CD8 in HV by interfering with the TCR induced metabolic reprogramming. Interestingly, while GZMB$^+$ Breg are functional in KTR with ABMR, CD8 T cells from ABMR are resistant to this regulation. Ongoing transcriptomic analysis that will be presented during the conference will identify potential targets that contribute to resistance to regulation. This resistance of T CD8 to regulation in KTR with ABMR provides new insights into the pathophysiology of this rejection.

BOS60_01_7 GENETIC ENGINEERING OF SILENCING MHC BY NORMOTHERMIC MACHINE PERFUSION MITIGATES ACUTE REJECTION OF RENAL ALLOGRAFT

Tong Chen[1], Li Lin[2], Shuangjin Yu[3], Qin Wang[4], Jiang Qiu[5]

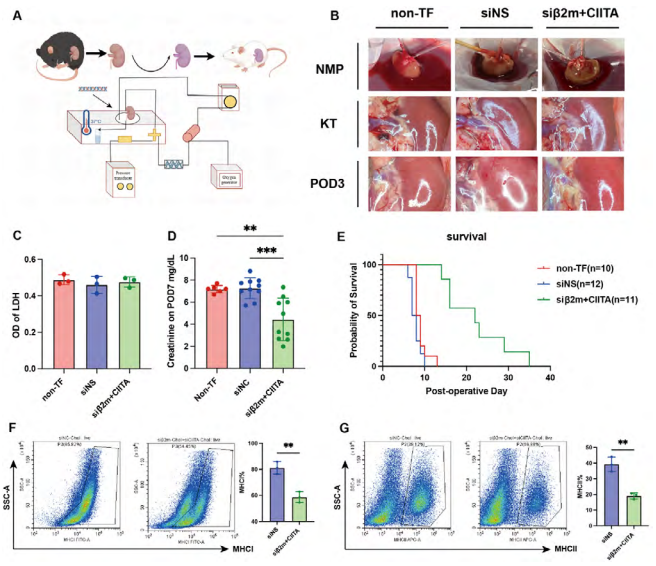
[1]Organ Transplant Center; Surgery, [2]Sun Yat-Sen University, [3]The First Affiliated Hospital of Sun Yat-Sen University; Surgery; Transplantation, [4]Zhongshan School of Medicine, Sun Yat-Sen University, [5]The First Affiliated Hospital of Sun Yat-Sen University

Background: Acute rejection (AR) significantly affects renal allograft outcomes, and MHC is a principal factor in AR.

Methods: we synthesized cholesterol-modified siRNA targeting β2m and CIITA, which were delivered to the renal graft of BN rats during 3 hours of normothermic machine perfusion (NMP). Non-transfection (non-TF) kidneys or kidneys perfused with non-specific siRNA (shNS) served as controls. Then, we transplanted allografts into the recipient rats (Lewis) and compared each group's graft function, survival rates, and the MHC expression on postoperative day(POD) 3 by FCM. The schematic representation is shown in Fig. A.

Results: Cholesterol-modified siRNA does not cause additional renal injury during NMP (Fig. B). No significant differences in LDH activity levels after NMP were between individual groups (Fig. C). The subsequence transplantation was successful (Fig. B), and renal grafts transduced with siβ2m+CIITA showed better renal allograft function. There were significant differences in serum creatinine on POD 7 (7.26 ± 0.94mg/dl in siNS and 4.45±1.91 mg/dl in siβ2m+CIITA, *P*=0.0003, Fig. D). All recipient rats with non-TF and siNS died within 12 days post-transplant. The Median survival of siβ2m+CIITA was longer than siNS (9 days vs 12 days, P=0.0069 Fig. E). Renal grafts were harvested on POD3 (Fig. B), and kidneys perfused with siβ2m+CIITA showed lower expression of MHC I and MHC II (Fig. FG).

Conclusions: This study shows that NMP can efficiently deliver siRNA to renal graft ex vivo, successfully downregulate MHC I and MHC II, and effectively mitigate AR, which potentially provides an organ-targeted, ex vivo approach to treat AR in kidney transplantation.



(A)The schematic representation; (B) Appearance of renal allografts during NMP, after kidney transplantation (KT), and on POD5;(C) The OD of LDH level in perfusate after NMP; (D)The creatinine of recipients on POD7; (E) Survival of recipients in non-TF, siNS, and siβ2m+CIITA group; (F)The MHCI expression level of allografts on POD3 in siNS and siβ2m+CIITA group (81.06±4.73% vs 58.62±4.23%, *P*=0.0036); (G) The MHCII expression level of allografts on POD3 in siNS and siβ2m+CIITA group (39.27±4.65% vs 19.06±1.94%, *P*=0.0023);.

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BOS60_01_8 INTRA-RENAL IL-33 INDUCED INDUCTION OF ILC2 CELLS PROTECTS FROM RENAL ISCHEMIA INJURY IN RENAL TRANSPLANTATION

Linda Marie Laura Thole[1], Janine Siegle[2], Karolin W. Hublitz[3], Efstathios Stamatiades[3], Claudia Dürr[4], Christoph Klose[3], Peter Boor[5], Roman Bülow[5], *Katja Kotsch*[6]

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Background: Innate lymphoid cells (ILCs) do not express antigen-specific receptors, persist mainly in solid tissues and play a critical role in regulating inflammation and tissue homeostasis. Especially the induction of ILC type 2 cells (ILC2s) by the exogenous application of the alarmin IL-33 has been shown to mediate reno-protective processes upon ischemia-reperfusion injury (IRI). However, the precise role of ILC2s for homeostasis and improved graft function following kidney transplantation (KTx) needs to be defined.

Methods: We studied the renal-protective effects of ILC2s applying a murine model of KTx.

Results: Kidney-resident ILC2s of the donor are completely lost following allogeneic BALB/c to C57BL/6 KTx. Although recipient-derived ILC2s infiltrate the graft already within 24 hours post KTx, the intra-renal ILC2 pool is not replenished until day 7 post KTx. However, in a syngeneic C57BL/6 to C57BL/6 KTx setting, donor pre-treatment with recombinant IL-33 (300 ng/day) for 5 consecutive days prior to KTx resulted in a significant expansion of intra-renal ILC2s and protected the kidney against prolonged cold ischemia (6 hours) reflected by reduced tubular injury and significantly improved creatinine levels. IL-33 pre-treatment was less protective in Nmur1CreID2flox (ILC2-deficient) mice supporting the renal-protective role of ILC2s. Moreover, IL-33 donor pre-treatment was verified in the BALB/c to C57BL/6 allogenic transplantation setting with prolonged cold ischemic time under co-stimulatory blockade (CTLA-4 Ig), resulting in significantly improved graft function. Of note, without co-stimulatory blockade, donor pre-treatment resulted in accelerated inflammation and graft deterioration reflected by elevated creatinine levels compared to controls. In contrast, although recipient-treatment with IL-33 for 7 days post KTx resulted in higher renal ILC2 numbers than control-treated recipients, administration of IL-33 did not improve early graft function in both, syngeneic or allogeneic transplantation.

Conclusions: In summary, we report on the functional relevance of the IL-33-ILC2 axis in experimental kidney transplantation pointing towards a new regulatory cell type in this setting.

BOS60_01_9 ANTI-CD38 TREATMENT ON MOLECULAR PHENOTYPE OF ANTIBODY-MEDIATED REJECTION IN KIDNEY TRANSPLANTS

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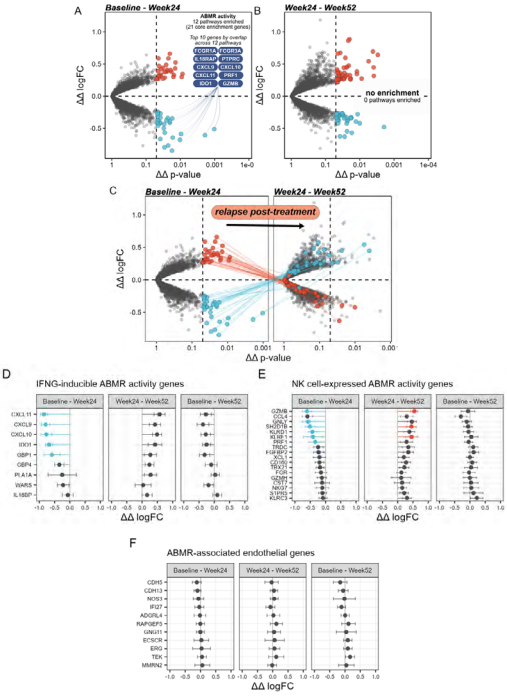
Background: A recent randomized controlled trial demonstrated that treatment with CD38 monoclonal antibody felzartamab suppressed antibody-mediated rejection (ABMR) in kidney transplant patients but with recurrence post-treatment in some patients.

Methods: This study examined the molecular effects of 6-months felzartamab treatment on biopsies from the trial using genome-wide microarray analysis, comparing pre-treatment, end-of-treatment (24 week) and post-treatment (week 52) biopsies from 10 felzartamab and 10 placebo patients.

Results: Felzartamab reduced molecular ABMR activity scores in all 9 patients with baseline ABMR activity, selectively suppressing interferon gamma (IFNG)-inducible and natural killer (NK) cell transcripts, with minimal effect on ABMR-induced endothelial transcripts and no effect on T cell transcripts. Suppression was often incomplete when ABMR activity was intense, and molecular recurrence was nearly universal by week 52. In genome-wide transcriptome analysis, felzartamab impacted 58 genes between baseline and week 24. Ten of the top 20 differentially expressed genes were decreased, including those associated with ABMR activity. Functional enrichment analysis confirmed the suppression of 12 ABMR-related pathways, reflecting downregulation of NK- and IFNG-induced genes. Of the top 20 differentially expressed genes, 10 were increased. These genes likely represented normal parenchymal genes previously suppressed by ABMR activity, all of which decreased after therapy as ABMR activity returned by week 52. Felzartamab suppressed both IFNG-inducible and NK-expressed ABMR activity genes. From baseline to week 52, felzartamab affected 166 genes. 17 of the top 20 genes were injury-inducible and decreased by week 52, indicating lasting recovery from ABMR-related parenchymal injury after 24 weeks of therapy.

Conclusions: Felzartamab selectively suppressed IFNG-inducible and NK cell transcripts, offering parenchymal benefits and potentially slowing progression to kidney failure despite near-universal molecular recurrence by week 52.



Genome-wide effect of felzartamab on gene expression during the study (A-C) and effect on interferon gamma (IFNG)-inducible (D), natural killer (NK) cell-expressed (E), and ABMR-associated endothelial genes (F).

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Next generation immune regulation and rejection

BOS60_01_10 FIRST CHARACTERIZATION OF LONG-TERM IMMUNE RESPONSE AFTER PIG-TO-HUMAN KIDNEY XENOTRANSPLANTATION

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Background: We previously characterized the short-term immune response after pig-to-human kidney xenotransplantation, but little is known about its long-term evolution. Here we aimed to decipher the long-term xenoimmune response in a human decedent model.

Methods: We analyzed a genetically modified pig kidney xenograft implanted for 61 days in a deceased human recipient with a pre-transplant negative xenoreactive crossmatch. We performed morphological evaluation, multi-immunophenotyping, 38-hyperplex complement cascade imaging, bulk transcriptomic profiling, and spatial transcriptomics at cellular and subcellular levels (NanoString CosMx®) at sequential time points (POD10, POD33, POD45, POD49, POD61). Controls included pre-implantation xenograft, wild-type pig kidney autografts, and brain-dead pig kidneys.

Results: From POD10 to POD61, we observed a membranoproliferative glomerulonephritis (MPGN)-like pattern characterized by microvascular inflammation, predominantly in glomeruli, associated with intense linear capillary C4d deposition, glomerular deposition of IgM and IgA, endothelial activation, and early post-xenotransplant *de novo* positive xenoreactive crossmatch. This pattern was accompanied by glomerular double contours, interstitial edema and endarteritis from POD45. Capillary inflammation primarily consisted of CD68+ and CD15+ innate immune cells throughout all follow-up time points. At POD45, we observed co-localized deposits of IgM, IgA, C1q, C3c, C4d, factor B, and complement factor H regulator along glomerular capillaries. The xenograft exhibited increased expression of genes related to humoral response, including monocyte and macrophage activation, NK cell burden, endothelial activation, interferon-gamma response, and T and B cell interaction, which improved over time after rejection treatment (**Figure**).

Conclusions: We described for the first time a new entity of xenoantibody-mediated injury characterized by an MPGN-like pattern, mainly driven by complement activation through glomerular xenoimmune complexes, which improved after rejection treatment. These findings support the development of personalized therapies to improve xenotransplantation outcomes.

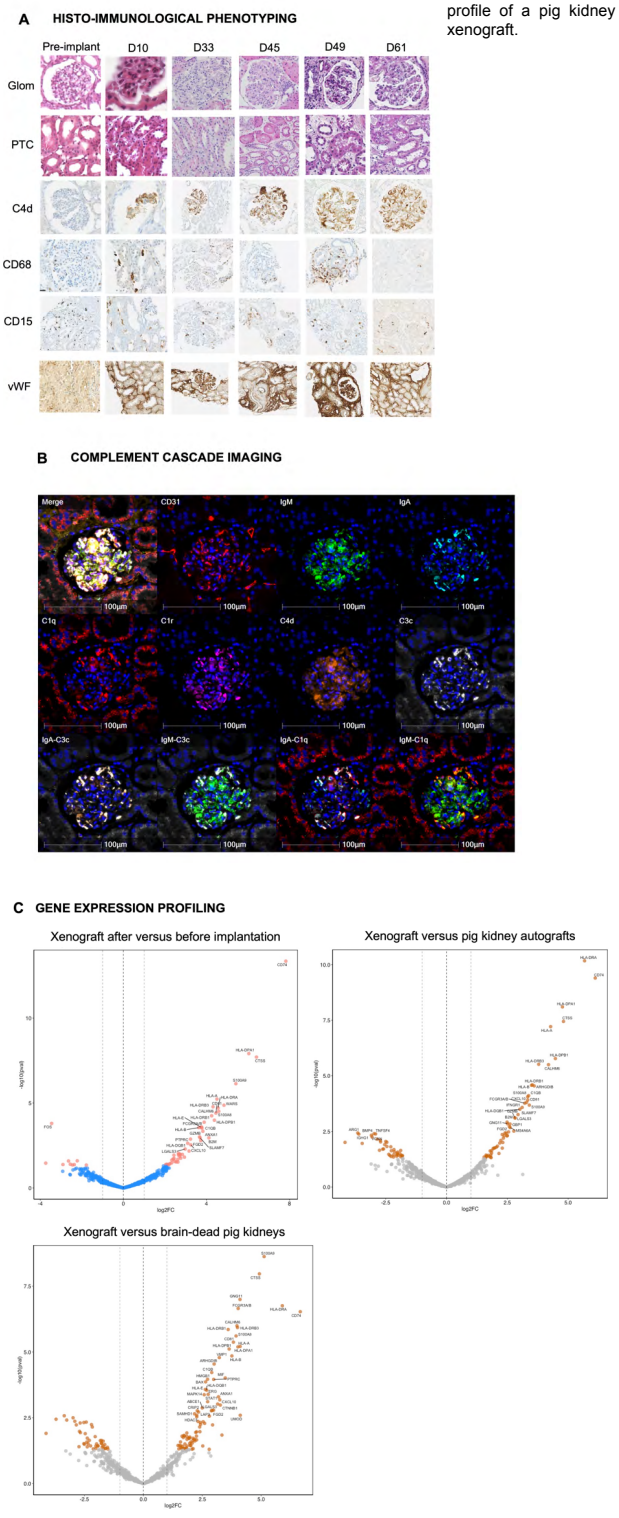

Figure. Longitudinal immune molecular profile of a pig kidney xenograft.

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BOS60_02_1 COMPARISON OF THE OUTCOMES OF RIGHT POSTERIOR SECTOR GRAFT AND LEFT LOBE GRAFT IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Living donor liver transplantation (LDLT) is life-saving procedure for individuals with decompensated chronic liver disease or acute liver failure. When right lobe of the liver is unsuitable for donation due to insufficient remnant volume (<30%), either left lobe graft (LLG) or right posterior sector grafts (RPSG) serves as a viable alternative.

Methods: This retrospective study examines 4036 adults who underwent LDLT between September 2006 and May 2023 and received RPSG or LLG at our centre. Study includes comparison of 51 cases of RPSG which is the largest case series in the world, and 72 cases of LLG which is first in the world to the best of our knowledge.

Results: RPSG donors had a significantly larger graft volume compared to LLG donors (p-value < 0.001). RPSG donors had a higher peak total bilirubin and INR compared to LLG donors (p-value = 0.007 and <.001 respectively). As per Clavien-Dindo classification there were no significant differences between RPSG and LLG donors in terms of minor complications (p-value = 0.760), major complications (p-value = 0.805), bile leak (p-value = 0.648), or hospital stay duration (p-value = 0.515). Recipients of RPSG had a significantly higher mean body weight (73.0 kg) compared to recipients of LLG (66.3 kg) (p-values = 0.003). There were no significant differences in MELD score, operation time and blood loss. Graft volume was significantly higher in RPSG than LLG recipients (576.8 vs 475.2 gm, P <0.001). Major complications (graded 3-4) were similar in both the groups (25.5% for RPSG vs 29.2% for LLG recipients, p-value = 0.377). Mortality rates were similar (7.8% for RPSG vs 8.3% for LLG recipients, p-value = 0.921). Long term survival (1,3 and 5 years) was similar on Kaplan Meier curve analysis (P value= 0.536)

Conclusions: We propose RPSG can be considered as viable option for LDLT to increase donor pool

BOS60_02_2 DONOR LIVER MICROBIOTA IN PRESERVATION SOLUTION AS AN EARLY BIOMARKER IN TRANSPLANTATION

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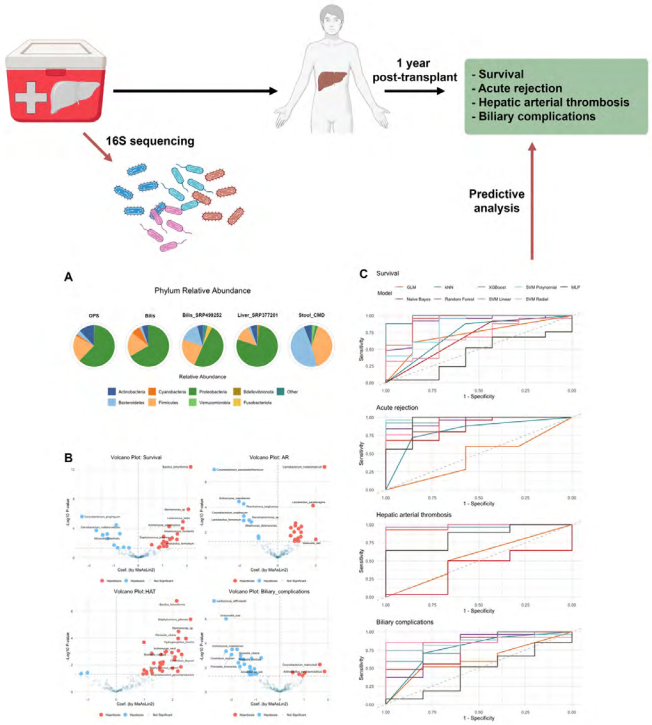
Background: Gut microbial dysbiosis has been linked to various diseases, including transplant rejection. However, the liver harbors a unique microbiota, distinct yet interdependent with the gut, which influences hepatic immunity. This suggests potential implications for liver transplantation outcomes that conventional immunosuppression does not address. This study examined the microbiome present in organ preservation solution (OPS) from donated livers after static cold ischemic storage, focusing on its impact on early transplant outcomes and predictive modeling of clinical variables.

Methods: **OPS** samples underwent amplicon sequencing, with adjustments for batch effects. Microbial profiles were compared to matched bile, published liver metagenomics, and stool datasets. Microbial diversity was assessed via the Shannon index across four clinical outcomes: patient survival, acute rejection (AR), hepatic arterial thrombosis (HAT), and biliary complications. Differentially abundant taxa were identified using MaAsLin2. Data mining in PubMed identified genes linked to these taxa, followed by gene set enrichment analyses to explore implicated pathways, focusing on inflammation. Predictive models were developed using machine learning algorithms, incorporating microbial data. Synthetic minority oversampling (SMOTE) addressed class imbalances, and performance was evaluated on test datasets.

Results: OPS microbiome resembled bile and liver microbiota more than stool (Fig.A). While microbial diversity did not significantly differ across clinical outcomes, several taxa showed differential abundance in relation to these variables(Fig.B). Data mining and gene enrichment linked these taxa to inflammatory pathways relevant to post-transplant complications. Predictive models achieved high AUCs: 0.99 for AR, 0.94 for survival, 0.98 for HAT, and 0.88 for biliary complications (Fig.C).

Conclusions: Metagenomic analysis of the post-ischemic OPS emerges as a reliable source for identifying distinct taxa linked to clinical outcomes and their association with inflammatory pathways. Predictive models based on microbial data provide accurate predictions of transplant outcomes, demonstrating the biological and clinical relevance of the donor liver microbiome.



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BOS60_02_3 LARGEST SINGLE CENTRE SERIES OF HYPOTHERMIC OXYGENATED PERFUSION (HOPE) IN LIVER TRANSPLANTATION

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Background: The use of Hypothermic Oxygenated Perfusion (HOPE) has emerged in recent years as a promising tool to improve clinical outcomes and organ utilisation in liver transplantion. The aim of this study is to compare the outcomes of HOPE perfused grafts to a historical cohort of static cold storage grafts.

Methods: Data was collected prospectively for all HOPE perfused livers from October 2020 to January 2025. The study cohort includes mainly DCD but also DBD donors and two devices were used: VitaSmart™ from Bridge to Life until October 2024 (single portal vein perfusion) and Liver Assist™ from XVIVO from then until currently (dual portal vein and hepatic artery perfusion). VitaSmart™ DCD HOPE perfused liver results were compared with a historical cohort of DCD SCS (static cold storage) in our centre to assess postoperative complications, biliary complications, early allograft dysfunction (EAD), acute kidney injury / dialysis requirement and long-term follow-up. NMP (normothermic machine perfusion), livers perfused with other technologies or livers perfused and not transplanted were excluded.

Results: A total of 92 livers (DCD n=88; DBD n=4) have been perfused using Hypothermic Oxygenated Perfusion (HOPE) in our centre. 82 livers were perfused using VitaSmart™ and 10 livers with the Liver Assist™. When compared with the DCD SCS cohort (80 livers), HOPE DCD had a lower rate of NAS (non-anastomotic strictures) n=4 (5.1%) in HOPE group vs n=20 (25%) in SCS group (p = 0.001). No significant difference was seen for mortality at 90 days/1 year or for the rate of complications greater than Clavien Dindo IIIA. An unexpected increased risk of AKI was seen in the HOPE group n=48 (60.85%) vs n=78 (47.3%) in SCS (p = 0.003). This could be explained by the expansion of recipient pool suitable for DCD which meant sicker patients receiving a DCD grafts with higher risk for AKI.

Conclusions: HOPE has allowed us to increase the use of DCD livers and we have demonstrated a significant reduction in rates of ischaemic cholangiopathy. The use of HOPE may help to increase organ utilisation by allowing to safely transplant more marginal and extended criteria organs in addition to facilitating improved liver transplantation logistics. This is one of the largest single centre experience of HOPE in liver transplantation reported in the literature.

BOS60_02_4 INTRACARDIAC THROMBOSIS AND ITS MANAGEMENT DURING LIVER TRANSPLANTATION: INTERNATIONAL, MULTI-CENTER, CASE-CONTROL STUDY

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Background: Intracardiac thrombosis (ICT) is an uncommon yet critical complication during liver transplantation (LT), with limited evidence on its risk factors, clinical management, and patient outcomes. This study aims to identify predictors of ICT, evaluate its intraoperative outcomes, and propose a novel classification and management strategy.

Methods: A retrospective, multicenter, international case-control study was conducted on liver transplant recipients from seven institutions between January 2005 and December 2023. ICT cases were diagnosed using transesophageal echocardiography (TEE) or autopsy and matched with controls by transplantation year, recipient age, BMI, MELD score, and transplant status

Results: Of 11,077 liver transplant recipients, 133 (1.2%) developed ICT, primarily after reperfusion (58%). ICT cases exhibited elevated preoperative INR (p=0.001) and fibrinogen levels (p=0.014) and required more intraoperative blood products (p<0.001). Post-reperfusion syndrome (p<0.001), disseminated intravascular coagulation (p<0.001), and primary graft failure (p=0.002) were more frequent in the ICT group. Continuous veno-venous hemofiltration (CVVH) during surgery (OR 8.20; p=0.004) and elevated INR (OR 3.96; p=0.006) were associated with ICT. ICT significantly increased cardiac arrest (53.4% vs. 1.55%; p<0.001) and intraoperative mortality (24.8% vs. 0.75%; p<0.001). Left-heart thrombus location was a major predictor of mortality (OR 20.7; p<0.001). ICT grades 2 and 3 were strongly linked to intraoperative cardiac arrest (p<0.05), and delayed TEE use correlated with higher intraoperative death risk (OR 6.27; p=0.014). ICT cases had higher 90-day (43% vs. 4.5%) and 1-year (46% vs. 10.5%) mortality compared to controls.

Conclusions: ICT during LT is a rare but severe complication characterized by hemodynamic instability, significant intraoperative mortality, and poor survival. Preoperative coagulation status, intraoperative interventions, and CVVH contribute to ICT risk. Early TEE utilization facilitates timely diagnosis and intervention, improving outcomes. A novel ICT classification based on thrombus location and hemodynamic instability provides a systematic framework for management and risk stratification, potentially reducing mortality.

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BOS60_02_5 HYPOTHERMIC OXYGENATED PERFUSION FOR HIGH-RISK DONOR-RECIPIENT MATCHING IN LIVER TRANSPLANTATION

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Background: End-ischemic hypothermic oxygenated perfusion (HOPE) of liver grafts from extended criteria donors (ECD) has been shown to improve post-transplant outcomes. However, data on the benefit of HOPE in the context of high-risk matching of an ECD graft with a high acuity recipient are currently lacking.

Methods: This is a case-control study conducted in two centers from 2017 to 2024, evaluating liver transplantation (LT) in a group of high acuity recipients matched to an ECD graft with or without HOPE. ECD grafts were defined by the presence of at least 1 criteria among the following; age >65 years, BMI >30, steatosis ≥20%, ICU stay >7 days, AST >150, ALT >170. High acuity recipients were defined as recipients with a MELD score >25. The aim of the study was to analyze the impact of adding a period of end-ischemic HOPE on post-LT morbidity (de novo dialysis, primary non-function, biliary complication, venous thrombosis, relaparotomies, retransplantation and early graft dysfunction EAD) and mortality.

Results: Seventy-five recipients were included in the study with 39 (52%) in the HOPE group and 36 (48%) in the control group. Donor characteristics were not significantly different between the two groups. In both groups, >50% of recipients had a MELD score >30 and were within Acute-On-Chronic Liver Failure (ACLF) criteria. A total of 13 (33%) and 10 (28%) recipients were on pre-LT dialysis in the HOPE and the control group, respectively (p=0.6). After LT, the HOPE group presented with a lower rate of Early Allograft Dysfunction (10% vs 31%, p=0.03), of post-LT de novo dialysis (10% vs 33%, p=0.01) and early relaparotomies (23% vs 44%, p= 0.05). One-year graft and recipient survival rates were 85.3% vs 72.2% (p=0.30) and 87.9% vs 72.2% (p=0.20) in the HOPE and control group respectively.

Conclusions: The use of HOPE in high-risk donor-recipient matchings reduces early post-LT morbidity and shows a trend towards improved graft and recipient survival. Switching the focus from grafts to donor-recipient matching opens up novel clinical perspectives for machine perfusion strategies.

Table 1 :

	End ischemic HOPE (n=39)	Static Cold Storage (n=36)	p-value
Recepient general characteristics			
Sex			
Male	28 (72%)	24 (67%)	0.60
Age (year)	56 (49-61)	56 (47-60)	0.80
BMI (kg/m2)	27 (23-31)	25 (22-30)	0.40
Previous abdominal surgery	11 (28%)	12 (33%)	0.60
Portal thrombosis	2 (5.1%)	8 (22%)	**0.04**
In ICU at time of LT	20 (51%)	23 (64%)	0.30
Intubated	*6 (16%)*	*NA*	
Pre-LT dialysis	13 (33%)	10 (28%)	0.60
At home at time of LT	14 (36%)	5 (14%)	**0.03**
ACLF	20 (51%)	19 (53%)	0.90
1	*2 (5.1%)*	*1 (27.8%)*	
2	*10 (25.6%)*	*7 (19.4%)*	
3	*8 (20.5%)*	*7 (19.4%)*	
Missing data	*0*	*4 (11.1%)*	
Indication for LT			NS
Alcoholic cirrhosis	29 (74%)	20 (56%)	
Metabolic cirrhosis	2 (5.1%)	6 (17%)	
Alcoholic + Metabolic cirrhosis	2 (5.1%)	2 (5.6%)	
Acute liver failure	Excluded	Excluded	
Viral hepatitis (VHB/VHC)	3 (7.7%)	9 (24.6%)	
Malignancy	7 (18%)	4 (11%)	
Other	2 (5.1%)	3 (8.3%)	
MELD Score	31 (27.5-36)	34.5 (29.8-38.3)	0.08
MELD >30	*20 (51%)*	*25 (69%)*	*0.11*
Donor general characteristics			
Age (year)	71 (62-75)	72 (68-75)	0.70
BMI (kg/m2)	25.3 (23-29)	26.7 (23.4-30.8)	0.60
Missing data	*1*	*0*	
ICU stay duration (days)	2 (1-4.5)	3 (1.8-4)	0.80
Donor after brain death	39 (100%)	36 (100%)	
Graft general characteristics			
Static cold storage	348 (280-398)	387 (339-473)	**0.03**
Missing data	*2 (5.1%)*	*18 (34%)*	
HOPE treatment	39 (100%)		
Perfusion duration	180 (101-208)		
Warm ischemia	50 (35-57)	*Missing data*	
Per operative data			
Operative time (min)	415 (355-475)	456 (406-501)	**0.03**
Per opertive dialysis	10 (26%)	24 (67%)	**< 0.001**
Blood transfusion	5 (3.5-7.5)	5 (3.75-8)	0.80
Post operative data			
Post operative dialysis	11 (29%)	19 (53%)	**0.04**
De novo dialysis	*4 (10%)*	*12 (33%)*	***0.01***
Missing data	*1 (2.6%)*	*0*	
PNF	1 (2.6%)	0	> 0.90
Biliary complication	11 (28%)	8 (22%)	0.60
Portal thrombosis	2 (5.1%)	2 (5.6%)	> 0.90
Hepatic vein thrombosis	0	1 (2.8%)	0.50
Acute rejection	8 (21%)	8 (22%)	0.90
Post operative ascitis	9 (24%)	*Missing data*	
Surgical reintervention within 90 days	9 (23%)	16 (44%)	**0.050**
Retransplantation	1 (2.6%)	0	> 0.90
EAD	4 (10%)	11 (31%)	**0.03**
Survie patient globale	84.6%	69.4%	
Survie patient 1 an	87.9%	72.2%	
Survie greffon globale	82%	69.4%	
Survie greffon 1 an	85.3%	72.2%	

Note: Data are expressed as n (%) or median (IQR).

Abbreviations : HOPE, hypothermic oxygenated perfusion; BMI, body mass index; MELD, model of end stage liver disease; ICU, intensive care unit; LT, liver transplantation; ACLF, Acute on chronic liver failure; PNF, primary non function; GRAE, graft related adverse event; IQR, interquartile range

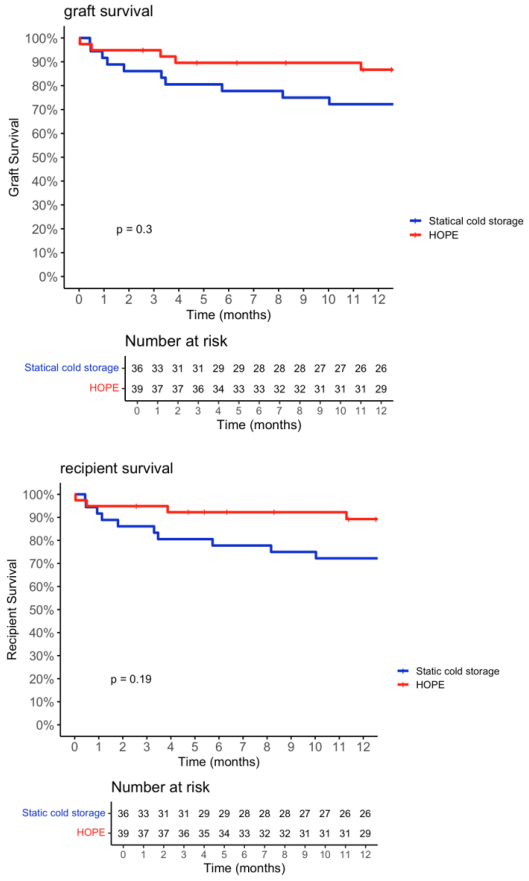

Figure 1. One-year graft and patient survival by HOPE Perfusion

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BOS60_02_6 OUTCOMES OF PORTAL VEIN THROMBOSIS IN LIVING DONOR LIVER TRANSPLANTATION: AN ANALYSIS OF 155 CONSECUTIVE PATIENTS

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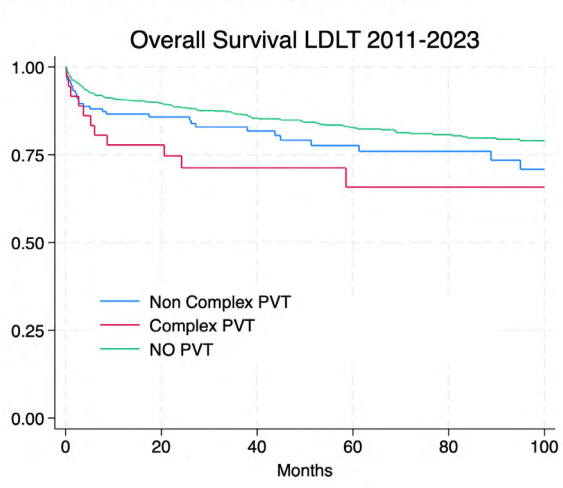
Background: The Banghui classification defines Complex Portal Vein Thrombosis (CPVT) as grade 4 Yerdel or grades 3–4 Jamieson and Charco. CPVT poses a significant challenge in living donor LT (LDLT) due to the reported higher rate of complications and lower survival. This study evaluates the impact of CPVT on perioperative and long-term outcomes in LDLT.

Methods: An analysis of a prospective database of 1132 adult LDLT performed in a single centre from 2011 to 2023 was evaluated. All patients with intraoperatively detected PVT were included. Based on preoperative contrast-enhanced radiology findings PVT were classified as Non-Complex (NCPVT) or CPVT. Perioperative and Long-Term outcomes were compared between patients with NCPVT and CPVT.

Results: Of the reviewed series, 155 (14%) had intraoperative PVT. Imaging included CT in 116 (68.6%) and MRI in 53 (31.4%), with a median interval of 50 days (IQR 20–107) before LDLT. PVT were classified as Non Complex in 119 (77%) and Complex in 36 (24%) cases. A complete PVT was found intraoperatively in 24 patients (15%) despite negative preoperative imaging. Management included thrombectomy with end-to-end anastomosis (TEEA) (122, 74%), jumping graft (10, 6%), portosystemic shunt anastomosis (5, 3%). It is noteworthy that TEEA was performed in 24/36 Complex PVT cases (67%). Regarding postoperative outcomes, no differences were observed in rates of major complications (NCPVT: 36 (32%) vs CPVT: 13(37%), p=0.630), CCI (NCPVT: 20.9 (IQR 0 - 39.7) vs CPVT: 26.2 (IQR 0-39.7), p=0.329). The number of surgical interventions for PV complication after LDLT did not differ (NCPVT: 6 (5%) vs CPVT: 2 (5.5%), p=0.903. Survival at 1, 3, and 5 years was not different in the CPVT group (78%, 72%, 66%) compared to NCPVT (87%, 84%, 79%; p=0.23).

Conclusions: Despite being technically challenging, LDLT can be performed safely also in patients with CPVT. Extensive thrombectomy can be performed without significantly impaired post-operative results.

Figure 1. Overall Survival Results Stratified per PVT Complexity



BOS60_02_7 PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION: A STRUCTURED APPROACH AIMED TO REDUCE BILIARY COMPLICATIONS

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Background: Biliary complications (BC) can compromise donor and recipient outcome in pediatric living donor liver transplantation (pLDLT).

Methods: Medical records of 503 consecutive pLDLTs performed from 1993 to 2022 were reviewed focusing on the donor/recipient biliary approach and outcome. Pre-operative magnetic resonance imaging (MRI) and intraoperative cholangiography (IC) results were compared with surgical findings after donors' hilar plate transection, with anastomoses number at graft implantation and correlated with recipient's BC.

Results: Donors MRI and IC were strongly correlated (87.6%, p<0.001). Number of bile ducts requiring anastomoses corresponded mostly to imaging prediction (81.8%, p<0.001). Complications occurred in 96 donors (19.1%) (none grade IV/V of Dindo-Clavien Classification); which 12 were biliary (2.3%) (all treated without surgical reintervention). One, 2, or 3 biliary anastomoses were performed on 390 (77.5%), 107 (21.3%), and 6 (1.2%) recipients respectively. BC occurred in 114 recipients (136 events) (Table 1). Rate was comparable among recipients with 1 or 2 anastomoses (107/390 (27.4%) vs. 25/107 (23.4%) (p=0.40)). It tripled among recipients with 3 anastomoses (4/6, 66,7%) (p=0.06). This discrepancy was reinforced when comparing anastomotic BCs (p=0.04) (Table 2).

Conclusions: A standardized approach combining donor MRI/IC well correlates with number of performed bile ducts anastomoses; improving donor and recipient outcomes. Recipient biliary morbidity did not increase with a 2nd biliary anastomose, suggesting that risky maneuvers during graft procurement to reduce biliary anastomoses number to perform are not always justified.

	Strictures		Cholangitis		Bile leak		Biloma		Total	
	N	%	N	%	N	%	N	%	N	%
# anastomoses										
1 (Total=390)	52	13.3	32	8.2	18	4.6	5	1.3	107	27.4
2 (Total=107)	13	12.2	9	8.4	2	1.9	1	0.9	25	23.4
3 (Total=6)	3	50.0	1	16.7	0	0.0	0	0.0	4	66.7
Total (=503)	68	13.5	42	8.4	20	4.0	6	1.2	136	27.4

Table 1. Recipient biliary complications in function of number of performed biliary anastomoses.

	Strictures		Bile leak		Total	
	N	%	N	%	N	%
# anastomoses						
1 (Total=390)	49	12.6	9	2.3	58	14.9
2 (Total=107)	13	12.2	0	0.0	13	12.2
3 (Total=6)	3	50.0	0	0.0	3	50.0
Total (=503)	65	12.9	9	1.8	74	14.7

Table 2. Recipient anastomotic biliary complications in function of number of performed biliary anastomoses.

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BOS60_02_8 SIMULTANEOUS VERSUS SEQUENTIAL REVASCULARIZATION OF THE LIVER GRAFT IN SPLIT LIVER TRANSPLANTATION

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Background: The technical sequence of graft revascularization during liver transplantation (LT) isn't standardized in split LT (SLT). Simultaneous declamping technique prolongs portal ischemia but may allow arterial anastomosis (AA) to be performed under better conditions compared to the sequential revascularization. This study aimed to compare the postoperative outcomes of patients who underwent SLT using either the simultaneous or sequential technique.

Methods: A retrospective cohort of patients undergoing SLT in one tertiary center between 2000 and 2023 was performed. Patients were divided into two groups: sequential revascularization (seq), where AA was performed after vena cava and portal reperfusion, versus simultaneous (sim), where AA was performed before veinous reperfusion. Patients' characteristics at baseline, SLT procedure, blood transfusion requirement, and postoperative outcomes were retrospectively collected and analyzed.

Results: From May 2000 to April 2023, 126 patients underwent SLT, including 35 Sim (27.8%) and 91 Seq (72.2%). Patient's outcomes were comparable at baseline. Operative time was significantly shorter in sim group (444 vs. 351 minutes, p < 0.001). Cold ischemia time was longer in sim group (675 vs. 708 minutes, p=0.008). No significant difference was observed in the blood transfusion rate (71.4% in sim vs. 62.3% in seq group, p=0.389). The arterial thrombosis rate did not differ significantly between sim and seq groups (2.9% vs. 12.2%, p=0.176) as well as the incidence of biliary stenosis (22.9% vs. 18.0%, p=0.536). No difference was observed for retransplantation rate (p=0.178), severe complication (p=0.464), and post SLT hospital stay (p=0.807). No difference was observed between the two groups in overall survival (p=0.128, graft survival (p=0.106) and ABC free survival (p=0.287).

Conclusions: Simultaneous revascularization is a feasible approach in SLT, with shorter duration of operation compared to sequential revascularization. No significant difference was observed in terms of post-operative outcomes, OS or ABC free survival between the two groups.

BOS60_02_9 TRANSITION FROM OPEN TO ROBOTIC SURGERY IN LIVING DONOR HEPATECTOMY: PRELIMINARY EXPERIENCE FROM A WESTERN CENTER

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Background: Open and laparoscopic living donor hepatectomies (LDH) are now well-standardized procedures that respect the necessary balance between donor safety, graft quality and recipient outcomes. Robotic-assisted hepato-pancreatobiliary surgery is rapidly expanding and robotic LDH now routinely performed in several centers worldwide. In this context, data evaluating the transition from an open to a robotic LDH program will further contribute to standardize this challenging procedure.

Methods: This retrospective, single-center study evaluates the transition from an open to a robotic LDH program for pediatric recipients in a high-volume tertiary HPB center in France. We included all living donor procedures performed at our institution from January 2018 to December 2024. This is an IDEAL Stage 2a study focusing on feasibility, logistics, and safety for both the donors and recipients. Donor complications were assessed using the Clavien-Dindo Classification (CD).

Results: The transition from open LDH to robotic LDH took place in 2023, six months after the initiation of our robotic HPB program and performance of > 40 robotic hepatectomies. Of note, our center had an extensive experience in laparoscopic liver surgery prior to the robotic program. We performed 21 LDHs during the study period with 16 (76 %) open LDHs and 5 (24%) robotic LDHs (table 1). The majority of the LDHs were G23 (n=19, 90%) and one G1234MHV was performed in the open LDH group and one G234 in the robotic LDH group. Operative time was longer (365 min vs 243 min, p=0.014) but intraoperative blood loss was significantly reduced (50 ml vs 125 ml p=0.011) in robotic LDH. Less than 50% of donors had a CD graded complication, without a significant difference. Overall, one donor complication graded CD≥III occurred (incisional hernia in the open LDH group). Graft survival in pediatric recipients was 100% at 6 months in both groups.

Conclusions: Transition from open LDH to robotic LDH allows respecting donor safety and graft quality standards. Although there is a learning curve and logistical adjustments, the background of a high-volume HPB center with experience in laparoscopic liver surgery facilitates standardization of robotic LDH.

		Open LDH (n =16)	Robotic LDH (n=5)	
Preoperative Donor characteristics				
Age, y (IQR)		36,5 (32;39)	32 (31;33)	ns
BMI, kg/m2 (IQR)		24,5 (20,75; 26,25)	22 (22; 23)	ns
Graft Type:				ns
G23, n (%)		15 (93)	4 (80)	
G234, n (%)		0 (0)	1 (20)	
G1234MHV, n (%)		1 (6)	0 (0)	
Operative time, min (IQR)		243 (223; 300)	365 (356; 380)	p = 0.014
Graft weight, g (IQR)		300 (262, 342)	270 (250, 300)	ns
Blood loss, mL (IQR)		125 (95; 212)	50 (0; 50)	p = 0.0106
Length of hospital stay, d (IQR)		7 (6,7; 7,2)	7 (7; 9)	ns
Post-operative complications according to Clavien-Dindo				
Patients with at least 1 complication, n (%)		5 (30)	2 (40)	ns
Early complications (<30d)	Cut surface collection, n	1 (CD II)	0	
	Infection (urinary, pulmonary), n	2 (CD II)	1 (CD II)	
	Urinary retention, n	0	1 (CD I)	
	Pain despite non-opioid analgesics, n	1 (CD I)	1 (CD I)	
Late complications (>30d)	Incisional hernia, n	1 (CD IIIb)	0	
Clavien Dindo I – II, n (%)		5	2	
Clavien Dindo >II, n (%)		1	0	
Readmission, n (%)		2 (12)	1 (20)	ns
Mortality, n (%)		0 (0)	0 (0)	ns

Table 1. Donor characteristics and post-operative outcomes in open and robotic LDH

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BOS60_02_10 EX-SITU SPLIT LIVER ON MACHINE PERFUSION IN THE COUNTRY OF IN-SITU SPLIT LIVER: A PILOT EXPERIENCE

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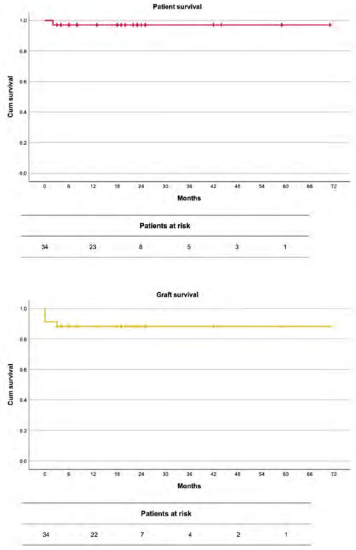
Background: Italy has a unique tradition of in-situ split liver transplantation (SLT), with reported 1-year patient and graft survival of up to 96% and 91% for conventional SLT, and of 73% and 63% for full left/full right (FL/FR) SLT. In countries where liver splitting is regularly performed ex-situ, SLT was shown to benefit from liver splitting during hypothermic oxygenated perfusion (HOPE-split). We analyzed the pilot Italian experience of SLT after HOPE-split, investigating its feasibility and safety, and comparing the outcomes of SLT after HOPE-split with those of in-situ SLT reported by the literature.

Methods: Multicenter, retrospective, cohort study. Primary feasibility endpoint: rate of completion of HOPE-split. Primary safety endpoint: mean number of graft-related adverse events (primary nonfunction, vascular or biliary complications, relaparotomy) per patient during the first post-SLT month.

Results: From December 2018 to September 2024, 18 HOPE-split procedures (16 splits, 2 reductions) were performed, and 34 patients (17 children, 17 adults) were transplanted at 6 institutions (100% completion rate).The indications for HOPE-split were: FL/FR SLT (10/18 cases, 56%), donor hemodynamic instability (4/18, 22%), complex logistics (3/18, 17%), extended criteria donation (1/18, 6%). The median (interquartile range, IQR) HOPE duration, cold ischemic time (excluding HOPE) and total preservation time (including HOPE) were: 238 (160-314) minutes, 421 (353-468) minutes, 651 (552-760) minutes. The HOPE-split procedures provided 22/34 FL/FL grafts (65%) and 12/34 left lateral/extended right grafts (35%); 4/16 paired grafts were shared between different centers (25%). The mean number (standard deviation) of graft-related adverse events per patient during the first post-SLT month was 0.24 (0.5) With a median (IQR) follow-up of 19 (8-23) months, 1-year patient and graft survival was: 97%, 88% (figure).

Conclusions: This pilot Italian experience suggests that conventional and FL/FR SLT after HOPE-split is feasible, safe, and allows for graft sharing between distant centers; moreover, its outcomes may be similar to those of in-situ SLT. A national study comparing matched recipients of SLT after HOPE-split versus in-situ SLT is ongoing.



BOS60_03_1 IMPACT OF CYTOMEGALOVIRUS VIREMIA CLEARANCE ON POST-TRANSPLANT MORTALITY: SOLSTICE POST-HOC ANALYSIS

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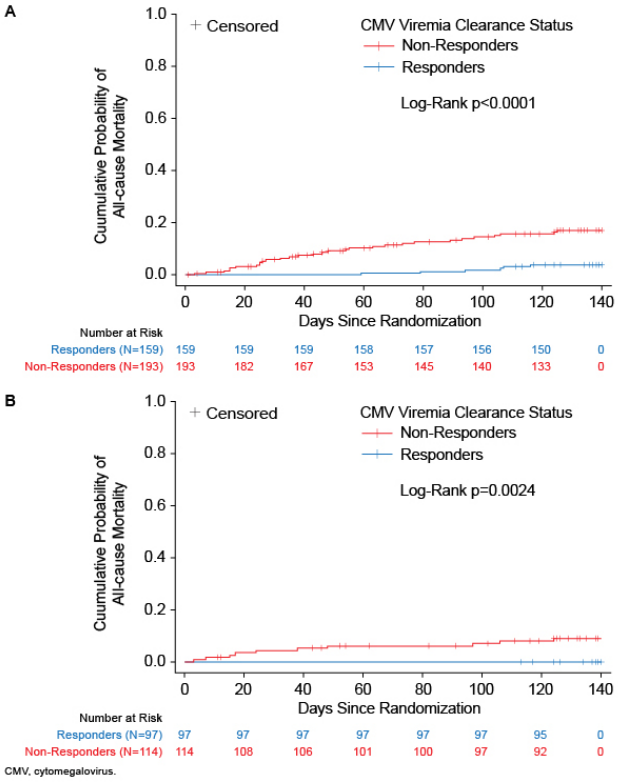
Background: The Phase 3 SOLSTICE study (NCT02931539) showed superiority of maribavir over investigator-assigned therapy (IAT; valganciclovir/ganciclovir, foscarnet, or cidofovir) for cytomegalovirus (CMV) clearance in transplant recipients with refractory CMV infection. We performed a post hoc analysis of SOLSTICE to examine the potential impact of CMV viremia clearance on mortality.

Methods: The primary endpoint of SOLSTICE was confirmed CMV viremia clearance at Week 8. In this analysis, all-cause mortality was assessed up to 20 weeks using the Kaplan–Meier method with log-rank test. Cumulative probability of all-cause mortality was plotted in responders and non-responders. CMV viremia clearance was defined as plasma CMV DNA level <137 IU/mL (lower limit of quantification) in two consecutive post-baseline samples, separated by ≥5 days, by end of Week 8. Non-responders did not achieve CMV clearance by end of Week 8 (including missing virologic data), discontinued the study, or received maribavir rescue or alternative treatment before the end of Week 8. Mortality was assessed for the overall study population (patients who received hematopoietic cell transplant or solid-organ transplant [SOT] and were treated with maribavir or IAT) and for the HCT and SOT populations separately. Here we present end-of-study (20-week) data for the overall and SOT populations.

Results: In total, 352 patients were randomized to maribavir or IAT in SOLSTICE (responders, n=159; non-responders, n=193). Among responders and non-responders, most patients were male (64.2% and 57.5%, respectively), with a median (range) age of 57 (19–77) and 55 (19–79) years, respectively. Of 211 SOT recipients, 97 were responders and 114 were non-responders. During the 20-week study, responders had a significantly lower probability of all-cause mortality than non-responders in the overall population (p<0.0001, **Fig A**) and in the subset of SOT recipients (p=0.0024) (**Fig B**).

Conclusions: In SOLSTICE, patients with CMV clearance at week 8 had a significantly lower probability of 20-week all-cause mortality than those who did not. Results were similar in the overall trial population and in patients who had undergone SOT. These data highlight the importance of sustained CMV clearance in transplant recipients who develop refractory CMV infection.

Figure. Cumulative probability of all-cause mortality by Week 8 CMV clearance status (cut off 20 weeks after randomization), among all patients **(A)** and among those who underwent SOT **(B)**



CMV, cytomegalovirus.

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BOS60_03_2 MARIBAVIR USE IN REAL-WORLD FOR REFRACTORY CMV INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Maribavir has demonstrated promising efficacy in treating refractory cytomegalovirus (CMV) infections among solid organ transplant recipients; however, the factors influencing favorable outcomes remain uncertain.

Methods: We conducted a retrospective cohort study involving 88 kidney transplant recipients (KTRs) from 20 transplantation centers, all of whom had refractory CMV infections treated with maribavir (68 with ganciclovir resistance mutations and 20 without). The endpoints included CMV clearance at week 8 post-maribavir, CMV clearance within 16 weeks post-maribavir without recurrence, and the emergence of maribavir resistance mutations.

Results: CMV clearance at week 8 was achieved in 33 KTRs (37.5%). Among the 51 KTRs (57.9%) who achieved CMV clearance within 16 weeks, only 37 (42%) did not develop CMV recurrence. Notably, CMV DNA levels <10,000 IU/mL at the time of maribavir initiation (HR 3.535, 95% CI 1.356-9.671) and symptomatic CMV infection (HR 0.287, 95% CI 0.10−0.767) were identified as independent factors associated to CMV clearance within 16 weeks without recurrence. Maribavir resistance mutations were observed in 17 KTRs (19.3%), primarily in those who failed to achieve CMV clearance within 16 weeks (38.9%) and in those who experienced CMV recurrence (21.4%).

Conclusions: Refractory CMV infections characterized by high levels of CMV DNA or symptomatic presentations pose greater treatment challenges with maribavir. These findings may inform more targeted use of maribavir and support the development of new strategies for patients at risk of poor outcomes.

BOS60_03_3 VALGANCICLOVIR DOSING FOR CMV PROPHYLAXIS IN RENAL TRANSPLANTATION AND ITS IMPACT ON CLINICAL OUTCOMES

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Background: Cytomegalovirus (CMV) is a common opportunistic pathogen following solid organ transplantation. CMV increases the risk of graft rejection and mortality and can be prevented by valganciclovir prophylaxis. Valganciclovir dosing is particularly challenging after kidney transplantation, where renal function can change rapidly in the weeks after surgery. This study at a large London transplant center explored the accuracy of valganciclovir dosing following kidney transplantation and its associations with clinical outcomes.

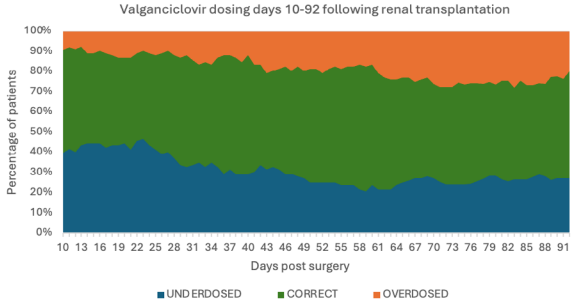
Methods: Electronic records between April 2017 and June 2019 were searched for patients receiving a kidney transplant and starting valganciclovir CMV prophylaxis. The primary outcome was the difference between prescribed and ideal valganciclovir dose (calculated according to creatinine clearance) on days 10-92 after surgery. Secondary outcomes included development of CMV viraemia, leukopenia and reduction in mycophenolate mofetil (MMF) dose.

Results: 92 patients on valganciclovir prophylaxis were included in analysis. Table 1 displays demographics and adverse outcomes. The indication for valganciclovir prophylaxis was use of anti-thymocyte globulin (ATG) induction immunosuppression regardless of CMV status in 63 patients (68.5%), or donation from a CMV sero-positive donor into a sero-negative recipient receiving anti-IL2 induction in 29 patients (31.5%). Patients spent an average of 31% of the study period underdosed on valganciclovir, 51% correctly dosed and 18% overdosed (Graph 1). Patients who developed CMV viraemia spent more time underdosed than those without viraemia (52.7% vs 27.5% respectively, (t(90) = -2.73, p < 0.01)), whilst those with MMF dose reductions spent more time overdosed compared to those on full MMF dose (29.6% vs 12.7% respectively, (t(44) = -2.65, p 0.01).

Conclusions: On average, patients were correctly dosed on valganciclovir for only 51% of the study period. Incorrect dosing associated with adverse outcomes including CMV viraemia and reduction in immunosuppressive medication. This highlights the importance of close monitoring of valganciclovir dosing. Embedding clinical pharmacists within transplant clinics, or making use of electronic dose calculators, may improve clinical practice.

Table 1: Demographics & outcomes

Variable	Characteristic	N (=92)	%
Age	10-24	5	5.4
	25-39	19	20.7
	40-54	39	42.4
	55-69	27	29.3
	70+	2	2.2
Sex	Male	58	63
	Female	34	37
Transplant type	DBD	51	55.4
	DCD	28	30.4
	LD (U)	4	4.3
	LD (R)	9	9.8
Induction agent	ATG	63	68.5
	IL-2	29	31.5
CMV status (donor / recipient)	+ / +	22	23.9
	+ / -	38	41.3
	- /+	16	17.4
	- / -	0	0
	Unknown/incomplete	16	17.4
Adverse outcomes	*Any adverse outcome*	55	59.8
	CMV viraemia	12	13.0
	MMF dose reduced	30	32.6
	WCC dropped <4.0	44	47.8
	Transplant rejection	3	3.3



Graph 1:

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BOS60_03_4 IMMUNOGUIDED PROPHYLAXIS FOR THE PREVENTION OF CMV DISEASE IN LOW-RISK LUNG TRANSPLANT RECIPIENTS

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Background: The standard prophylaxis treatment for CMV disease in CMV-seropositive lung transplant recipients is associated with adverse events and risk of resistance. The current study aims to demonstrate that immunoguided prophylaxis is effective and safe in seropositive lung transplant recipients.

Methods: Phase III, multicentre, randomized, open-label, noninferiority clinical trial conducted in adult lung transplant recipients. Patients were randomized (1:1) to: (1) immunoguided prophylaxis (IP), consisting of 3 months of universal prophylaxis followed by CMV-specific cell-mediated immunity-guided discontinuation, or (2) standard prophylaxis (SP), consisting of 6 months of prophylaxis followed by pre-emptive therapy, both for a total of 12 months. The primary and secondary efficacy endpoints were CMV disease and asymptomatic CMV replication at month 18. The primary and secondary safety endpoints were the incidence of neutropenia (neutrophil count < 1500 cells/μL), incidence of rejection, and number of days of valganciclovir prophylaxis. A post-hoc composite efficacy/safety endpoint (CMV disease plus neutropenia) was included. This trial was registered in EudraCT (2018-003300-39) and ClinicalTrials.gov (NCT03699254).

Results: A total of 150 patients were randomized. Incidence of CMV disease at month 18 did not differ among groups (18.7% vs. 16%; risk difference [RD] -0.03 [95% CI -0.15% to 0.06%]; *P*=0.62). The proportion of patients who developed CMV disease at ≤ 180 days after transplant was higher in the IP group compared with the SP group (8% vs. 0%; RD -0.08 [95% CI -0.14 to -0.02; *P*=0.009]). Asymptomatic CMV replication was reduced in the IP group (4% vs. 16%; adjusted RD 0.12 [95% CI 0.03-0.21; *P*=0.009]). A total of 30 patients (40%) in the IP group did not require prophylaxis from month 4 to 12. No significant difference was observed in the proportion of patients with neutropenia during months 4 to 7 (14.7% vs. 25.3%; RD 0.11 [95% CI -0.02 to 0.23]; *P*=0.09) or rejection (33.3% [25 patients] vs. 30.7% [23 patients]; RD -0.03 [95% CI -0.18 to 0.12; *P*=0.690]). The median days of valganciclovir was lower in the IP group than in the SP group (137 vs. 198; *P* < 0.001).

Conclusions: Immunoguided prophylaxis was noninferior to the standard of care in preventing CMV disease in lung transplant recipients.

BOS60_03_5 EFFECTOR-MEMORY T GD LYMPHOCYTES PREDICT CMV DISEASE AFTER THE WITHDRAWAL OF PROPHYLAXIS IN KTR

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Background: Evaluation of CMV-specific cell-mediated immunity (CMI) has enhanced strategies for preventing post-transplant CMV disease. This study aims to analyze the occurrence of CMV disease in relation to the absolute count of TEMRA effector/memory γδ T cells at the end of universal prophylaxis in kidney transplant recipients (KTR).

Methods: We retrospectively included 262 R+ patients and 82 D+R- KTR who received antiviral prophylaxis and underwent quantification of TEMRA γδ T cells at the end of prophylaxis. The primary endpoint was the incidence of post-prophylaxis CMV disease within the first two years following transplantation.

Results: A total of 43 out of 344 (12.5%) patients developed post-prophylaxis CMV disease after withdrawal of prophylaxis. Using a ROC curve, we determined a threshold of 4.65/mm³ for the absolute count of TEMRA γδ T lymphocytes, where higher count was associated with a lower incidence of CMV disease. However, in the overall study population (D+R- and R+), multivariate analysis revealed no significant association between an absolute count of TEMRA γδ T lymphocytes over 4.65/mm³ and CMV disease. In contrast, in the R+ population, the positive predictive value (indicating protection against CMV disease in patients with a TEMRA γδ T lymphocyte count > 4.65/mm³) was 97.7%, while the negative predictive value was only 10.7%. The multivariate analysis showed that a TEMRA γδ T lymphocyte count > 4.65/mm³ was independently associated with post-prophylaxis CMV disease-free survival [HR: 0.2695 (95% CI: 0.08554 – 0.8493), p=0.0252].

Conclusions: Incorporating the easy evaluation of TEMRA γδ T lymphocyte counts into the arsenal of CMV cell-mediated immunity assays could enhance immune-guided CMV prevention in R+ patients.

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BOS60_03_6 LEVERAGING FRENCH COMPASSIONATE PROGRAM DATA TO DESCRIBE MARIBAVIR USE IN REFRACTORY CYTOMEGALOVIRUS INFECTION

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Background: Maribavir is indicated for treating CMV infection/disease refractory to prior therapies in transplanted patients. The treatment was first used in France outside the pivotal trial through a compassionate use program (CUP) initiated in 2021. In addition to the maribavir use/safety data reported to French authorities, and as part of a research protocol, further analyses of the CUP database can allow for generating additional evidence. This study described the overall maribavir effectiveness and the resistance profile during the CUP follow-up.

Methods: Retrospective longitudinal study of patients included in the maribavir CUP. Patients were followed from the maribavir initiation and up to 20-weeks after initiation. Maribavir effectiveness was assessed by estimating the percentage of patients achieving clearance (<137 IU/mL for plasma or <411 IU/mL for whole blood) overall, and by the time-to first CMV clearance under treatment (regardless of treatment duration). Kaplan Meier estimator was used to describe median time-to clearance and respective 95% CIs. Resistance profile was described at maribavir initiation and after treatment using descriptive statistics, and frequency and percentages were reported.

Results: Among 79 patients who completed initiation/end of treatment data, 84.8% were solid organ recipients (median age 58.6 years, 69.6 % male). At baseline, resistance to standard antivirals was reported in 57 (72.1%) patients, showing mutations in UL97 (67.1%); UL54 (21.5%) and UL56 (5.1%). Post-treatment, emergent maribavir resistance was detected in 13.9% (11/79) patients; all mutations being located in UL97 (T409M, 33.3%; C480F, 26.7%; F342Y, 20% and/or H411L, 20%). Regarding effectiveness, 53.2% of patients achieved clearance at least once anytime under maribavir treatment during follow-up, with a median time-to first clearance of 59 days [39-63].

Conclusions: The present analysis is the first to report maribavir resistance profile and effectiveness over time outside the pivotal trial. The maribavir resistance rate was lower than the findings from the pivotal study, while effectiveness was consistent with the trial findings with the additional patients who achieved CMV clearance beyond 8 weeks of treatment.

BOS60_03_7 QUANTIFYING GAMMA-INTERFERON DEFINES CLINICALLY SIGNIFICANT CMV INFECTION IN HIGH-RISK RECIPIENTS

Elisa Ruiz-Arabi[1], Juan Jose Caston[2], Aurora Paéz Vega[3], Raquel Fernandez Moreno[4], Federico Giovagnorio[5], Belen Gutierrez Gutierrez[6], Angela Cano[7], Alberto Rodriguez Benot[8], Jose Manuel Vaquero Barrios[9], Isabel Machuca[2], Elisa Vidal[7], Sara Cantisan[10], Julian de la Torre-Cisneros[11]

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Background: The cutoff value of the QuantiFERON®-CMV (QF-CMV) assay proposed by the manufacturer is generally assumed to be predictive. This study aims to determine the optimal cutoff value for predicting protection from clinically significant CMV infection within 30 days.

Methods: We conducted a subanalysis of two cohorts derived from different clinical trials: adult CMV seropositive kidney transplant (KT) recipients with antithymocyte globulin (ATG) induction from the TIMOVAL study and seropositive lung transplant (LT) patients from the CYTOCOR study. The optimal cutoff value was established using the Youden's index. We estimated the predictive capacity of the cutoff value through the AUROC and assessed the diagnostic accuracy of the assay at the different cutoff values. We evaluated clinical variables that improve the predictive ability of the assay on a predictive score.

Results: Four hundred-four samples from 130 transplant recipients were analyzed. The optimal cutoff value was ≥ 2.2 IU/mL for both KT and LT recipients. It increments the test's specificity, with a positive predictive value for protection of 99% (95% CI, 98-100%) and 99.5% (95% CI, 98-100%) for KT and LT recipients, respectively. The AUROC of the predictive score was 0.85 (95% CI, 0.73–0.97).

Conclusions: Using the proposed cutoff value and the Quanti-CMV score may allow individualization of the length of prophylaxis and provide an objective tool to aid decision-making in clinical practice.

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BOS60_03_8 MONITORING OF CYTOMEGALOVIRUS-SPECIFIC CELL-MEDIATED IMMUNITY IN HEART TRANSPLANT RECIPIENTS

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Background: Valganciclovir prophylaxis is recommended for solid organ transplant recipients to prevent cytomegalovirus (CMV) infection but is frequently associated with leukopenia. Assays measuring CMV-specific T cell-mediated immunity may individualize the duration of antiviral prophylaxis after heart transplantation. Data remain scarce in heart transplant recipients.

Methods: This prospective, observational, single-center study included all CMV-seropositive adults who underwent heart transplantation at our center between January 2021 and January 2023. All patients received primary valganciclovir prophylaxis for 90 days. QuantiFERON®-CMV assays were performed at 3, 6, and 12 months post-transplant. The primary outcomes were the assessment of CMV immunity restoration and the ability of the QuantiFERON®-CMV assay to predict a protective immune status against CMV infection.

Results: We included 11 adult heart transplant recipients CMV-seropositive, most of whom had received antithymoglobulin (ATG)-based induction therapy. At 3, 6 and 12 months post-transplant, the QuantiFERON®-CMV assay was positive in 8 patients (73%) and negative in 3 patients (27%). Results remained stable throughout the follow-up period. Eight patients experienced significant CMV infections during the follow-up, including 7 with a positive QuantiFERON®-CMV assay and only 1 patient with a negative assay.

Conclusions: The QuantiFERON®-CMV assay may not accurately predict CMV infection and would not have contributed to refining the duration of primary prophylaxis in this study.

BOS60_03_9 CELL-MEDIATED IMMUNITY TO ASSIGN THE CMV STATUS IN LIVER TRANSPLANT RECIPIENTS WITH PASSIVE IMMUNITY

Tina Schmidt[1], Stefanie Marx[2], Urban Sester[3], Christian Klein[4], Andreas Pascher[5], Lutz Fischer[6], Björn Nashan[7], Martina Koch[8], Martina Sester[9]

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Background: Correct determination of the cytomegalovirus (CMV) infection status of the recipient and the donor is essential to guide management strategies to prevent CMV complications. As serology may be falsely positive in patients with passive immunity, guidelines identified a need for assessing the utility of CMV-specific cell-mediated immunity (CMI) as an alternative to assign the CMV infection status.

Methods: In a multicenter HEPHAISTOS substudy, blood samples from 92 liver transplant recipients (52.9±9.1 years of age, 24 female/68 males) were tested at transplantation, and 43 patients were tested on follow-up after transplantation. CMV-specific antibodies were determined using ELISA, CMI was quantified after stimulation based on intracellular cytokine staining using flow-cytometry.

Results: Serology and CMI were concordantly negative in 39 (42.4%), and concordantly positive in 41 (44.6%) of the 92 patients. A discordant positive serological test and a negative CMI test indicative of passive immunity was found in 12 (13.0%) patients. Median antibody levels in seropositive patients with discordant results were significantly lower as compared to patients with concordant results (29.3 (IQR 20.6) versus 182.7 (IQR 226.8) RU/ml, p<0.0001). Median CMI levels in concordantly positive patients were significantly higher (1.89 (IQR 2.66) % CMV-specific CD4 T cells) as compared to patients with concordantly negative or discordant results (0.01 (IQR 0) % CMV-specific CD4 T cells), p<0.0001). Among 22 CMI negative patients with follow-up data, 11 underwent primary infection with conversion of both antibodies and CMI, whereas 11 patients remained negative. All 21 longitudinally tested patients with positive CMI remained positive on follow-up.

Conclusions: Evidence for passive immunity was found in more than 10% of liver transplant recipients. While a truly positive infection status is associated with high levels of both antibodies and T cells, low CMV-IgG antibody levels should raise suspicion of a falsely positive CMV infection status, which may be confirmed by absence of CMV-specific T cells.

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Cracking CMV

BOS60_03_10 CMV-IVIG MODULATES CD8 DR+ LEVEL AND ANTI-CMV RESPONSES IN ORGAN RECIPIENTS WITH DIFFICULT TO CONTROL CMV INFECTION

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Background: CMV immunoglobulin (CMV-IVIG) has been reported to decrease overactivation status of CD4+ and CD8+ T-cells in high risk heart recipients (D+/R-) when used as adjunctive therapy for prophylaxis of clinical manifestations of CMV infection. In vitro studies have demonstrated that it can also increase CD8+ anti CMV specific responses. Looking for a rational for the use of CMV-IVIG in the setting of difficult to control CMV infection (DCCMV) we performed an immunophenotypic evaluation to assess if CMV-IVIG is associated with immunomodulatory changes in vivo.

Methods: In a prospective observational multicenter study, the immunophenotype of CD4+, CD8+ and CD19+ subsets was evaluated in patients at the time of detection of DCCMV in solid organ recipients (n=27). 17 transplant controls without infections during the first 3 months after transplantation were evaluated. The functional activity of CD8+ T cells that produce IFN-gamma was evaluated after stimulation with CMV IE1 peptide. Overactivation status of CD4 and CD8 T cells was evaluated by analyzing coexpression of HLA-DR or CD38 markers by flow cytometry. Inclusion criteria: Refractory, recurrent or resistant CMV infection; presence of neutropenia secondary to antivirals; severe IgG hypogammaglobulinemia (IgG < 4 g/L). 13 solid organ recipients who developed DCCMV were treated with standard of care therapy (SOC) and 14 with SOC + CMV-IVIG. The immunological study was performed at the time of diagnose of DCCMV and after completion of therapy.

Results: DCCMV patients showed lower percentages of CD8+IFNgamma+ T cells to CMV IE1 antigen (0.27 vs 0.56%, p=0.02) and significantly higher percentages of CD8+DR+ T-cells (64.9 vs 39.9%, p=0.00026) vs transplant controls. CMV-IVIG was associated with a significant decrease of CD8+DR+ cells (p=0.048) and a significant increase of CD8+IFN-gamma+ T cells (p=0.022) while no differences were observed in solid organ recipients using SOC (p=0.36 and p=0.83, respectively).

Conclusions: Overactivation of CD8+ and lower anti-CD8 cellular specific immunity was demonstrated at the time of DCCMV in SOT recipients. Interestingly, CMV-IVIG demonstrated to modulate both components. These observations warrants further evaluation in a randomized clinical trial.

Life after transplantation: risks, resilience, and recovery

BOS60_04_1 PERSISTENT HEMATURIA AFTER IGA NEPHROPATHY RECURRENCE INCREASES THE RISK OF KIDNEY ALLOGRAFT LOSS

Emilio Rodrigo Calabia[1], Luis F. Quintana[2], Ana Sánchez-Fructuoso[3], Anna Buxeda[4], Eva Gavela Martinez[5], Juan Manuel Cazorla[6], Sheila Cabello-Pelegrin[7], Isabel Beneyto[8], Hernando Trujillo[9], Maria Ovidia Lopez Oliva[10], Domingo Hernández[11]

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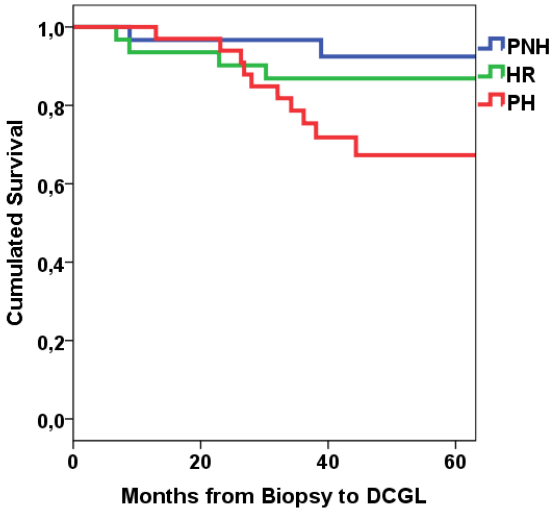
Background: Recurrence of IgA nephropathy (IgAN) after kidney transplantation (KTx) is associated with a worse long-term prognosis. Although hematuria is a hallmark of IgAN, the role of hematuria in its progression remains controversial. Similarly, in patients with recurrence of IgAN after KTx, whether hematuria or its persistence influences a worse renal graft outcome has not been well studied.

Methods: A multi-centre retrospective study was conducted in kidney transplant recipients with biopsy-proven IgA nephropathy as the underlying disease. Recurrence of the primary disease was assessed by graft biopsy. Hematuria was analysed at the time of graft biopsy for IgAN recurrence and two years later. Persistent hematuria (PH) was defined if the number of red blood cells per high-power field (RBC/HPF) was greater than 10 at the diagnosis of recurrence and two years later. Hematuria remission (HR) was defined as RBC/HPF > 10 at baseline and ≤ 10 at two years. Persistent no hematuria (PNH) was defined if RBC/HPF was ≤ 10 at both time points.

Results: 122 kidney transplant recipients were included with an age at recurrence of 46 ± 14 years, 79% male, with a mean time to biopsy of 65 ± 67 months and a post-transplant follow-up of 122 ± 72 months. After recurrence, 34 (28%) grafts were lost at 36 ± 27 months, excluding death. The AUC-ROC of baseline hematuria for discriminating death-censored graft loss (DCGL) at three years was 0.720 (95%CI 0.602-0.837, p = 0.002). Baseline hematuria increased the risk of DCGL at three years in univariate analysis (OR 2.083, 95%CI 1.291-3.359, p = 0.003), but not in multivariate analysis (OR 1.779, 95%CI 0.997-3.175, p = 0.051) after adjustment for estimated GFR and proteinuria. According to Kaplan-Meier survival analysis (Figure 1), patients with PH had worse DCGL than those with PNH or HR (60-month survival: PH 67.3%, PNH 92.5% and HR 86.9%, log-rank p = 0.030). PH increased the risk of DCGL (HR 1.618, 95%CI 1.076-2.432, p = 0.021) independent of estimated GFR and proteinuria.

Conclusions: Persistent hematuria is associated with an increased risk of DCGL independent of other variables. The persistence of hematuria should be considered as a marker of IgAN activity and may represent a treatment response marker.



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Life after transplantation: risks, resilience, and recovery

BOS60_04_2 KIDNEY TRANSPLANTATION IN OLDER PEOPLE (KTOP) STUDY: IMPACT OF FRAILTY ON OUTCOMES

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Background: Frailty is common in waitlist (WL) candidates and is set to increase with the ageing ESKD population. Frailty has been associated with adverse outcomes post-transplant, but evidence of the longitudinal impact of frailty on quality of life (QoL) and patient experience in elderly WL and transplant patients is lacking.

Methods: The Kidney Transplantation in Older People (KTOP) study is a prospective, single centre longitudinal study of WL patients >60 years, designed to assess patient reported outcome (PRO) changes following transplantation by frailty status. Frailty was assessed by the Edmonton Frail Scale. Patient experience/QoL was assessed as part of 12 validated questionnaires whilst remaining on the WL and then at 3- and 12-months post-transplant.

Results: 210 patients were recruited, 120 were transplanted. 36.6% were frail/vulnerable to frailty, and 37.4% had ≥mild cognitive impairment. At 12 months post-transplant, frailty was independently associated with lower health and mental related QoL, depression and increased symptom burden and illness intrusion (**figure 1**). Whilst longitudinally treatment satisfaction and illness intrusion improved post-transplant, frail patients experienced worsening symptom burden, mental QoL and depression. One-year death censored allograft (95.8%) and patient survival (91.7%) was no different between the frail and non-frail participants. Frail patients were more likely to experience delayed graft function (p=0.03), longer length of stays (p=0.01) and have inferior allograft function at 12 months, p=0.01. Frail patients on the WL experienced more infections (p<0.001), and were more likely to spend greater time suspended (p=0.03).

Conclusion: Frailty status in WL and post-transplant recipients is associated with inferior patient reported outcomes. In addition, frailty impacts clinical outcomes, and reduces time active on the WL, influencing chances of transplantation. Frailty assessments as part of WL workup may help inform patient experience and outcomes.

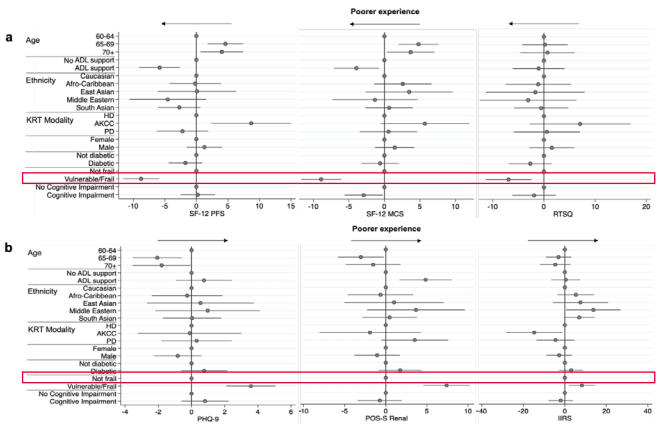

Figure 1. Association of clinical characteristics on Patient Reported Outcome Scores at 12 months post-transplant

BOS60_04_3 TRAJECTORIES OF FEV1 AFTER LUNG TRANSPLANTATION AND PATIENT OUTCOMES

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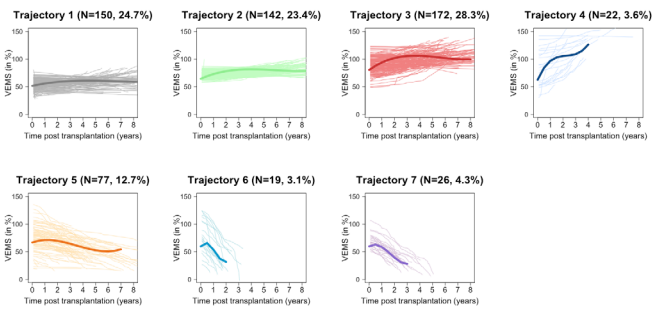
Background: The forced expiratory volume in one second (FEV1) is the standard measure for monitoring lung allograft function. However, little is known about FEV1 trajectories and their associations with clinical outcomes.

Methods: Adult patients who received a bilateral lung transplantation were included from 15 centers in France, Belgium, Austria and the US, between 2010 and 2021. All centers performed routine spirometry measurements post lung transplantation at regular intervals. All centers performed routine spirometry measurements commencing shortly after lung transplantation and continuing at regular intervals of maximum three months afterwards. Recipient, donor and transplant characteristics were collected for each patient. Latent class mixed models were used to identify FEV1 trajectories.

Results: A total of 2,305 patients were included with 59,034 FEV1 measurements performed. The median follow-up post-transplantation was 6.5 years (IQR 4.0-9.0). In the development cohort, the best latent class mixed model identified seven clinically meaningful FEV1 trajectories (Figure). Trajectory #1 (24.7%) was characterized by patients with moderate and stable lung function (5-years patient survival = 79.1%); trajectory #2 (23.4%) and #3 (28.3%) were characterized by patients with moderate/high and stable lung function (5-years patient survival = 94.2% and 90.7% respectively) ; trajectory #4 (3.6%) was characterized by patients with increasing lung function (5-years patient survival = 72.7%) ; trajectory #5 (3.6%) was characterized by patients with a slow decline (5-years patient survival = 68.9%) ; and trajectory #6 (3.1%) and #7 (4.3%) were characterized by patients with accelerated decline (5-years patient survival = 21.1% and 42.3 % respectively). Similar FEV1 trajectories and patient outcomes were identified in the external validation cohorts on the basis of independent analyses. The trajectories were also confirmed in a series of subpopulations. Last, FEV_1 value and slope assessed at 1 year post transplant were strongly associated with FEV_1 trajectories.

Conclusions: We identified FEV1 trajectories that capture different clinical scenarios associated with lung recipients outcomes. Our results provide the basis for a trajectory-based assessment of lung transplant patients.



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Life after transplantation: risks, resilience, and recovery

BOS60_04_4 HEALTH RELATED QUALITY OF LIFE IN THE FIRST YEAR POST KIDNEY TRANSPLANTATION - A COHORT STUDY

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Background: For patients suffering from end-stage renal disease, a kidney transplantation is the treatment of choice to improve health-related quality of life (HRQOL). An in-depth understanding of individual factors affecting HRQOL might help to develop strategies to support the process of HRQOL improvement. The AdTorque study was designed to prospectively assess HRQOL in the context of patient-related characteristics and follow-up data associated with HRQOL.

Methods: This cohort study screened all 283 consecutive adult kidney graft recipients transplanted at the Medical University of Vienna between January 2018 and December 2019. HRQOL was monitored within the first-year post-transplant applying the WHOQOL-BREF questionnaire at 3 study-visits (first outpatient visit – P1, 3 months post-transplant – P2 and 12 months post-transplant – P3). The WHOQOL-BREF assesses the HRQOL in 4 domains: physical health, psychological health, social relationships and environmental health. Each domain is scored between 0 and 100 and a total score for overall HRQOL is calculated by the sum of all domains (0-400). For subgroup analysis all patients were stratified according to sociodemographic, psycho-social and transplant-related variables.

Results: In the total cohort of 183 patients [33% females; median age 56 (IQR 46-53)] the median overall HRQOL was 315 (IQR 278-340) at P1, 322 (IQR 277-351) at P2 and 328 (IQR 289-359) at P3. A significant improvement was only detected in the physical health domain: 71 (IQR 54-79) at P1 to 79 (IQR 56-89) at P3; p=0.006]. While male sex, younger age, higher education and donation from a living donor had a positive influence, smoking and living-alone negatively affected the improvements in HRQOL. Patients with psychological disorders (n=67; 37%) reported significantly reduced median overall HRQOL compared to patients without such disorders (279 [IQR 251-323] vs. 329 [IQR 307-347; *p<0.001*] at P1, 284 [IQR 244-335] vs. 333 [IQR 297-354; *p<0.001*] at P2 and 302 [IQR 267-335 vs. 354 [IQR 307-371; *p<0.001*] at P3).

Conclusions: Patients with a psychological disorders and fewer social relations perceived less improvement in their HRQOL in the first year post kidney transplantation. Our study emphasizes the need for psycho-social support in post-transplant routine care.

BOS60_04_5 OUTCOMES AND RISK FACTORS FOR DE-NOVO MAJOR DEPRESSIVE DISORDER AFTER LIVER TRANSPLANTATION

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Background: Major depressive disorder (MDD) is a major psychiatric complication of liver transplantation (LT). Here, we aimed to analyze the impact of de novo MDD on survival post-LT and identify risk factors for this disorder among LT recipients.

Methods: A retrospective analysis was conducted on 1350 LT recipients at Severance Hospital, Korea, from July 2005 to December 2022. Patients with MDD were matched 1:5 with controls using a nested case-control design to control for immortal time bias.

Results: During follow-up post-LT, 58 patients (4.3%) were newly diagnosed with MDD. The median time from LT to MDD diagnosis was 316 (interquartile range 46–920) days. Patients with MDD had significantly lower graft survival rates than controls at 1, 3, and 5 years after matching (89.5%, 75.3%, and 66.5% vs. 95.5%, 91.5%, and 86.4%, respectively; P=0.003). Multivariable Cox regression identified de novo MDD as an independent risk factor for reduced graft survival (hazard ratio 2.39, 95% confidence interval [CI] 1.15–4.98, P=0.003). Independent risk factors for de novo MDD included female sex (odds ratio [OR] 2.29, 95% CI 1.16–4.53, P=0.017), alcoholic liver disease (OR 2.36, 95% CI 1.16–4.75, P=0.016), pre-transplant encephalopathy (OR 2.95, 95% CI 1.49–5.79, P=0.002), and lower hemoglobin levels (OR 0.85, 95% CI 0.73–0.98, P=0.025).

Conclusions: In our matched population of nested case controls, de novo MDD significantly reduced the survival of LT recipients. Screening and early intervention are required for LT recipients with risk factors for MDD.

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Life after transplantation: risks, resilience, and recovery

BOS60_04_6 PREGNANCY OUTCOMES FOLLOWING PANCREAS TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background: Pregnancy in diabetic patients presents unique challenges due to glycemic control difficulties, increased maternal health risks, fetal complications, and higher adverse pregnancy outcome rates. Diabetes mellitus (DM), a leading cause of end-stage renal disease (ESRD), often results in menstrual irregularities and infertility. This study evaluates pregnancy outcomes in pancreas transplant recipients at a single center.

Methods: We retrospectively analyzed 32 pregnancies in 23 pancreas transplant recipients among 501 recipients (268 women, 208 of childbearing age). Maternal, fetal, and graft outcomes were collected and analyzed. Pre-conception immunosuppressive regimens were adjusted, primarily replacing or discontinuing mycophenolate mofetil with azathioprine in combination with tacrolimus.

Results: Of 32 pregnancies in 23 recipients, there were 11 miscarriages and 21 live births among 20 recipients. The mean age at transplantation was 28.6 years, with an average interval between transplantation and pregnancy of 65.3 months (range: 18-146). The mean gestational age was 35.0±4.2 weeks, with an average birth weight of 2326.2 g. Among 21 live births (11 male, 10 female), 6 required neonatal intensive care. Preterm delivery occurred in 10 cases, 5 due to preeclampsia. One case of pancreas graft failure occurred during pregnancy, and 4 recipients experienced rejection episodes (2 kidney, 2 pancreas) within the first postpartum year. At median follow-up of 84 months (range, 15~158 months) post-childbirth, 15 recipients maintained graft function, 5 resumed insulin therapy (including 1 who underwent pancreas re-transplantation), and 2 SPK (simultaneous pancreas-kidney transplant) recipients required kidney re-transplantation.

Conclusions: Pregnancy following pancreas transplantation is feasible but carries significant risks, including miscarriage, preterm delivery, fetal complications, and graft dysfunction. Successful maternal and fetal outcomes necessitate close monitoring and coordinated multidisciplinary care involving nephrologists, obstetricians, endocrinologists, and pediatricians.

BOS60_04_7 PIONEERING PROSPECTIVE STUDY ON VISCOSITY AND ELASTICITY IN LIVER TRANSPLANTATION

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Background: The need to address the precise diagnosis of early post-transplant complications remains challenging due to prognosis and overall patient survival. While liver biopsy provides definitive diagnostic accuracy, its invasiveness entails considerable risks. Therefore, developing non-invasive diagnostic techniques is essential. This study aimed to evaluate whether changes in hepatic elasticity and viscosity along with Doppler Ultrasound could predict complications following liver transplantation (LT) and to determine if these parameters could enhance the accuracy of non-invasive diagnosis.

Methods: Between January 2022 and November 2023, patients with LT underwent ultrasound with detection of viscosity and elasticity at post operative day 1, 2, 3, 4 and 7 (P1,P2,P3, P4,P7).Measurements were performed with Aixplorer® Super Sonic ultrasound system equipped with ShearWaveTM Elastography and ViscosityPLUS Imaging.Uni-and multivariate analyses identified elasticity and viscosity values associated with surgical complications (Clavien-Dindo ≥ 3).The best cut-off was determined using the Youden Index.

Results:131 patients who had undergone LT were analyzed. The median elasticity values at 1-2-3-4 and 7 were 13,12.2,12.8,12.1 and 12.2 kPa. The median difference in elasticity between P1 and P7 was +0.40 (IQR-2; +2.9). The median viscosity values at 1-2-3-4 and 7 were 2.7 Pa.s, 2.7 Pa.s, 2.7 Pa.s, 2.7 Pa.s, respectively and 2.5 Pa.s. The median viscosity difference between P1 and P7 was +0.15 (IQR -0.3;+0.5). 46 patients (35.1%) developed severe postoperative complications (Clavien-Dindo ≥ 3). In multivariate analysis, elasticity in P1 (OR 1.106, p=0.004, 95% CI=1.034-1.184) and difference in viscosity (OR 0.407, p=0.008, 95% CI=0.210-0.788) were significantly associated with the onset of severe surgical complications after LT. The analysis ROC curve identified the optimal cut-offs as 13.1 kPa for elasticity (AUC=0.624, 95%CI=0.517-0.732) and 0.15 Pa.s for delta viscosity (AUC=0.620, 95%CI 0.512-0.727).

Conclusions: Further studies are needed to continue validating this technology, but in the light of the results obtained, we could say that it is a promising tool to assess complications in the immediate post-transplant period and can be used as a non-invasive method for LT follow-up.

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BOS60_04_8 DONOR-DERIVED DISEASE TRANSMISSION IN ORGAN DONATION AND SOLID ORGAN TRANSPLANTATION IN GERMANY FROM 2016-2023

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Background: In many cases, organ transplantation is the only option that has been proven to improve the life expectancy and quality of life of patients with terminal organ failure. Despite continuous improvement in the evaluation of organs, there remains a residual risk of unrecognized transmission of infections, tumors or other diseases from the donor to the recipients. A careful analysis of serious adverse event (SAE) and serious adverse reaction (SAR) reports can help to identify potential risks and increase the safety of recipients

Methods: All incoming SAE and SAR reports from January 1st 2016 to December 31st 2023 related to a possible donor-derived disease (DDD) were evaluated by a special team of qualified physicians of the Deutsche Stiftung Organtransplantation (DSO). In case of a possible transmission of a disease to one or more recipients, an assessment of imputability was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).

Results: Between 2016 and 2023, 27919 patients were transplanted with organs from 9771 deceased donors. In the same period, the DSO received 612 SAE/SAR reports. 68 of the 612 reports (11 %) were proven or probable (P/P) transmissions of infectious diseases, malignancies or other diseases to 95 recipients. 20 of 95 (20/95; 21 %) recipients died due to the transmitted disease. Infections were the most frequently reported disease transmission occurrences (40/68; 59%). In 18 cases bacteria were responsible, in 14 cases fungi, in 7 cases viruses and in one case a parasite with together 6 attributable deaths. In 20 cases, a malignant tumor was transmitted to 28 recipients, 14 of whom died. In addition, 8 other diseases were transmitted to 10 recipients, none of them died.

Conclusions: The transmission of donor-derived disease is a rare event (68/9771; 0,7%), but when it does occur, it has a high morbidity and mortality rate in the recipients, especially when a malignant disease is transmitted. The evaluation of SAE and SAR reports can help to better assess possible risks in organ donation and solid organ transplantation and to improve donor characterization and increase awareness of transmission events.

BOS60_04_9 BLACK ETHNICITY IS ASSOCIATED WITH INCREASED GRAFT FAILURE AND TCMR

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Background: Kidney transplant recipients of Black ethnicities experience inferior allograft survival. Potential explanations include reduced access to living donors, inferior HLA matching and increased socioeconomic deprivation. In addition, heightened alloimmune responses leading to increased rates of rejection have been suggested but confirmatory and mechanistic data are lacking.

Methods: The OuTSMART trial is the largest UK analysis of 2094 renal transplant recipients with median follow-up of 3.9 years providing an ideal opportunity to investigate associations between rejection and allograft failure with ethnicity. In this trial, transplant biopsies were taken 'for cause'. The mean time to biopsy was 14.9 months after recruitment.

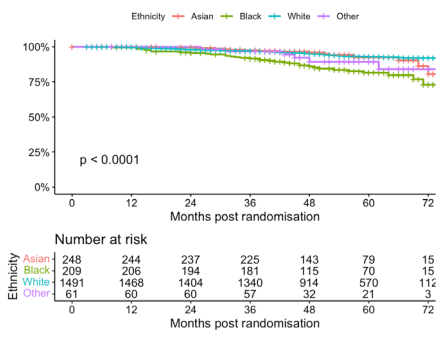
Results: 11% of participants were of Black ethnicity (self-reported) (Table 1). Recipients of black ethnicity had lower baseline eGFR, were more likely to be male and receiving their first kidney transplant compared with patients of White, Asian and other ethnicities. Time from transplantation to recruitment into OuTSMART was shorter and primary cause of kidney disease more likely to be hypertension in patients of Black ethnicity compared with other ethnicities. Tacrolimus levels were significantly higher at baseline in Black patients compared with other ethnicities, but similar rates of *de-novo* DSA formation were found in all ethnic groups despite inferior number of HLA mismatch in patients of Black ethnicity. Patients of Black ethnicity had increased risk of late T cell mediated rejection (TCMR) 4.1% Black v 1.2% White v 1.1% Asian v 0% Other; P=0.02 (Table 1), lower end of study GFR and increased risk of allograft failure (16.7% Black v 5.9 White v 7.3% Asian v 9.8% Other P<0.01 (Figure 1). Survival analysis showed that HLA mismatch, presence of previous transplant and taking prednisolone did not impact graft failure. In Cox regression analysis, the only significant risk factor for allograft failure was ethnicity (HR 1.9 (1.02-3.47), P<0.04). Polycystic kidney disease as a cause of end stage kidney disease was found to be protective (HR 0.29 (0.08-0.66), P=0.02).

Conclusions: This is the first UK based study to demonstrate increased late TCMR in patients of Black ethnicity which may explain the inferior allograft outcomes.

Table 1

n=2094	Asian (n=264, 12.6%)	Black (221, 10.6%)	White (1542, 73.6%)	Other (67, 3.2%)	P (chisq, fisher, ANOVA)
Baseline Variables					
Recipient age at time of randomisation (range)	47.8 18-76	51.9 20-71	50.7 18-78	49.7 18-75	**<0.01**
Time from transplant to randomisation (years)	6.63	5.61	8.22	7.84	**<0.01**
Male (%)	68.6	71	68.1	67.2	0.84
Cause of CKD (%)					
Diabetes	8.7	7.4	3.5	8.1	**<0.01**
GN	11.5	12.1	14.4	19.4	
PKD	5.5	8.4	16.1	6.5	
Hypertension	6.3	23.3	4.9	3.2	
Congenital	4	0	5.1	3.2	
Obstructive	0.4	1.4	2	1.6	
Other	47.8	31.2	45	43.5	
Unknown	15.8	16.3	8.76	14.5	
Previous Transplant (%)	9.1	7.9	15.8	14.5	**<0.01**
Number of HLA Mismatches (%)					
0	5.5	7.1	13.1	1.8	**<0.01**
1	3.6	2.8	9.9	7.4	
2	15.9	13.2	23.0	16.7	
3	33.6	28.3	28.8	27.8	
4	22.3	25.9	15.3	27.8	
5	14.5	15.6	6.7	14.8	
6	4.5	7.1	2.5	3.7	
DSA positive at time of transplantation (%)	1.9	3.6	1.9	6	0.56
OuTSMART randomisation					
Biomarker Led (%)	53.4	50.9	49.9	45.9	0.67
Standard of Care (%)	46.6	49.1	50.1	54.1	
Immunosuppression					
Prednisolone	51.6	69.8	53.6	61.3	**<0.01**
Prednisolone dose	5.06	5.13	6.31	4.9	0.98
Tacrolimus	74.3	71.6	72.8	77.4	0.81
Tacrolimus level	6.89	7.48	6.69	6.85	**<0.01**
Mycophenolate mofetil	69.2	72.6	65.5	77.4	0.05
Mycophenolate mofetil dose	1074	1053	1069	1014	0.84
Ciclosporin	20.5	21.9	17.8	16.1	0.38
Azathioprine	15.5	11.2	15.7	11.3	0.29
Everolimus	0	0.5	0.1	0	0.39
Sirolimus	2	4.2	3.2	3.2	0.56
Baseline eGFR (ml/min/1.73m²)	58.1	48	53.4	53.9	**<0.01**
Baseline UPCR mg/mmol (range)	49.8 (3-607)	47.2 (3-559)	40.6 (2-706)	40.7 (4-179)	0.46
Outcome Variables					
End of Study eGFR (ml/min/1.73m²)	57	51.4	53.3	51.9	**0.03**
End of Study UPCR mg/mmol (range)	115 (4-2640)	103 (0-2820)	63.6 (0-2960)	78.3 (15-1191)	**<0.01**
Biopsy proven antibody mediated rejection (n,%)	5(1.8)	9 (4.1)	32 (2.1)	1.5 (1)	0.29
Biopsy proven T Cell Mediated Rejection (n, %)	3 (1.1)	9 (4.1)	18 (1.2)	0	**0.02**
% Graft failure at end of study (median 3.9 years) (n)	7.3 (18)	16.7 (35)	5.9 (89)	9.8(6)	**<0.01**

Figure 1



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Life after transplantation: risks, resilience, and recovery

BOS60_04_10 KIDNEY GRAFT SURVIVAL BENEFIT THANKS TO THE FRENCH ACCEPTABLE MISSMATCH PROGRAM

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Background: Specific national or supranational strategies to improve kidney graft access for hypersensitised patients (HS) are often required because of scarcity of the HLA compatible donor pool leading to a long waiting time. Acceptable mismatch priority is a way to increase the number of potential matched donors without increasing the immunological graft failure risk. In 2005, the French acceptable mismatch program (AMP) was introduced with success as a strategy toward improving kidney allocation to HS patients. The AMP was improved in 2015: no more than 4 HLA A B DR DQβ mismatch are authorized but each must be an acceptable antigen (Ag), regarded as such when the bead with the highest normalised MFI for this Ag < 500 by SAB assays (on historical and recent serum). Our study compared graft survival between AMP allocation and the others among HS recipients.

Methods: We selected all French DBD single renal transplant recipients transplanted between 2016 and 2022 with cPRA above 85% (N=2986).

Results: AMP recipients were older and more comorbid. They were less often pre-emptive but with shorter dialysis duration. Non-AMP had more often previous history of renal transplant, source of more than cPRA 99-100% (20.6 vs 16.9%) and transplanted with more HLA mismatches. In Kaplan Meier, 5-years graft survival is 71.4% (95% CI 68.7% - 73.9%) and graft survival with death censored is 85.6% (95% CI 83.4% - 87.5%). After adjustment on donor and recipient characteristics with a Cox regression, non-AMP recipients have an excess risk of failure of 1.21 (95% CI 1.05-1.38).

Conclusions: The French AMP, in place for 20 years to improve access to kidney transplant for HS patients, also offers better post-transplant survival than other kidney allocation modalities, possibly due to the presence in historical and recent serum of preformed DSAs for non-AMP recipients, associated to a greater risk of rejection.

Beyond insulin: the promise of beta cell therapy

BOS60_05_1 AUTOMATED ABDOMINAL ORGAN SEGMENTATION USING DEEP LEARNING FOR RETRIEVAL PHOTOGRAPHS

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Background: Photography at time of organ retrieval is routine and enables remote assessments and decision-making regarding utilisation. These assessments are subjective and reliant on surgeon experience. Artificial intelligence (AI) models could offer an objective alternative, but computers must first accurately and reliably identify organs within the image. To date AI research in this field has relied on humans first outlining the organs (segmentation). We present the first set of automated segmentation models for retrieval photographs across abdominal organs.

Methods: Transfer learning was applied to open-source segmentation algorithms to generate novel segmentation models for backbench kidney, liver, pancreas, and in situ liver photographs. For each organ, main datasets were split 70:30 for training and testing. Entirely independent images from a different source were used for external validation. Ground truth annotations were verified by a transplant surgeon.

Results: Compared to human segmentation, kidney and liver segmentation with Detectron2 and YOLOv8 demonstrated high performance, achieving over 90% across multiple computer vision metrics (Intersection over Union, Dice similarity coefficient, Area Under the Curve). Performance below 90% was observed for pancreas and in situ liver segmentation, likely due to the smaller sample size of training images. The models exhibited strong generalisability, with no evidence of overfitting during external validation. Full results reported in Table 1. These custom deep learning models outperformed standard background removal/segmentation software. Human annotation took a median of 64 (IQR:54-78) seconds/image. Detectron2 was 64 times faster at 0.95 (0.87-1.07) seconds, while YOLOv8 was 640 times faster at 0.10 (0.09-0.10) seconds.

Conclusions: Deep learning models can achieve accurate and significantly faster segmentation than manual methods. Effective segmentation ensures that AI analysis remains focused on organ tissue, enhancing both the explainability and trustworthiness of AI-driven organ quality assessments. Accurate segmentation methods, such as these, will form the foundation for any AI based visual organ quality assessment tools.

Table 1. Performance summary of segmentation models across various organs and visual assessment metrics. The number of images in the training and internal validation cohorts is denoted as n_1, while the images from a smaller independent dataset used for external validation are denoted as n_2.

Organ	Segmentation Task	Model	Intersection over Union (IoU)		Dice Similarity Coefficient (DSC)		Area Under the Curve (AUROC)	
			Internal Validation	External Validation	Internal Validation	External Validation	Internal Validation	External Validation
Kidney $n_1 = 821$ $n_2 = 203$	Whole Organ	Detectron2	0.93	0.93	0.96	0.96	0.98	0.97
		Yolov8	0.94	0.94	0.97	0.97	0.99	0.98
	Clear View	Detectron2	0.92	0.91	0.96	095	0.97	0.98
		Yolov8	0.92	0.90	0.96	0.95	0.98	0.99
Liver $n_1 = 400$ $n_2 = 208$	Whole Organ	Detectron2	0.97	0.92	0.98	0.96	0.97	0.97
		Yolov8	0.97	0.91	0.99	0.95	0.97	0.97
	Clear View	Detectron2	0.89	0.7	0.94	0.82	0.95	0.96
		Yolov8	0.89	0.64	0.94	0.78	0.95	0.94
Pancreas $n_1 = 305$ $n_2 = 64$	Whole Organ	Detectron2	0.91	0.88	0.95	0.93	0.96	0.95
		Yolov8	0.92	0.89	0.96	0.94	0.97	0.97
	Clear View	Detectron2	0.45	0.58	0.57	0.70	0.86	0.88
		Yolov8	0.41	0.37	0.49	0.47	0.79	0.77
Liver – in situ $n_1 = 254$ $n_2 = 58$	Whole Organ	Detectron2	0.84	0.84	0.89	0.87	0.93	0.95
		Yolov8	0.87	0.82	0.92	0.87	0.95	0.95

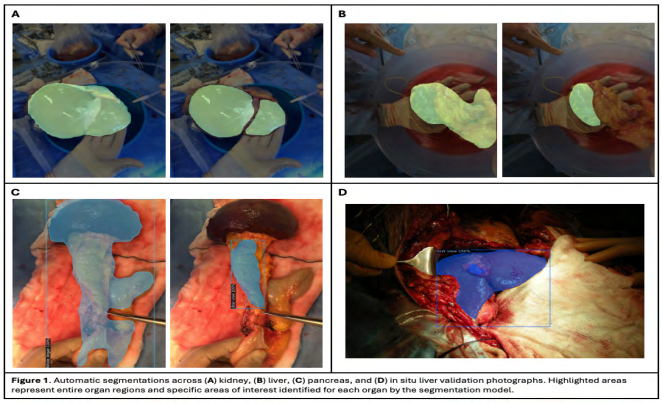

Figure 1. Automatic segmentations across **(A)** kidney, **(B)** liver, **(C)** pancreas, and **(D)** in situ liver validation photographs. Highlighted areas represent entire organ regions and specific areas of interest identified for each organ by the segmentation model.

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Beyond insulin: the promise of beta cell therapy

BOS60_05_2 PANCREATIC BETA CELL HETEROGENEITY IN ADULT HUMAN ISLETS: INSIGHT FROM SINGLE-ISLET TRANSCRIPTOMIC PROFILING USING DISCO

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Background: Pancreatic β-cell heterogeneity within adult human islets plays a critical role in maintaining glucose homeostasis and has profound implications for diabetes pathophysiology and therapeutic development. Conventional single-cell RNA sequencing (scRNA-seq) methods often require pooling multiple islets, potentially obscuring intra-islet variability.

Methods: To overcome this limitation, we employed the deterministic mRNA-capture bead and cell co-encapsulation system (DisCo), developed by Bart Deplancke's group at EPFL. DisCo is optimized for low-input samples, achieving >70% capture efficiency and processing up to 350 cells per hour, making it ideal for single-islet, single-cell transcriptomic analyses. Using DisCo, we analyzed dissociated islet cells from three human donors. Cells were co-encapsulated with mRNA-capture beads in microfluidic droplets for immediate lysis and mRNA hybridization, ensuring high capture efficiency with minimal technical variability. Captured mRNA was reverse-transcribed, amplified, and sequenced, enabling comprehensive profiling of individual β-cell populations.

Results: Our analysis revealed significant intra- and inter-islet heterogeneity, with variations in gene expression related to insulin secretion, cellular stress responses, and β-cell maturation states. Notably, distinct β-cell subpopulations were identified within islets from the same donor, underscoring the limitations of bulk transcriptomic approaches. By preserving individual islet compositions, DisCo provided a more accurate and detailed representation of β-cell diversity.

Conclusions: These findings offer critical insights into the functional heterogeneity of β-cells, advancing our understanding of islet biology and informing the development of targeted, personalized therapies for diabetes. The DisCo system represents a significant step forward in diabetes research by enabling high-resolution transcriptomic analyses of single islets, paving the way for innovations in β-cell replacement and regenerative medicine strategies.

BOS60_05_3 LONG TERM OUTCOMES OF PANCREAS TRANSPLANTATION ALONE FROM DONATION AFTER CIRCULATORY DEATH

Francess Adlard[1], Rumyana Smilevska[2], Edward Sharples[3], Irene Mosca[4], Srikanth Reddy[4], Isabel Quiroga-Giraldez[5], Sushma Shankar[6], Emilio Canovai[7], Sanjay Sinha[8], Rutger Ploeg[9], Peter Friend[10], Simon Knight[11]

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Background: Decreased graft survival and increased risk of postoperative complications are key factors contributing to the infrequent use of donation after circulatory death (DCD) in pancreas transplantation worldwide, due to assumed higher risk. This study aims to compare the outcomes associated with DCD and donation after brain death (DBD) in the context of pancreas transplantation alone (PTA) within a large, single-centre cohort.

Methods: PTA recipients' prospectively maintained database was analysed for the period from July 2004 to December 2024. The DBD and DCD cohorts were compared for demographic and transplant variables. Kaplan-Meier and Cox regression were used for analysis of graft survival and associated risk factors.

Results: 223 PTA were performed during the study period, of which 20 cases were excluded due to early graft loss in the first 30 postoperative days. 203 PTA were included in the analysis: 53 (26.1%) from DCD and 143 (73.9%) from DBD. Demographic data for recipients, postoperative complications and length of hospital stay showed no statistical difference. Donor BMI was statistically lower in the DBD group (25.97 vs 24.68kg/m^2, p=0.035). Cold ischemia time (CIT) was not significantly different (705 vs 674 min, p=0.27). There was no significant difference in 5-year and 10-year patient and pancreas graft survival (Table 1). Cox regression analysis identified age at transplant, recipient body mass index (BMI), and CIT as significant risk factors for graft failure, while donor category was not found to be a significant predictor.

Conclusions: The findings of this study support that DCD should be considered a safe alternative for PTA without compromising long-term outcomes. Recipient selection and minimising CIT are essential for optimising graft survival.

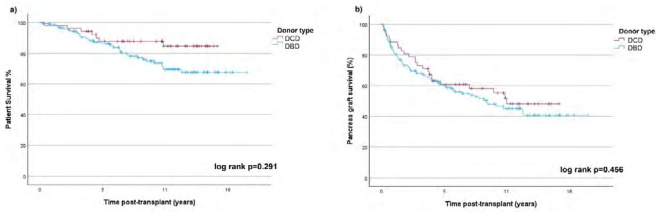

Figure 1: Patient (a) and pancreas graft survival (b) for PTA

	Coefficient	p-value	HR	95% CI
Recipient age	-.039	**.002**	0.962	0.939 -0.985
Recipient BMI	-.057	**.040**	0.944	0.894 -0.997
Donor age	.012	.186	1.012	0.994-1.029
Donor BMI	-.021	.590	0.979	0.905-1.058
Donor category (DBD/DCD)	-.246	.339	0.782	0.473-1.295
CIT	.002	**.011**	1.002	1.000-1.003

Table 1. Cox regression analysis for risk factors for graft survival

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BOS60_05_4 HEPATITIS C POSITIVE ORGAN DONATION AND DIRECT ACTING ANTIVIRALS IN PANCREAS TRANSPLANTATION: APPLICATION IN THE UK

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Background: Pancreas transplantation (PT) provides euglycaemia for patients with complicated diabetes mellitus. Renal and liver transplants from HCV+ donors have been transplanted to HCV- recipients alongside directing acting antivirals (DAA) with success in small trials. We aimed to review this strategy in PT while analysing the opportunity for potential increases in organ utilisation in the UK.

Methods: A literature search evaluated MedLINE, PubMed and EMBASE regarding the use of HCV+ organ donors for PT in HCV- recipients alongside DAA therapy. In addition, retrospective NHSBT registry analysis reviewed characteristics and outcomes of HCV+ organ donors in the UK from 2014-2024.

Results: Database analysis produced 5 articles (4 single centre retrospective, 1 case report). This included a total of 65 patients, 15 of which received PT. Three studies employed prophylactic DAA's, while 2 examined treatment post-transplantation. 100% of patients achieved a sustained virological response (SVR) at 12 weeks after only one case of HCV transmission and good medium-term graft function. 188 potential HCV+ PT donors were offered in the time period (mean age 43.3±9.1years, 75.0% male, 60.1% DBD, mean BMI 25.2±4.6kg/m^2, 89.1% drug users). Only 2 organs were used for PT, with the primary reasons for decline either virology (60.8 %) or past history (23.1%). 38.8% of donors had other organs utilised for transplanted.

Conclusions: The use of DAA therapy is safe and effective for HCV+ donors to HCV- transplant in early reported studies. This approach could increase successful utilisation of HCV+ organs from already identified high quality donors. Pancreas transplantation specific studies are required to further analyse outcomes.

BOS60_05_5 MAGNETIC RESONANCE ELASTOGRAPHY OF PANCREATECTOMY SPECIMENS: A NOVEL APPROACH TO ASSESS ISLET YIELD PRIOR TO ISOLATION

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Background: Magnetic resonance elastography (MRE), a non-invasive phase-contrast MRI technique used to assess mechanical tissue properties *in vivo* for many organs, has not yet seen any application in evaluating the pancreatic parenchyma prior to islet isolation. This study aims to explore the viscoelastic properties of pancreatectomy specimens using MRE, and to investigate potential correlations between MRE findings, histological assessment by pathologists regarding grade of fibrosis/pancreatitis/lipomatosis, and islet yield and functionality.

Methods: To date, 29 MRE measurements and isolations from pancreatectomy specimens of patients undergoing a pancreas surgery at the Department of Surgery, Charité – Universitätsmedizin Berlin could be performed. After retrieval, the specimen was cylindrically cut to a diameter of 8 mm and the MRE analysis, followed by islet isolation was performed (**Figure 1A**). Islet yield was correlated to viscoelastic properties of the specimen (α-, μ- and c-value) as measured with MRE.

Results: An average of 2117.5 IEQ per gram pancreatic tissue were isolated. Isolations were separated into low yield (LY) and high yield (HY, **Figure 1B**). The dispersion of patient-, specimen, and surgery-related characteristics between both groups is described in **Table 1**. The shear viscosity μ was significantly higher in the LY than in the HY group (p=0.03, **Figure 1C**). Shear wave speed *c* was also found to be significantly higher for the LY group (LY vs. HY for 2900 Hz; 4.451 ± 1.19 vs. 3.38 ± 0.55, p=0.02, **Figure 1D**). Our correlation analysis showed stiffer tissue with a higher vibration frequency *c* yielded significantly less islets than softer tissue (r=-0.3901, p=0.03, **Figure 1E**). To date, a correlation analysis between consistency of pancreatic parenchyma as evaluated from the pathologist, and *α*, *μ* and *c* could only be performed for three isolations. The analysis showed a significant positive correlation between the μ-value and fibrosis as evaluated from the pathologist (r=0.997, p=0.04, **Figure 1F**).

Conclusions: While further analysis is currently ongoing, our findings up until now suggest that MRE could serve as a valuable tool for predicting islet yield before the time-consuming and costly islet isolation process, potentially enhancing the sustainability of islet transplantation.

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Isolation Characteristics	IEQ < 2000 (n=21)	SD	IEQ > 2000 (n=8)	SD	p
Age (Median)	64 (40-84)	12.7	67 (64-74)	3.29	0.65
Sex (Male), n (%)	12 (57 %)		2 (25 %)		0.21
Body mass index (BMI)	23.75	3.2	26.78	5.2	0.12
Comorbidities, n (%)					0.31
Diabetes mellitus, type 2	5 (24 %)		2 (25 %)		
Acute pancreatitis	0 (0 %)		2 (25 %)		
Chronic pancreatitis	5 (24 %)		3 (37 %)		
None	11 (52 %)		1 (13 %)		
Diagnosis, n (%)					0.99
Benign	8 (38 %)		3 (37 %)		
Malignant	13 (62 %)		5 (63 %)		
Histological diagnosis, n (%)					0.92
IPMN	7 (33 %)		1 (13 %)		
NET	3 (14 %)		1 (13 %)		
PDAC	5 (24 %)		3 (37 %)		
Other	6 (29 %)		3 (37 %)		
Neoadjuvant chemotherapy, n (%)					0.99
Yes	0 (0 %)		0 (0 %)		
No	21 (100 %)		8 (100 %)		
Type of Surgery, n (%)					**0.03**
Open total pancreatectomy	5 (24 %)		1 (13 %)		
Open PPPD	11 (52 %)		1 (12 %)		
Robotic-assisted distal pancreatectomy	4 (19 %)		6 (75 %)		
Open distal pancreatectomy	1 (5 %)		0 (0 %)		
Duration of Surgery (min)	260	83	204	46	0.18
Tissue Weight (g)	1.88	1.4	2.001	0.78	0.39
Localization of Specimen, n (%)					
Head	11 (52 %)		0 (0 %)		**0.02**
Corpus	3 (14 %)		3 (37 %)		
Tail	7 (33 %)		4 (50 %)		
Unknown	0		1 (13 %)		

Table 1: Isolation Characteristics. Depiction of patient-, surgery-, and specimen-related characteristics separated into two groups based on islet yield. IEQ, islet equivalent; SD, standard deviation; BMI, body mass index; IPMN, intraductal papillary mucinous neoplasm; PDAC, pancreatic ductal adenocarcinoma; NET, neuroendocrine tumor; PPPD, pylorus preserving pancreatoduodectomy.

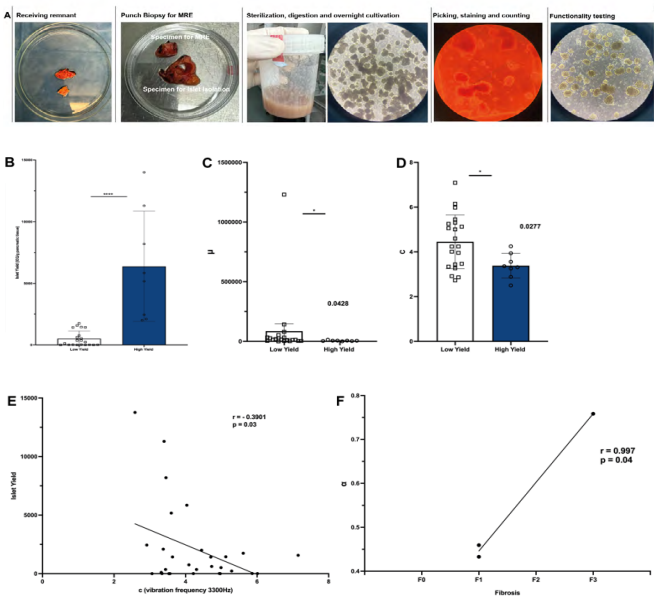

Figure 1: A) The process of islet isolation. **B)** A total of n=29 isolations were performed, and the isolations were separated into low yield (< 2000 IEQ, n=21) and high yield (> 2000 IEQ, n=8). The difference between both groups was statistically significant (504.1 ± 825.58 vs. 6381.72 ± 4478.54, p<0.0001). **C)** The shear viscosity μ was significantly higher in the LY group (86268.08 ± 271319.5 vs. 5735,96066 ± 3945,13, p=0.03). **D)** Shear wave speed c for the LY group was found to be significantly higher than for the HY group (2900 Hz: 4.451 ± 1.19 vs. 3.38 ± 0.55, p=0.02). **E)** Stiffer tissue with a higher vibration frequency c yielded significantly less islets than softer tissue (r=-0.3901, p=0.03). **F)** For n=3 isolations a significant positive correlation between the p-value and grade of fibrosis as evaluated from the pathologist was detected (r=0.997, p=0.03).

BOS60_05_6 ADENOSINE: A KEY REGULATOR OF ISLET INSULIN CONTENT AND A SHIELD AGAINST HYPOXIA INJURY

Quentin Perrier[1], Iori byers[2], Wonwoo Jeong[3], Rita Bottino[4], Christopher A. Fraker[5], Alice Tomei[5], Giuseppe Orlando[6], Amish Asthana[2]

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Background: Islet transplantation is an effective cell therapy for treating type 1 diabetes. However, a high therapeutic dose is required to achieve optimal glycemic control, as a significant proportion of islets is destroyed shortly post-transplantation due to oxidative stresses. Adenosine has been shown to decrease the metabolism of rat islets and, also to provide protection against ischemia-reperfusion injury. Therefore, the objective was to assess the impact of adenosine in preventing hypoxia-associated adverse effects on human islets viability and function.

Methods: Adenosine-treated human islets (1mM for 24h) were then subjected to 48h of hypoxia (1% O_2), followed by 2h of reperfusion (culturing in full oxygenated medium, 21% O_2), and then directly analyzed for viability (confocal imaging) and function by glucose-stimulated insulin secretion (GSIS) index (an index>2 suggested functional islets).

Results: Preconditioning of human islets with adenosine was able to prevent the deleterious effects of hypoxia. Hypoxia reduced islet viability compared to non-hypoxic control (72.7±6.8% vs. 91.4±0.3%, p<0.01), but adenosine treatment prevented the reduction in viability (81.5±5.3%, p<0.01 vs. hypoxia). Hypoxia also decreased the GSIS index compared to the control (0.68±0.42 vs. 4.80±1.98, p < 0.01), and adenosine prevented this reduction in the GSIS index (3.41±0.80, p<0.01 vs. hypoxia).

Conclusions: Adenosine preconditioning can protect human islets from the impact of hypoxia. These findings provide a strong support for incorporating adenosine preconditioning in bioengineered islet grafts for cell therapy in diabetes, to protect islets from necrosis that often occurs early during the engraftment period due to insufficient oxygen supply.

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BOS60_05_7 ASSESSING ONE-YEAR HBA1C AS A MARKER OF GRAFT SURGICAL AFTER PANCREAS TRANSPLANTATION

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Background: One-year graft survival is a key indicator of long-term function in pancreas transplantation. However, for patients with functional grafts at the one-year mark, reliable predictors of long-term outcomes remain poorly defined. This study investigates HbA1c levels at one year as a predictor of sustained graft function over the long term.

Methods: A retrospective cohort study using the UNOS registry on all simultaneous pancreas-kidney (SPK) transplants between 2017-2024. Regression models with multiple imputations for missing data were used to evaluate predictors of long-term function. Non-linear relationships were modelled with restricted cubic splines (RCS). Power calculations were conducted to compare the sample sizes between different outcome measures.

Results: There were 4,215 SPK transplants during the study period, of which 2,915 (69%) had a functioning graft at one year and >1 year of follow-up data. Median length of follow-up was 44 (IQR 25-60) months. HbA1c at one-year post-transplant was the strongest predictor of subsequent graft survival (Figure 1A). The relationship was non-linear in RCS analysis (p<0.01,Fig 1B). A higher one-year HbA1C of 6.8% (95th percentile) compared to 4.4% (5th percentile) was associated with poorer subsequent graft survival (aHR=4.13, 3.56-4.88). Sample size calculations found that one-year HbA1C, being a continuous measure, required fewer patients per group to achieve adequate power compared to using the binary outcome for graft failure at one year (Figure 2).

Conclusions: Recipient HbA1c at one year was the most important predictor of long-term pancreas graft function. This highlights its usefulness as a surrogate marker of outcome and supports its role in post-transplant monitoring. As a continuous outcome it can be an effective clinical trial endpoint, requiring far fewer participants than a trial powered for graft loss.

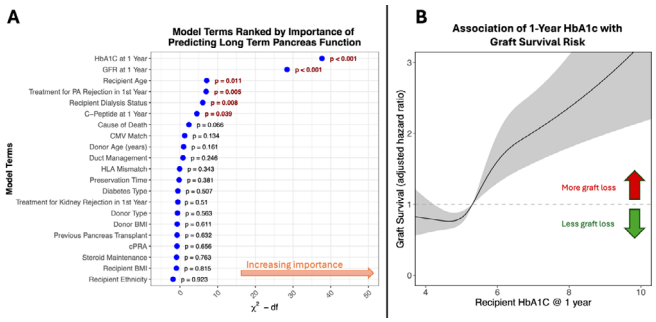

Figure 1. (A) Model terms ranked by significance in predicting long-term function. (B) Adjusted hazard ratio for graft survival based on recipient HbA1c at one year.

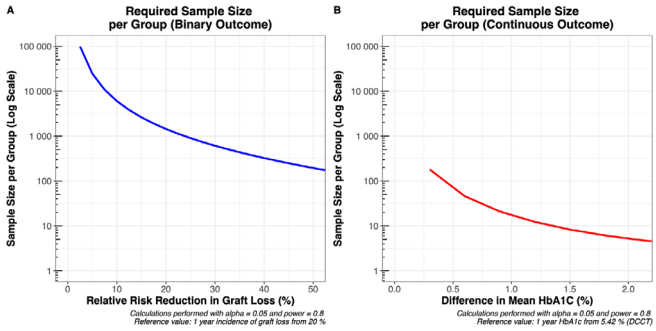

Figure 2. Sample sizes needed to detect the desired minimum clinically important difference along the range on the x-axis: (A) relative risk reduction in graft loss from 20% at one year, and (B) change in one-year mean HbA1c from 5.42%.

BOS60_05_8 BREAKTHROUGHS IN 3D PRINTING: FUNCTIONAL HUMAN ISLETS IN AN ALGINATE-DECM BIOINK

Quentin Perrier[1], Wonwoo Jeong[2], Arunkumar Rengaraj[2], Iori byers[3], Grisell Gonzalez[4], Emma Peveri[2], Jake B. Miller[2], emmanuel Opara[5], Rita Bottino[6], Alexei V. Mikhailov[7], Christopher A. Fraker[8], Alice Tomei[8], Sang J. Lee[9], Giuseppe Orlando[10], Amish Asthana[3]

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Background: Bioprinting human islets (HI) for beta-cell replacement therapy for treating type 1 diabetes (T1D) holds immense potential but faces challenges due to shear-induced HI damage, reduced functionality, and HI aggregation. Previous studies have mainly focused on animal-derived islets, with limited research addressing HI-specific bioink optimization and bioprinting parameters. This study aims to develop a scalable HI bioprinting methodology that preserves islet viability, functionality, and construct structural integrity for clinical applications.

Methods: HI were bioprinted in clinically applicable alginate-based bioinks, supplemented with decellularized human pancreatic extracellular matrix (dECM). Bioinks were optimized for rheological behavior, shear-thinning properties, and mechanical stability. Constructs were printed with an extrusion-based bioprinter using optimized parameters to minimize HI shear stress. Viability and functionality were assessed via live/dead assays, glucose-stimulated insulin secretion (GSIS), and immunostaining over 21 days in culture. Construct pore size and mechanical stability were evaluated for structural integrity, while high-density bioprinting (10,000 iEQ/mL) addressed scalability challenges.

Results: The optimized bioprinting parameters resulted in over 90% viability of HI (2,500 iEQ/mL, N=3 donors), with stable stimulus index (SI) comparable to free islets over 7 days. High-density printing demonstrated the potential for volumetric tissue manufacturing. The printing conditions resulted in over 90% viability and a significantly higher SI on day 21 compared to free islets (3.7 ± 0.6 vs. 2.6 ± 0.4). dECM-enriched constructs demonstrated long-term HI viability, with a significant absence of glucagon-insulin co-expressing cells.

Conclusions: This study has established a HI bioprinting platform for T1D therapy, by optimizing bioink formulations and printing parameters that resulted in enhanced HI viability, functionality, and construct structural stability. Functional high-density HI constructs were also successfully printed, paving the way for therapeutic applications. This strategy could address the delivery system requirements of various groups developing clinically relevant beta-cell replacement therapies.

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BOS60_05_9 CRYOGEL-BASED, PREVASCULARIZED BIOLOGICAL PLATFORM FOR ISLET TRANSPLANTATION

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Background: Intrahepatic islet transplantation restores insulin independence but is limited by donor scarcity, immunosuppression, and poor engraftment due to instant blood-mediated inflammatory reaction and inadequate vascularization. Subcutaneous transplantation is safer but hindered by hypoxia and slow revascularization. Hydrogels provide structural support but restrict cell migration, while cryogels, with large, interconnected pores, show promise but struggle to replicate native extra-cellular matrix (ECM) and support vascularization. Placenta-derived cryogels can closely mimic islet ECM, offering a promising alternative.

Methods: This study tested whether placenta-derived cryogels enhance islet transplantation outcomes by supporting islet survival and function. Hydrogels from human placenta were blended in varying ratios and crosslinked at subzero temperature into cryogels. Quality assessments included DNA quantification, structural integrity, and LC-MS/MS protein analysis. Pore interconnectivity, porosity, density, and water swelling capacity were measured. Rat (100 IEQ, n=4) or human islets (50 IEQ, n=3) were seeded on cryogels, function was assessed using static incubation.

Results: Cryogels showed DNA removal, successful decellularization, and intact structure. Composition analysis revealed collagen and glycoproteins comparable to commercialized Matrigel®. Different hydrogel ratios showed no differences in interconnectivity, density, porosity, though higher Collagen I content increased water uptake significantly. By Day 14, islets on cryogels showed improved or stable stimulation index (SI) values (1.54±0.57 to 2.18±0.4), while conventional cultures declined (1.15 to 0.90) and Matrigel dropped sharply (2.12 to 0.60).

Conclusion: These results highlight human placenta-derived cryogels as a sustainable, biocompatible, and functional promising scaffold for improving islet transplantation outcomes, providing an animal-free alternative to matrices like Matrigel®.

BOS60_05_10 EXPANDING PANCREAS DONOR POOL BY EVALUATION OF UNALLOCATED ORGANS: EXPLORE STUDY

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Background: Pancreas transplantation (PTx) is a widely accepted treatment for patients with type 1 diabetes mellitus (DM) and for patient undergoing total pancreatectomy due to benign diseases. However, the availability of suitable pancreas grafts remains limited by strict selection criteria. This study aimed to investigate histopathological features of pancreas organs from brain-dead donors that were unallocated to further characterize potentially suitable grafts.

Methods: This multicenter prospective study was conducted from November 2019 to November 2022. A total of 100 unallocated pancreases from brain-dead donors were evaluated. Donor quality of unallocated pancreases was assessed through Pancreas Allocation Suitability Score (P-PASS) and the Pancreas Donor Risk Index (pDRI). Macroscopic and histopathological assessments of discarded pancreases were also recorded. Associations between microscopic quality of pancreases with donor quality and macroscopic quality were analyzed.

Results: Nineteen percent of the pancreases had P-PASS < 17 and 24% had pDRI < 1. In addition, 35% of pancreases had unremarkable macroscopic and 31% had unremarkable microscopic characteristics. Out of 31 pancreases with unremarkable microscopic characteristics, seven pancreases (22.6%) had P-PASS < 17, 10 pancreases (32.2%) had pDRI < 1, and 14 pancreases (45.2%) had unremarkable macroscopic characteristics. There were no significant association between microscopic characteristics with P-PASS ($p = 0.541$), pDRI ($p = 0.194$), and macroscopic characteristics ($p = 0.153$).

Conclusions: Current allocation criteria for pancreas transplantation are failed to detect pancreases with unremarkable microscopic characteristics. Incorporating histopathological assessment into the allocation process could improve donor selection criteria. Further research is needed to correlate these findings with post-transplant outcomes and develop standardized evaluation protocols.

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BOS60_06_1 ETHICS OF IN-SITU AND EX-SITU PERFUSION TECHNOLOGY FOR ORGAN TRANSPLANTATION: A SCOPING REVIEW

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Background: Perfusion technology is increasingly utilized to check and/or enhance organ viability and improve transplant outcomes by circulating blood or preservation solutions through organs. While both ex-situ and in-situ techniques are used, they raise distinct ethical considerations which must be considered in deliberations about their implementation. Insight into the perspectives of patients, families, and the public is useful for understanding relevant ethical and psychosocial factors. This review aims to map the discussion in the literature on the ethical and psychosocial issues with organ perfusion technology, comparing in-situ and ex-situ techniques.

Methods: We employed a scoping review method to search Embase, Medline (all), CINAHL, PsycINFO, and Google Scholar for discussions on ethical issues or patient/family/public perspectives of perfusion technology in organ transplantation, with no date limits. Peer-reviewed journal articles and book chapters in English were included. Thematic analysis was utilized to extract and synthesize ethical and psychosocial themes and arguments.

Results: Of 2,377 records screened, 336 full texts were reviewed and 141 included. 89% of articles discussed in-situ normothermic regional perfusion (NRP) (67% in depth), most focusing on thoracoabdominal NRP and potential negation of death determination, harm to donors, and concerns about stakeholder trust and communication. 60% of articles discussed ex-situ machine perfusion (MP) (16% in depth), highlighting effects on allocation and its potential to ameliorate or exacerbate inequities. See Table 1 for descriptions of the themes. Research on stakeholder perspectives of perfusion and ethical analyses of MP were lacking.

Conclusions: Ex-situ MP has sparked less ethical debate than in-situ NRP, but MP requires attention, especially considering its impact on organ allocation. Qualitative research could clarify debated issues. This review can provide input for policy development.

Table 1. Description of ethical and psychosocial themes discussed in the literature on perfusion technology

Ethical or psychosocial theme	Description of Content
Determination of Death	- Negation or complication of death determination - Whether or not the dead-donor-rule (DDR) is violated by the technique - Impact on definition of death or DDR as a concept
Non-maleficence / Harm	Harm - Donor's ability to experience harm - Pre-mortem interventions (e.g. cannulation) - Risks of the procedure Conflict of interest (COI) - COI between donor (treatment or end of life care) and recipient - COI between transplant program and individual patient(s)
Dignity / Respect for Persons	Donor integrity and dignity - Whether or not respect owed due to the person or deceased body is fulfilled Autonomy: a person's freedom to decide what happens to their own body - Whether patient/family wishes are respected or not - Degree of patient/family involvement in decision making - Patient preferences
Beneficence / Utility (vs. costs)	Weighing the benefits of the procedure against costs/burdens - Clinical outcomes and quality of life for recipient - Societal outcomes: waitlist outcomes, organ utilization, lives saved - Costs and resources needed - Burdens and drawbacks - Current and future applications
Justice / Equity	Justice: Fairness or equity in distribution of resources, benefits, and burdens - Impact on access to transplantation/procedures and barriers to access (e.g. geographic) - Disparities / inequities improved or worsened Allocation and prioritization - Recipient selection - Patient prioritization - Impact of the technique on allocation patterns
Informed Consent and Communication	Informed consent and authorization (clinical and research) - Timing and content of conversations with patients/families about the technique - Communication with potential donors and the public about the technique Transparency and trust - Interplay between transparency about the technique and public trust in organ transplantation
Stakeholder Engagement	- Engaging patients, family, public, and healthcare workers in decisions about these techniques - Consideration of diverse beliefs and views - Degree of public acceptance and understanding of the technique
Sociocultural and Psychological Aspects	- Effects on grieving/dying process and rituals surrounding death - Cultural and religious issues - Interplay with societal understanding of life and death - Psychological effects on family and healthcare workers

BOS60_06_2 SOCIOECONOMICS, IMMIGRATION, ETHNICITY AND HEART TRANSPLANTATION IN ITALY: INTERSECTIONAL INSIGHTS

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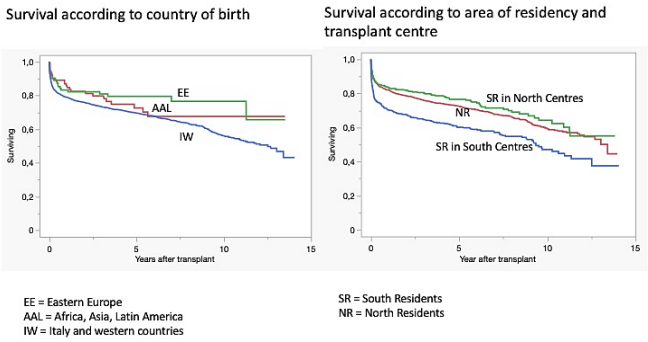
Background: The interplay between socioeconomic factors and ethnicity, highlighting the role of intersectionality, has been extensively related to transplant outcomes, particularly in private healthcare contexts. Yet, this interplay is less well understood in publicly funded healthcare settings. This study examines how factors potentially linked to disadvantage or discrimination affect heart transplant (HT) outcomes in Italy's public healthcare system.

Methods: This retrospective cohort study analyzed national data of all adult patients listed for HT in Italy (2010-2023). Indicators of potential disadvantage included immigrant status, non-Western background, socio-economic status (SES), and Southern Italian residency. Immigrant status, inferred from country of birth, was grouped into Italy/Western countries (IW), Eastern Europe (EE), and Africa/Asia/Latin America (AAL). SES was derived from residency ZIP codes. Endpoints included waitlist (WL) outcomes (transplantation, death) and post-HT survival.

Results: 4,527 patients were listed for HT (23% women; 8% foreign-born; 38% Southern residents, SR). SRs had significantly lower income than Northern residents (NR) (P<0.01) and worse 5-year HT survival (66% vs. 72%; P<0.01). EE and AAL patients were younger than IW (P<0.01) and had better unadjusted 5-year HT survival (72% vs. 79% vs. 69%; P=0.03), but the difference was age-dependent. While 99% of NRs were listed in their area, only 64% of SRs were listed locally. SRs transplanted in Northern centers had HT survival comparable to NRs (72%, 5-year); those in Southern centers had worse survival (59%; P<0.01) (**Figure**). WL mortality was similar across groups (P=0.4), but yearly WL rates per million were lower for Southern vs. Northern residents (4.9?0.8 vs. 6.1?1.8; P=0.07).

Conclusions: This study highlights the association of geographic and socioeconomic disparities with HT access and outcomes in Italy, particularly in Southern regions, where income levels are markedly lower. While the publicly funded healthcare system guarantees access to HT preserving good post-HT outcomes irrespective of birthplace or residency, healthcare infrastructure in underserved and economically deprived regions needs appropriate funding and support to ensure equitable HT access and outcomes across Italy.



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BOS60_06_3 ACCESS TO KIDNEY TRANSPLANTATIION FOR HIGHLY SENSITIZED PATIENTS: INSIGHTS FROM A FRENCH MULTICENTER STUDY

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Background: Kidney transplantation is the preferred treatment for end-stage renal disease, offering superior survival and quality of life compared to dialysis. However, highly sensitized patients face significant challenges in accessing transplantation due to anti-HLA antibodies developed during sensitizing events such as blood transfusions, pregnancies, or previous transplants. These antibodies prolong waiting times, increase mortality risk, and reduce transplantation opportunities. This study evaluates access to transplantation for highly sensitized patients in France, focusing on the cPRA (TGI: Incompatible Graft Rate) as a metric for prioritization and potential desensitization strategies.

Methods: A retrospective cohort analysis was conducted across 13 French centers, including 14,485 patients listed for kidney transplantation between 2011 and 2021. Patients were stratified into TGI categories: low (0%), moderate (1-84%), high (85-95%), and very high (96-100%). Cumulative incidence functions (CIFs) and Cox proportional hazards models assessed transplantation rates and competing risks of death.

Results: Results revealed that patients with TGI ≥96% had significantly reduced transplantation rates (50.6%) compared to those with lower TGI scores (e.g., 77.5% for TGI 0%). These patients also exhibited higher mortality risks, with 14.9% deaths in TGI ≥96% compared to 7.3% in TGI 0%. Access disparities were most pronounced in the highest TGI categories, with hazard ratios for transplantation decreasing to 0.08 (95% CI 0.05–0.12, $p < 0.0001$) in TGI 100%. Kaplan-Meier analysis demonstrated prolonged waiting times and reduced survival for highly sensitized patients, emphasizing the need for targeted interventions.

Conclusions: This study highlights the urgency of optimizing organ allocation policies and exploring desensitization strategies to improve transplantation access for highly sensitized patients. The findings underscore the critical need for prioritizing these patients in transplantation programs and developing standardized approaches to address their unique immunological challenges.

BOS60_06_4 OUTCOMES OF A SPECIALIZED BRAZILIAN HEART TRANSPLANT CENTER: AN 11-YEAR REVIEW

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Background: Multidisciplinary approaches are recognized as key to improving outcomes in heart transplantation (HTx), supported by public health policies and scientific evidence. In line with this, a Thoracic Organ Transplant Center was established at Brazil's largest university hospital. This study aimed to evaluate the impact of this center by comparing outcomes in two distinct periods: before (pre-center period - PCP) and after its establishment (center period - CP).

Methods: A retrospective cross-sectional study was conducted from 2002 to 2023, analyzing 1264 patients listed for HTx using data from the São Paulo State Health Department's Transplant Registry. Two eras were compared: PCP (2002–2012) and CP (2013–2023). Data were presented as absolute and relative frequencies, with statistical significance assessed using the Chi-square test ($p < 0.05$).

Results: In the PCP, 469 patients were registered, with 343 (73.1%) meeting priority criteria. Inotropic support (IS) was the most common prioritization (66.2%). During this period, 222 HTx were performed, 72.5% of which were for prioritized recipients, but 53.1% of prioritized patients died while waiting. In contrast, the CP saw a 70% increase in registrations (795 patients), 90.1% of whom were prioritized, representing a 108.7% rise compared to PCP. Intra-aortic balloon pump (IABP) emerged as the predominant prioritization method (53.8%), with a 288.9% increase in IABP-prioritized cases ($p < 0.001$). Despite a stable number of IS-prioritized patients (227 in PCP vs. 223 in CP), HTx for IS-prioritized patients decreased by 51.25%. During the CP, HTx procedures increased by 135% to 521, with 52.8% of recipients prioritized under IABP. Pre-HTx mortality also fell by 15.83%, and non-prioritized HTx cases dropped to 4.99% of procedures.

Conclusions: The establishment of this specialized center significantly increased transplant activity and prioritization rates, reflecting greater recipient severity. However, the persistent high waiting-list mortality underscores the need for improved allocation processes. Specialized centers like this play a crucial role in optimizing the use of available organs and enhancing outcomes in HTx.

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BOS60_06_5 EVOLUTION OF RACIAL EQUITY IN UK KIDNEY TRANSPLANTS: A 20-YEAR ANALYSIS. COBIT-UK STUDY

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Objective: To analyse ethnic disparities in kidney transplant access and outcomes between Black and White recipients in the UK (2000-2019).

Design: Retrospective cohort study using UK Transplant Registry data (COBIT-UK Study), employing multivariable Cox proportional hazards models, competing risk analyses, and time-varying coefficient models.

Setting: Comprehensive UK Transplant Registry & UK Renal Registry database.

Participants: 19,385 first-time kidney transplant recipients (Black: n=1,878, 9.7%; White: n=17,507, 90.3%), with a median follow-up of 8.4 years (IQR 4.2-12.7).

Main Outcome Measures: Primary outcomes included death-censored graft survival, all-cause mortality, and waitlist outcomes. Secondary outcomes included acute rejection episodes, delayed graft function, and cardiovascular events.

Methods: Time-to-event analyses using Cox regression models, adjusted for demographic, clinical, immunological, and geographical covariates. Competing risk analyses accounted for death as a competing event for graft failure. Sensitivity analyses explored regional-level variations.

Results: Annual transplant rates among Black recipients increased five-fold (49 to 250, p<0.001). Black recipients had lower odds of receiving living donor organs (OR 0.43, 95% CI 0.39-0.48, p<0.001) and longer median waiting times (948 vs 640 days, p<0.001). After adjustment for confounders, death-censored graft survival at 5 years was comparable between groups (HR 1.04, 95% CI 0.89-1.21, p=0.64). While Black waitlist candidates showed higher mortality (HR 1.56, 95% CI 1.32-1.85, p<0.001), post-transplant survival benefit was significant (HR 0.42, 95% CI 0.35-0.51, p<0.001). Competing risk analysis revealed no differences in cause-specific hazard of graft failure (sub distribution HR 1.08, 95% CI 0.92-1.27, p=0.34). Regional-level analysis showed minimal variation in outcomes (ICC=0.03).

Conclusions: Despite improved access to transplantation for Black recipients, disparities persist in living donation rates and waiting times. Post-transplant outcomes are comparable between groups. Targeted interventions to increase living donation in Black communities may further improve access to transplantation.

BOS60_06_6 INTERNATIONAL TRAVEL FOR ORGAN TRANSPLANTATION: A SURVEY OF GLOBAL ACTIVITY (1 JAN 2023-31 AUG 2024)

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Background: International travel for organ transplantation (ITOT) is widespread; World Health Organization data show 31 countries reported at least 600 patients had travelled abroad for transplantation in 2022; 22 countries reported 2600 transplants of non-residents.(1) However underreporting is common, and the global picture of current ITOT activities remains obscure.(2)

Methods: An international anonymous survey of transplant professionals was conducted online (16 Sep-15 Dec 2024). The questionnaire (available in English, French, Mandarin and Spanish) assessed respondents' most recent case experiences of providing care to individuals who had traveled to or from a country for living donation or transplantation. Data were analysed with descriptive statistics.

Results: 353 individuals from 64 countries completed the survey. 313 were clinically active between 1 Jan 2023 and 31 Aug 2024, during which 28% (n=89) had provided care for ≥1 incoming transplant recipient (iTR); 23% (n=72) for ≥1 incoming living donor (iLD); 27% (n=83) for ≥1 outgoing TR (oTR); and 8% (n=24) for ≥1 outgoing LD (oLD). Considering only their most recent iTR cases, 34% (n=30) were children <18 years; 52% received LD transplants; 51% received kidneys (29% liver; 22% heart or lung; 3% pancreas). Considering oTR cases, 12% (n=10) were children; 64% received LD transplants; 70% received kidneys (22% liver; 9% heart or lung; 1% intestinal). 69 countries were identified as destinations for transplantation among these cases. 40% of iTR and oTR cases reported were performed in the private health sector.

Conclusions: This study provides a novel snapshot of contemporary ITOT activities during a defined period, revealing the diversity of such activities and the complexity of global routes of travel. It confirms the substantive role of the private health sector in ITOT and highlights the need for more effective data collection and reporting mechanisms in many regions to ensure all transplant activities are recorded in national and global registries.

https://www.transplant-observatory.org/wp-content/uploads/2016/02/2022-data-global-report_VF_2.pdf.

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BOS60_06_7 DIAGNOSTIC YIELD OF KIDNEY DISEASE GENE PANEL TESTING DURING KIDNEY TRANSPLANT EVALUATION

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Background: Approximately 15% of patients with end-stage kidney disease (ESKD) do not have a primary renal disease diagnosis. Monogenic diseases are estimated to account for 10-15% of the overall prevalence of ESKD in adults. Since knowledge of the underlying kidney disease is crucial for ESKD management in the context of kidney transplantation (KT), we conducted genetic testing using massively parallel sequencing (MPS) to access the diagnostic yield in patients on the KT waitlist.

Methods: A total of 161 patients, waitlisted for KT between January 2023 and July 2024 in a single transplant center, underwent MPS kidney disease gene panel testing, containing 282 genes. We classified the variants according to the classification of the American College of Medical Genetics and Genomics.

Results: Out of the 161 patients on the KT waitlist, 46.6% of patients (n=75) did not have a definite renal diagnosis, while 53.4% (n=86) had a known etiology of ESKD after a thorough clinical evaluation. Patients with a known etiology were subcategorized by their primary causes as hereditary (n=9, all of whom had autosomal dominant polycystic kidney disease) or non-hereditary (n=77). Among the 152 genetically analyzed patients with non-hereditary or without a definite renal diagnosis, 9.2% (n=14) were found to carry pathogenic or likely pathogenic variants. Of these 14 patients, 6 had mutations that constitute the primary cause of their ESKD. 66.7% (4 out of 6) were found to carry *COL4A* mutations, and in two patients, variants other than the *COL4A* mutation (*COQ8B, PAX2*) were observed. In another 62.5% (n=96), we identified variants of unknown significance. Among them, one patient had a *CFH* mutation and was diagnosed with atypical hemolytic uremic syndrome after KT. As a result, MPS gene panel testing increased the proportion of hereditary cases from 5.6% to 9.3%.

Conclusions: MPS gene panel testing has benefits for defining precise renal diagnoses and unraveling the etiology of ESKD.

BOS60_06_8 FROM ENABLER TO PREDICTOR: THE TRANSFORMATIVE ROLE OF TECHNOLOGY IN ORGAN TRANSPLANTATION IN INDIA

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Background: The shortage of organs for transplantation is a global challenge, particularly in developing countries. South Asia, which comprises 25% of the world's population, accounts for only 10-11% of global transplants, with 90% of these procedures conducted in India. This disparity arises from systemic barriers such as limited awareness, mistrust in healthcare systems, and financial inaccessibility. Technology has emerged as a transformative tool to address these challenges, enhancing accessibility, affordability, and awareness in organ donation and transplantation programs.

Methods: MOHAN Foundation, a 28-year-old NGO, has utilized technology to drive progress in organ donation and transplantation through: • **Raising Awareness:** Utilizing social media and online courses to educate the public and training volunteers.• **Expanding Access:** Deploying telemedicine to enhance healthcare access in rural areas, significantly boosting women's participation in consultations. • **Educating Professionals:** Providing the only e-learning program for Transplant Coordinators in South Asia, training 1,530 professionals between 2020 and 2024. • **Enhancing Affordability:** Using crowdfunding platforms to support economically disadvantaged patients. • **Building Trust:** Developing digital organ-sharing registries and transparent processes to foster public trust. • **Results**: **Awareness**: Creation of a broad network of ambassadors who actively lead public education initiatives, triggering a chain reaction of awareness. • **Access**: Improved healthcare access through telemedicine. • **Professional Training**: Over 1,530 Transplant Coordinators trained online.

Affordability: Successful crowdfunding campaigns enabling approximately 100 economically underprivileged patients to undergo transplant surgeries during 2021-2024. • **Trust**: Increased transparency and trust through digital waitlist registries.

Conclusion: Technology has significantly reduced barriers to organ donation and transplantation in India. From raising awareness to employing predictive AI models, digital innovations are revolutionizing healthcare systems. By addressing these challenges and fostering collaboration, technology will continue to enhance equitable and high-quality organ transplant services globally.

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BOS60_06_9 DETERMINANTS OF KIDNEY ALLOGRAFT SURVIVAL IN THE EUROTRANSPLANT SENIOR PROGRAM (ESP)

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Background: Selecting suitable organs from elderly donors remains challenging. We aimed to identify prognostic factors to further improve allocation and utilization of kidneys donated in the European Senior Program (ESP).

Methods: 64 ESP-recipients transplanted at our center between 2017 and 2022 were retrospectively analyzed to identify factors associated with allograft survival. We also assessed the potential impact of an innovative deep-machine-learning-based (automated) analysis tool to assess IFTA and glomerulosclerosis – also applicable during allocation at typical off duty pathologist-times - by (re-)analyzing the 51 available corresponding pretransplant-biopsies.

Results: BMI disparities of ≤ 2.5 kg/m² between donors and recipients were associated with significantly lower prevalence of DGF (11.1%), compared to >2.5 kg/m² (36.9%, P<0.05). Univariable analyses indicated that BMI mismatch, higher recipient BMI, presence of heart disease and prolonged ischemia (CIT) significantly increased the odds of DGF. Each additional hour of CIT increased DGF-risk by 24% (P<0.05). In addition, we could not confirm the positive impact of HLA-DR matching recently reported for ESP-graft survival. Using a semi-automated deep learning quantification tool agreed very well with the pathologists-report (ICC = 0.913; 95% Confidence Interval = 0.85-0.95). Univariable analyses identified IFTA, the percentage of arteriolosclerosis, and glomerulosclerosis as significant risk factors for future graft failure. Glomerular density and arterial fibrosis did not reach statistical significance.

Conclusions: Overall, our ESP cohort benefits from transplantation, demonstrating superior survival when compared to data on continued dialysis. BMI disparity – as a potential matching parameter during allocation and in contrast to absolute BMI or heart disease as non-modifiable static factors- could be an easy tool for more individualized and successful allocations. Furthermore, automated histopathological AI analysis during allocation decisions may further optimize the organ-acceptance process and improve allograft survival within the ESP.

BOS60_06_10 BEREAVED RELATIVES' EXPERIENCES AND PERSPECTIVES ON DONATION AFTER OUT-OF HOSPITAL CARDIAC ARREST: A QUALITATIVE STUDY

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Background: Introducing novel donation processes such as uncontrolled donation after circulatory death, Maastrich category II (uDCD) have the potential to increase the donor pool and thus help reduce the gap between the demand and supply of donor organs. For countries that have not yet introduced uDCD, obtaining consent from relatives is a crucial factor that complicates implementation. Therefore, the aim of this study was to explore relatives´ experiences of a family member´s circulatory death after out of hospital cardiac arrest and to explore relative's perspectives of being asked to decide on organ donation in this situation

Methods: A qualitative design consisting of 13 semi structured interviews, conducted between March and September 2024. Reflexive Thematic Analysis was used as analytical tool for an inductive, descriptive analysis.

Results: The analysis generated three themes: 'Fluctuating between hope and despair', 'Exposed to vulnerability' and 'Balancing a major life change'. The main findings can be summarized as being vulnerable and feeling lonely in an extremely stressful situation. Trust in health care professionals was important to how experiences were perceived. Participants' reflections on organ donation immediately after death in out of hospital cardiac arrest were perceived as complex and difficult to decide on. However, if the deceased's wishes were known, communication was clear, the behaviours of the health care staff were compassionate and personal, relatives were given the opportunity to confirm death themselves and were given enough time to say goodbye, the decision about organ donation could be facilitated. Support and follow-up from healthcare was needed after a family member's circulatory death after out of hospital cardiac arrest.

Conclusions: To provide comprehensive quality care for relatives, knowledge and skills among the health care personnel and specific guidelines are needed for structured proactive support and follow-up, taking into consideration the specific context, communication and needs of relatives.

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BOS60_07_1 INEQUALITIES IN LIVER TRANSPLANTATION: DATA FROM EPA-RITY STUDY

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Background: Social determinants of health (SDOH) are increasingly recognized as key drivers of health outcomes. Income inequality, in particular, has emerged as a critical factor influencing access to care and treatment outcomes. Despite Italy's universal healthcare system, disparities persist, often challenging to quantify due to limited socio-economic data. Liver transplantation (LT) outcomes may be affected by factors such as income, education, and geographic location, influencing waitlist entry and progression. While these disparities are well-documented in countries with private or mixed systems, they remain underexplored in Italy. This study investigates the role of SDOH—particularly income—in shaping LT pathways, from waitlist enrollment to outcomes

Methods: This multicenter, retrospective study analyzed anonymized data from the national transplant database for patients listed for LT between 2010 and 2020. Income data were assigned to geographic areas based on postal codes. Linear and logistic regression models (odds ratios) were used to evaluate associations between income levels and LT outcomes, adjusting for individual and contextual confounders.

Results: We analyzed 9,397 patients with complete postal code data from a total of 13,947 listed for LT during the study period. Among these, 30.7% were under 50 years old, 40.6% were 51–60, and 28.7% were over 60; 73.6% were male. MELDNa scores at listing were 0–14 in 43.7%, 15–19 in 23.4%, 20–29 in 21.8%, and >29 in 9.9%. Foreign-born patients were 33% more likely to have a MELDNa >29 at listing (OR 1.33, p=0.07). Patients from higher-income areas (>€20,000) were 20% more likely to have a MELDNa <15. Waitlist durations were longer for women (+53 days) and residents of lower-income areas (+38–41 days). Organ failure at 6 months and 1 year increased with higher MELDNa scores but unexpectedly also with rising income levels.

Conclusions: Despite Italy's universal healthcare system, SDOH—especially income, gender, and migration status—significantly affect LT access and outcomes. These findings highlight the need for policies that integrate socio-economic factors into transplant planning to ensure equitable care.

BOS60_07_2 SURVIVAL ADVANTAGE OF PRE-EMPTIVE WAIT-LISTING IN ELDERLY KIDNEY TRANSPLANT CANDIDATES

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Background: In elderly patients, the survival benefit of organ transplantation from a deceased donor is controversial. We hypothesized that, in this vulnerable population, a successful transplant is more likely if patients are transplanted preemptively or shortly after dialysis initiation. This can be achieved by wait-listing kidney transplant candidates before starting dialysis to improve their chances of finding a match.

Methods: We analyzed data from the Catalan Registries of Organ Transplantation and Kidney Diseases (2014–2022). The study included patients aged ≥70 years who were either wait-listed preemptively ("Waiting List-First") or after starting dialysis ("Dialysis-First"). An inverse probability of treatment weighting (IPTW) for being wait-listed preemptively was calculated using a propensity score based on age, sex, diabetes, hypertension, BMI, cause of CKD, blood group, and maximum cPRA. Imbalance between groups was assessed using the absolute standardized difference (ASD). The primary outcome (death) was analyzed using IPTW-weighted Cox regression analysis.

Results: The final population included 1142 patients, of whom 912 were wait-listed after dialysis initiation, and 230 were wait-listed preemptively. Differences between the two groups showed adequate balance after IPTW application (Table 1). In the Dialysis-First group, 651 patients (71.4%) were transplanted a median of 711[470–1106] days after starting dialysis, while in the Waiting List-First group, 74 patients (32.2%) were transplanted preemptively, and 85 patients (36.9%) were transplanted a median of 369 [166–728] days after starting dialysis—a significantly shorter time compared to their counterparts (P<0.001). IPTW-weighted Cox regression analysis demonstrated lower mortality in the Waiting List-First group, with an HR[95%CI] of 0.55[0.41–0.74], P<0.001. Sensitivity analyses confirmed the robustness of the model in patients with diabetes (P=0.009) and without diabetes (P<0.001), as well as after excluding the 99th IPTW percentile (P<0.001).

Conclusions: Wait-listing elderly kidney transplant candidates before dialysis initiation substantially decreased the time required to find a match and significantly improved their survival.

	Dialysis First (n=912)	Wait List First (n=230)	ASD unweighted	ASD weighted
Age (years)			**0.280**	0.046
- 70-74	474/912 (52.0%)	151/230 (65.7%)		
- 75-79	342/912 (37.5%)	60/230 (26.1%)		
- > 80	96/912 (10.5%)	19/230 (8.3%)		
Sex (%males)	610/912 (66.9%)	153/230 (66.5%)	0.008	0.023
BMI	27.76 ± 24.40	26.56 ± 17.38	**0.263**	0.002
cPRA (%)			0.084	0.032
- 0%	431/912 (47.3%)	99/230 (43.0%)		
- 1-49%	242/912 (26.5%)	63/230 (27.4%)		
- 50-89%	184/912 (20.2%)	50/230 (21.7%)		
- > 90%	55/912 (6.0%)	18/230 (7.8%)		
Diabetes (%yes)	478/912 (52.4%)	79/230 (34.3%)	**0.370**	0.015
Hypertension (%yes)	807/912 (88.5%)	209/230 (90.9%)	0.078	0.035
Cause of CKD (%)			0.155	0.034
- Unknown	297/912 (32.6%)	92/230 (40.0%)		
- Diabetes	253/912 (27.7%)	35/230 (15.2%)		
- Hypertension	111/912 (12.2%)	29/230 (15.6%)		
- Systemic disease	24/912 (2.6%)	9/230 (3.9%)		
- Glomerular	116/912 (12.7%)	30/230 (13.0%)		
- Tubulo-interstitial	64/912 (7.0%)	17/230 (7.4%)		
- Hereditary	47/912 (5.2%)	18/230 (7.8%)		
Blood group (%)			0.063	0.007
- A	386/912 (42.3%)	102/230 (44.3%)		
- B	80/912 (8.8%)	18/230 (7.8%)		
- AB	22/912 (2.4%)	8/230 (3.5%)		
- 0	424/912 (46.5%)	102/230 (44.3%		

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BOS60_07_3 BRIDGING THE GAP: A PEER-SUPPORT PILOT TO INCREASE LIVING KIDNEY DONATION IN BLACK COMMUNITIES

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Background: Pre-emptive living donor kidney transplantation (LD) offers the best outcomes for end-stage kidney disease patients, yet significant disparities persist, particularly for Black patients. Over the past five years, the UK has seen a 29% increase in Black patients on the transplant list but a 10% decline in Black living donors. The Gift of Living Donation (GOLD) charity aims to address disparities by providing tailored peer support for Black patients & potential donors.

Methods: A one-year pilot program was implemented through an NHS-community partnership at 3 London hospitals. The program included clinical staff, a data team & GOLD's 70 trained & certified "phone buddies" to enhance support for living donation. The quality improvement initiative was iteratively adapted to address barriers such as patient identification, clinic referrals, & equitable access to information via multimodal methods (e.g., written materials, community events, & patient-approved SMS via Accurx).

Results: Of 2,002 Black and mixed-Black patients across 3 sites, 635 (32%) were identified as potentially eligible for transplantation and GOLD referral. Of these, 91% (575/635) were offered referral. From Feb 2023-24, 149 referrals were made, resulting in >180 hours of conversations about kidney transplantation. 17 potential living donors were identified, with 11 contacting their local transplant teams, leading to one successful transplant so far. A mixed-methods service evaluation, with a 28.1% response rate (36/128), revealed strong patient satisfaction. 35/36 respondents would recommend GOLD, 80.6% (29/36) reported a shift in their views on transplantation and health & 69.4% (25/36) felt confident discussing transplantation with loved ones. Key themes included enhanced understanding, confidence and sense of community support.

Conclusions: This NHS-community partnership demonstrates a scalable, effective model for increasing awareness & consideration of LD in Black communities. While behaviour changes & transplantation outcomes take time, this initiative has shown promising results, with high patient engagement and satisfaction. Future work will focus on integrating this model into the transplant pathway & refining approaches based on patient feedback to further support equitable access to transplantation.

Figure 1: Outline of eligible patients offered referral and interactions with GOLD peer buddy. Key outcome measures being number of eligible patients referred and potential living donors identified

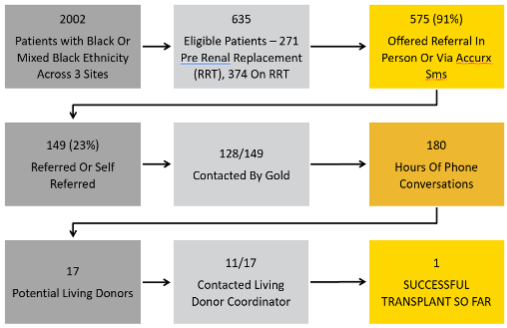
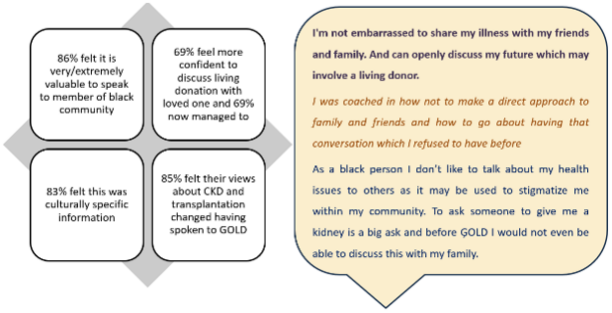


Figure 2: Patient feedback from service evaluation questionnaire offered to all referred patients with 36/128 respondents.



BOS60_07_4 THE LIVE PROJECT: ADVOCATE VOICES BRIDGING GAPS IN LIVING KIDNEY DONATION IN ITALY

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Background: Preemptive kidney transplantation is the best treatment for chronic kidney disease (CKD). Living donor kidney transplantation (LDKT) offers shorter waiting times and better outcomes compared to deceased donor transplantation. However, LDKT remains limited in Italy due to insufficient awareness among healthcare professionals (HCPs), patients, families, and the public, with the potential for inequitable LDKT opportunities. Promoted and led by the Italian Association for Hemodialysis and Transplant Patients (ANED) and partnering with the Italian National Transplant Center, the LIVE (LIVing kidnEy donation) project aims to increase LDKT uptake in Italy by enhancing knowledge, awareness, and attitudes. A unique aspect of the project involves individuals with personal LDKT experience educating HCPs, supporting potential donors and patients, and informing the public.

Methods: The project will target HCPs (e.g. nephrologists, nurses), patients/families, and the public. Focus groups and/or interviews will identify barriers, educational needs, and communication strategies. Individuals with LDKT experience will co-develop and deliver workshops, educational materials, and public campaigns, promoting evidence-based experiential messaging. Key Performance Indicators will assess changes in knowledge, awareness, attitudes, LDKT activity, and LDKT likelihood. Participant feedback and periodic reporting will monitor impact and guide continuous improvement.

Results: Expected outcomes include improved HCP knowledge and communication skills, increased discussions about LDKT benefits and risks, and greater patient and family empowerment in decision-making. Public campaigns aim to foster a more informed social environment. Leveraging lived experiences can enhance empathy and relatability across all stakeholder groups.

Conclusions: The LIVE project addresses knowledge gaps and inequitable LDKT opportunities in Italy. By actively engaging individuals with personal LDKT experience into education and advocacy, the initiative aims to foster collaboration among stakeholders, strengthen educational efforts, and enhance informed decision-making. Studies will assess the outcomes and sustainability of these interventions, establishing a replicable model for other contexts.

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BOS60_07_5 ASSOCIATION BETWEEN SOCIO-ECONOMIC FACTORS AND KIDNEY TRANSPLANTATION IN MUSLIM MAJORITY COUNTRIESGING GAPS IN LIVING KIDNEY DONATION IN ITALY

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Background: Muslim majority countries have heterogeneous stages of socio-economic development and infrastructure that may limit kidney transplantation opportunities. The aim of this study was to explore this data in Muslim countries and explore associations with socio-economic metrics.

Methods: Data was analysed for 50 global Muslim countries (classified if >50% of population described as Muslim). Organ donation/transplantation rates were obtained from the Global Observatory for Donation and Transplantation and International Registry on Organ Donation and Transplantation. Chronic kidney disease (CKD) data was obtained from the Global Burden of Disease Study 2021. Supplementary socio-economic and health data were obtained from data repositories including World Health Organisation, International Monetary Fund and the World Bank. Descriptive and comparative statistical analyses were performed using R version 4.4.2.

Results: The global Muslim population in 2023 was 1,877,263,750. Prevalence and death rates from CKD were 134,048,251 and 207,102 respectively. Organ donation and transplant activity data was only reported for 21/50 countries, with total kidney transplant activity 12,440 (deceased and living donor transplants 2,084 and 10,356 respectively). Countries that practiced deceased/living versus living donor only transplantation had higher GDP per capita ($12,986 versus $4,482, p=0.023) but no other significant difference. Countries that reported any kidney transplantation activity versus none had higher GDP per capita ($7,849 versus $2,211, p=0.013), higher adult literacy rates (96% versus 76%, p=0.017), higher life expectancy (74 years versus 68 years, p=0.007) and higher world economy ranking (66 versus 121, p<0.001).

Conclusions: People living with kidney failure in the Muslim world have sub-optimal access to kidney transplantation. While socio-economic factors are important, all barriers that prevent establishment of comprehensive organ donation and transplantation services must be overcome.

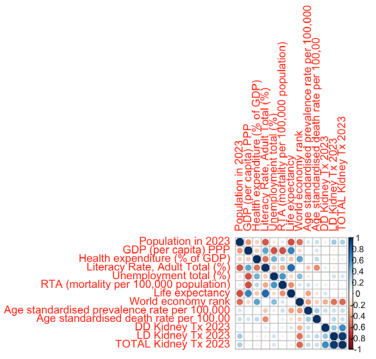

Figure. Heatmap showing correlations between socio-economic indicators with kidney disease rates and kidney transplant activity

Variable	Deceased donor kidney transplantation		Living donor kidney transplantation		Total kidney transplant activity	
	r	p value	r	p value	r	p value
Population in 2023	0.11	0.647	0.37	0.095	0.34	0.126
Gross Domestic Product (per capita)	0.02	0.929	-0.05	0.832	-0.04	0.880
Health Expenditure (% of GDP)	-0.03	0.896	-0.06	0.782	-0.06	0.786
Literacy Rate (& Adult Total)	0.09	0.692	-0.09	0.700	-0.05	0.841
Unemployment rate (%)	-0.03	0.896	0.07	0.777	0.05	0.844
Road Traffic Accidents (mortality per 100,000)	0.03	0.896	-0.12	0.593	-0.09	0.684
Life expectancy	0.17	0.453	0.03	0.904	0.08	0.742
World Economy rank	-0.38	0.088	-0.56	0.008	-0.59	0.005
Age standardized CKD prevalence rate (per 100,000)	0.19	0.402	0.17	0.448	0.21	0.372
Age standardized CKD death rate (per 100,000)	-0.06	0.808	0.41	0.396	0.64	0.527

Table. Correlations between socio-economic indicators with kidney disease rates and kidney transplant activity

BOS60_07_6 A MULTIDISCIPLINARY APPROACH TO IMPROVING PROCESSES: A TASK FORCE IN CHILE WITHIN THE ORGAN PROCUREMENT SYSTEM

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Background: Over the last decade, the use of machine learning (ML) techniques in problem modeling and solving has increased significantly, including in kidney transplantation. Numerous studies have used ML to predict outcomes such as delayed graft function (DGF). This study compares various ML models with logistic regression (LR) in predicting DGF, focusing on donor characteristics.

Methods: We analyzed 831 deceased donor kidney transplants performed between 1989 and 2020 across three transplant centers. The dataset included 14 donor, 7 transplant, and 60 recipient features. Four problem types were defined based on variable combinations: donor-only (D), donor + transplant (DT), donor + recipient (DR), and donor + transplant + recipient (DTR). The dataset comprised 44.7% DGF-positive and 55.3% DGF-negative patients, split into 80% for training and 20% for validation/testing. Six ML models—Support Vector Machine (SVM), Decision Trees (DET), Random Forest (RF), Gradient Boost (GB), Extreme Gradient Boost (XGB), and Multilayer Perceptron (MLP)—were compared with LR. Hyperparameters were optimized using Random Search and 10-fold Cross Validation. Accuracy was the primary performance metric.

Results: The best-performing model for each problem type achieved accuracies of 55% (SVM), 58% (XGB), 58% (RF), and 64% (XGB) respectively for D, DT, DR, and DTR. LR results were 47%, 62%, 55% and 60%. Across most models, significant predictors included donor creatinine and age, cold and warm ischemia times (transplant variables), and recipient calcium levels.

Conclusions: While most ML models outperformed LR, the differences were not substantial.This may be attributed to the small dataset size, which likely contributed to the overall poor performance. We recommend using these complex models with high-quality datasets that include a sufficient number of variables and observations to fully leverage their potential. The key question for future research is determining the dataset size required for ML to become the primary analytic tool for predicting kidney transplant outcomes.

	Accuracy	
Models	Best ML model	Logistic Regression
Donor	SVM: 55%	47%
Donor + Transplant	XGB: 58%	62%
Donor + Recipient	RF: 58%	55%
Donor + Transplant + Recipient	XGB: 64%	60%

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BOS60_07_7 PATIENT ENGAGEMENT IN EVALUATING CARDIOTHORACIC TRANSPLANT SERVICES AND POLICIES

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Background: The project explored how to align UK heart and lung transplant rates with international best practice[1]. The patient, carer and family perspective was integral to this activity, to evaluate current services and identify areas of best practice/ opportunities for improvement.

Methods: Government, healthcare and heart and lung transplant patient and family representatives worked collaboratively to co-create an online survey, which sought views about experience along the transplant care pathway. There was no time limit on when patients had received treatment or their current stage of the pathway. Patient representatives and transplant teams circulated the survey to their members/ patients. Responses were anonymous. Regular reviews were undertaken to inform targeted re-circulation to any groups with low response rates. Quantitative analysis of the results was undertaken of the multiple-response questions. Qualitative analysis was used for free text.

Results: There were 605 responses to the survey, a higher rate than anticipated. A breakdown of respondents is provided in Table 1. The responses have been vital to writing a report by three external experts.

Conclusions: The collaboration with patient and family representatives meant the survey language/ design was user-friendly for the target audience. Circulating the survey through 'trusted' routes including local and national charities rather than being publicised through Government, supported high levels of engagement. This, with the anonymity of responses, gave reassurance to respondents to provide honest feedback without fear of care being adversely impacted. Collaboration with patient groups also meant that specific patient groups could be targeted, to address gaps in survey responses. The collaborative approach led to an unprecedented level of response. The resulting data and feedback is being used to inform the future direction of heart and lung adult and paediatric transplant services in the UK.

Table 1 Demographic characteristics of patients surveyed

Factor	Level	N	%
Total		605	100
Type of respondent	Patient	528	87.3
	Carer	73	12.1
	Unknow	4	0.7
Age Group	0-5	5	0.8
	6-18	22	3.7
	19-35	59	9.8
	36-50	127	21.1
	51-65	273	45.3
	65+	116	19.3
	Unknown	3	0.5
Sex	Male	344	57.1
	Female	258	42.9
	Not specified	3	0.5
Ethnicity	White	538	88.9
	Asian	24	4.0
	Black	14	2.3
	Mixed	16	2.6
	Other	3	0.5
	Unknown	10	1.7
Stage of transplant process	Referred for assessment	28	4.7
	Completed assessment and awaiting decision	11	1.8
	Completed assessment and not suitable for waiting list	15	2.5
	On waiting list	40	6.6
	Suspended from waiting list	6	1.0
	Received a transplant in the last year	56	9.3
	Received a transplant over a year ago	433	71.9
	Unknown	16	2.7
Organ type	Heart	374	61.8
	Lung	198	32.7
	Heart and Lung	30	5.0
	Unknown	3	0.5

1. Organ and Tissue Donation and Transplantation Activity Report 2023 - 24, NHS Blood and Transplant, July 2024

BOS60_07_8 VALUE-BASED SURGICAL OUTCOME SCORE: A NOVEL METRIC TO PRIORITIZE PATIENT-CENTERED CARE IN HEALTHCARE ASSESSMENT

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Background: Rising healthcare costs demand a strategic reallocation of resources and the development of metrics that evaluate financial, patient-reported, and clinical outcomes comprehensively. Traditional surgical metrics often overlook cost and patient experiences. The novel Value-Based Surgical Outcome Score (VBS) integrates these aspects to enhance resource allocation and patient care across surgical disciplines.

Methods: The VBS Score combines patient satisfaction, quality of life (QoL), cost, and traditional surgical outcomes into a unified metric. It categorizes surgical disciplines and procedures into high, middle, and low priorities to guide resource distribution. This study utilizes simulation data of 5200 cases generated through Python, and surgical expertise to replicate real-world clinical scenarios. Data analysis was conducted using R.

Results: The VBS Score using simulation data ranked for example Cardiac, HPB Surgery, and Organ Transplantation as top priorities, with scores of 70, 69, and 69 respectively, indicating high patient satisfaction and QoL impacts. Lower-priority disciplines like Maxillofacial and Plastic/Reconstructive Surgery scored 53 and 51, respectively, showing lesser patient satisfaction and QoL. Statistical analysis revealed patient satisfaction and QoL as the most influential factors in the VBS Score ($r=0.81$&$r=0.80$, $p<0.001$).

Conclusions: The VBS Score effectively demonstrates the importance of integrating patient satisfaction, QoL, and cost into surgical prioritization. This framework aids in optimizing resource allocation and enhancing patient outcomes. By focusing on patient-centered care, healthcare institutions can improve clinical outcomes and potentially receive more funding and support. The VBS Score offers a comprehensive tool for assessing and prioritizing surgical care, promoting a value-driven approach in healthcare.

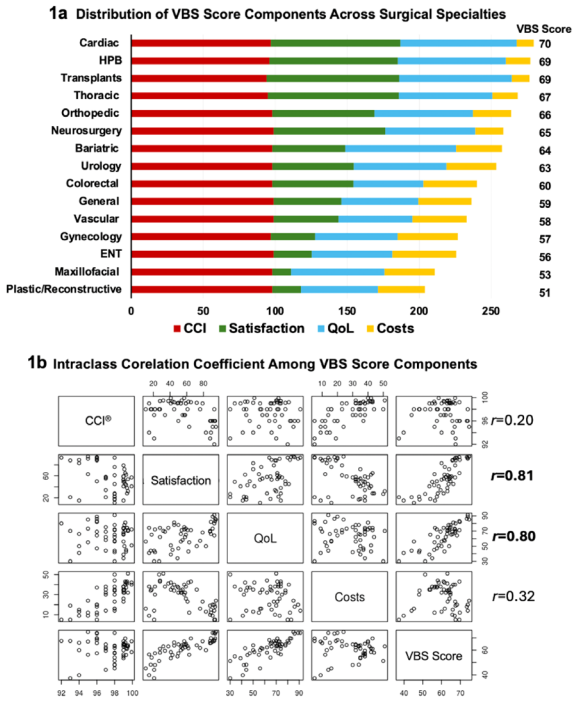

Figure 1a. Value-Based Surgical Outcome Scores (VBS) across surgical specialties. **Figure 1b.** Scatter plot illustrating the Intraclass Correlation Coefficient (ICC) among components of the Value-Based Surgical Outcomes Score (VBS).

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BOS60_07_9 IMPROVING PROMS FOR LIVING DONORS: BENEFITS AND CLINICAL PRACTICE INSIGHTS

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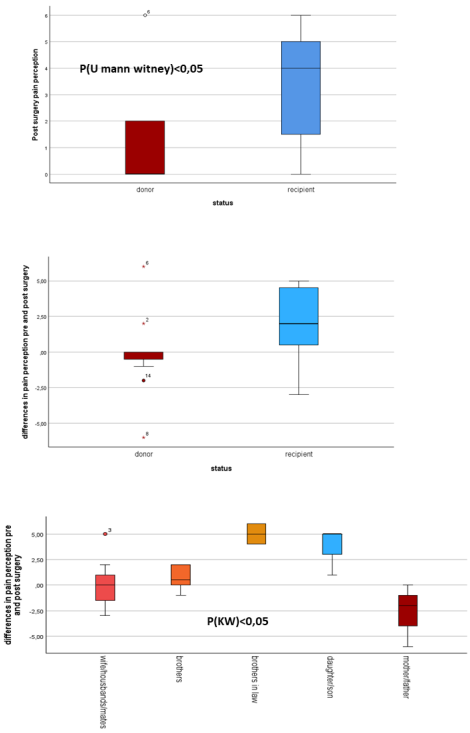
Background: Focusing on Patient-Reported Outcome Measures (PROMs) may reduce anxiety, shortens hospital stays, and improves compliance during the postoperative period. Rehabilitation interventions enhance minute ventilation, lowering the risk of pulmonary complications, fever, and coughing. These interventions are also associated with a higher prevalence of normal thoracic examinations and improved muscular strength levels, aligning with the principles of ERAS (Enhanced Recovery After Surgery).

Methods: These interventions have been evaluated in pairs enrolled in the living donor transplant pathway, introducing an informational and educational class with the surgeon and a facilitator nurse as part of quality improvement (DMAIC methodology). Data from 13 pairs over two years (2023–2024) were independently collected by the nursing coordinator.

Results: The multidisciplinary group handled the preoperative phase mapping the actual needs of patients. Functional assessments were effective for both donors (69,2 % women) and recipients (76,9% men), with average ages of 52,6 years (SD 14,4) and 52,6 years (SD 11,2), respectively. Non-parametric tests revealed significant differences pain levels based on donor status but there were no differences when variations in pre and post-surgery levels were evaluated (Mann-Whitney U test, p > 0.05). Some differences emerged in pain perception sorted by role, with brother in law, daughters and sons at higher level Data derived from donor committee revealed a general common fear concerning the graft function, and for all pairs a specific psychological support was required

Conclusions: Overall Patients experience improves with multidisciplinary team support, so dedicated preoperative discussions were included as part of standard procedures. Future directions include: to assess the correlation with predictive clinical outcomes, such as BMI and gain a better insight into the gender gap adjusting for specific clinical indicators.



1. Organ and Tissue Donation and Transplantation Activity Report 2023 - 24, NHS Blood and Transplant, July 2024

BOS60_07_10 THE NHSBT/OTDT ENVIRONMENTAL SUSTAINABILITY IN TRANSPLANTATION WORKING GROUP

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Background: Recognising the need to respond to the climate emergency, the Organ and Tissue Donation and Transplantation (OTDT) directorate of NHS Blood and Transplant (NHSBT) has set up the Environmental Sustainability In Transplantation (ESIT) working group.

Methods: Membership of ESIT was sought from across professional groups and organ types to cover the whole process from donation/retrieval through to transplantation and longer term care. Representation is included from the British Transplant Society (BTS), the Centre for Sustainable Healthcare (CSH), and wider NHSBT professionals working towards net-zero.

Results: ESIT convened in March 2023 and was formally integrated into the OTDT Clinical Team in July 2024, rapidly producing Terms of Reference, and a guide to immediate actions, available to all UK transplant centres. The “Top Tips on Making Transplantation Green in Your Unit” guide is available online[1] and has been circulated e.g. via NHSBT newsletters. ESIT provided consultative support to the Assessment and Recovery Centres Summer 2024 Spending Review bid and is a partner in NHSBT’s Transport Taskforce (currently being established). Deeper vision/strategy exercises have been undertaken in Dec 2024 / Jan 2025 clarifying scope and next key priorities e.g. embedding sustainable practice to reduce the environmental impact of transplantation, developing self-scoring dashboard metrics for units to understand their environmental impact, analysis of clinical pathways, and working towards reporting of environmental metrics via NHSBT. Formal launch is planned for March 2025 with a full communication strategy to engage with transplant healthcare professionals, and other organisations (including ESOT). Work has also begun on creation of a multi-agency Taskforce incorporating NHSBT, BTS, CSH and industry partners to leverage further funding.

Conclusions: Enabling the UK transplant community to respond effectively to the climate emergency is of critical importance. The creation of the ESIT working group within the OTDT Clinical Team is a key step in ensuring the right data, tools, and resources are made available to UK transplant centres to ensure the environmental sustainability of their services.

1. https://www.odt.nhs.uk/transplantation/making-transplantation-green/

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Challenges and breakthroughs in liver transplantation

BOS_08_01 MITOCHONDRIAL THERAPY DURING MACHINE PERFUSION RESTORES DCD LIVERS: A CROSS-CIRCULATION ASSESSMENT OF TRANSPLANTABILITY

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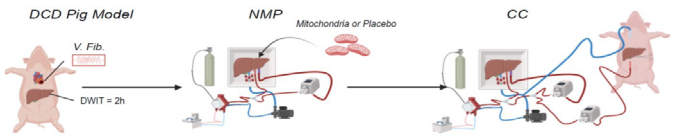
Background: Machine perfusion technology has improved DCD liver utilization, but with little expansion in the duration of acceptable warm ischemic time (WIT). To use livers with prolonged WIT, new strategies must be developed. Mitochondrial transplantation is such an innovative strategy.

Methods: Mitochondria were isolated from liver tissue of the C57BL/6 mice. In a porcine DCD model, following a 2 hour WIT, explanted livers were connected to normothermic machine perfusion (NMP) for 4 hours (n=12), and randomized to receive 5x10^9 xenogeneic mitochondria(n=6) or placebo(n=12). Upon completion of NMP, three livers from each group were connected to cross circulation (CC) (n=6) to test transplantability. The DCD cohort was compared to healthy control animals (n=9).

Results: After DCD donation, cell lysates exhibit a two-fold reduction in ATP levels, suggesting a loss of endogenous mitochondria. When exogenous mitochondria were added to healthy and ischemia reperfusion injury (IRI) exposed hepatocytes in vitro, only the IRI cells took up the mitochondria, confirmed by the change in ATP from baseline and through live single cell imaging. After 4 hours of NMP, treated livers demonstrated a significant increase in bile production, improved bile quality, and restored cytoarchitecture. After 6 hours of CC, untreated livers became edematous, and showed marked cellular degeneration, and near-complete loss of Kupffer cells and CK19+ cholangiocytes. In contrast, mitochondria treated livers maintained function and were comparable to healthy controls. There was a twenty-fold increase in TUNEL+ cells in the untreated livers. The proteomic profiles of bile and liver tissue revealed distinct differences in expression between treated and placebo groups during NMP. These differences became significantly pronounced following CC. Ultra high-plex spatial imaging using MACsima™ found differential populations of CD3, CD4, HH3, PCNA, Ki67, CD45, vimentin, IBA1, CD163 and LEA positive cells between both NMP cohorts and the treated CC cohort with very few viable cells in the non-treated CC samples.

Conclusions: These data confirm that NMP alone cannot restore a DCD liver with extended WIT. Mitochondrial transplantation restores function in these livers, presenting a promising approach to further expand the donor pool.



Experimental overview and technique for mitochondrial transplantation, machine perfusion and cross circulation. To produce a DCD model ventricular fibrillation was induced. Warm ischemic time (WIT) was 2 hours after which livers were retrieved and then perfused using normothermic machine perfusion (NMP) for 4 hours, receiving either mitochondrial transplantation or placebo. Finally, livers were connected via NMP to a living recipient to establish a cross circulation (CC) approach for evaluation of translatability. In the CC model the a. hepatica and the portal vein were ligated on the recipient. CC was maintained for 6 hours.

BOS_08_02 LONG-TERM FOLLOW-UP AFTER HYPOTHERMIC OXYGENATED MACHINE PERFUSION IN DCD LIVER TRANSPLANTATION

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Background: Transplantation of liver grafts from donors after circulatory death (DCD) is associated with an increased risk of nonanastomotic biliary strictures (NAS) post-transplantation. Previous studies have shown that dual hypothermic oxygenated machine perfusion (DHOPE) of DCD liver grafts reduces the incidence of NAS and acute cellular rejection (ACR). However, long-term outcomes are scarce. The aim of this study is to assess the 5-year incidence of NAS and ACR in a post-hoc analysis of our multicenter international randomized controlled DHOPE-DCD Trial (ClinicalTrials.gov number NCT02584283).

Methods: Between January 2016 and July 2019, recipients of DCD liver grafts in six European centers were randomly assigned to receive the liver either after DHOPE (machine perfusion group) or after (conventional) static cold storage group (control group). Primary endpoint was incidence of symptomatic NAS at 5-year follow-up. Secondary endpoints included ACR, graft and patient survival.

Results: A total of 78 patients were included in the machine perfusion (MP) group and 78 patients in the control group. The incidence of NAS was 6% vs 18% at 6 months and 14% vs 26% at 5 years, respectively, in the MP group compared to the control group (HR 0.47, 95% CI 0.23-0.99; p = 0.048). Incidence of ACR was 9% vs 15% (p = 0.221) in the MP group vs control group. In a subgroup of patients with immune-mediated diseases, who are at a higher risk of ACR, the incidence of ACR was significantly lower in the MP group: 0% vs 32% (p = 0.036). Graft and patient survival were similar.

Conclusions: Long-term results of DHOPE were excellent, with a significantly reduced incidence of NAS at 5 years follow-up and in patients at higher risk of ACR the incidence of ACR was reduced.

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Challenges and breakthroughs in liver transplantation

BOS_08_03 IMPACT OF EXTRACORPOREAL BLOOD FLOW ON CELIAC TRUNK FLOW DURING ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION: A PILOT STUDY

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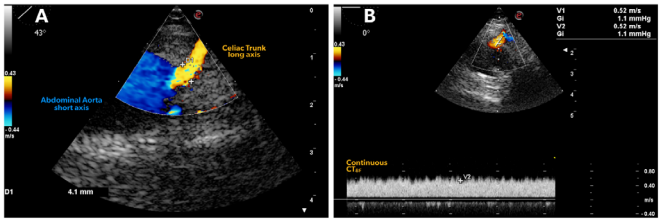
Background: The ideal extracorporeal blood flow (EBF) to be provided during abdominal-normothermic regional perfusion (A-NRP) is still debated. To evaluate the impact of variable EBF on restoring perfusion, we measured the blood flow through the celiac trunk (CT_{BF}) in donors undergoing circulatory determination of death (DCDDs) and A-NRP.

Methods: In this pilot study, we assessed CT_{BF} in six controlled DCDDs. CT was visualized antemortem with transesophageal ultrasound (TEU). The use of TEU is our standard of practice to guide cannulation, and endovascular balloon occluder positioning/inflation. The TEU probe was advanced to transgastric position, with abdominal aorta in short axis (figure). If normal anatomy, CT appeared as the first major branch. CT diameter was measured before withdrawal of life sustaining measures. Being a cylinder-like structure, CT cross sectional area (CSA_{CT}) was calculated as: $CSA_{CT} = [(CT\ diameter)/2]^2 \times \pi$. The velocity of CT_{BF} over time was visualized by pulsed-wave doppler, and its curve traced to obtain velocity-time integral (VTI_{CT}). VTI_{CT} was multiplied by CSA_{CT} to achieve systolic CT_{BF}, which was multiplied by antemortem heart rate to obtain CT_{BF} in L/minute. During NRP, post-mortem, a continuous EBF is generated by the circuit pump, so velocity/time profile becomes linear. The VTI_{CT} was assessed over one second and multiplied by 60, to obtain CT_{BF} in L/minute (figure). This measurement was repeated with EBF set at 40% (CT_{BF40}), 60% (CT_{BF60}), and 80% (CT_{BF80}) of the predicted cardiac index (CI) commonly used during normothermic cardiopulmonary bypass in adults (2.4 L/min/m^2 multiplied by body surface area).

Results: Results of CT_{BF} measurements during NRP, and their relationship with antemortem CT_{BF}, are displayed in the table. $CI_{40\%}$ was never enough to reproduce antemortem CT_{BF}. $CI_{60\%}$ was adequate in half of the donors, specifically if BSA < 2 m_2. $CI_{80\%}$ was above or largely above antemortem CT_{BF} in all but one donor.

Conclusions: Targeting an optimal, donor adapted, EBF during A-NRP could improve the results of organ recovery form DCDDs. Too high EBF may be harmful for splanchnic circulation, and difficult to be maintained without an excessive volume expansion. Too low EBF might impair organ perfusion. Implementing CT_{BF} assessment in larger cohorts of DCDDs may assist in defining this goal.



CT_{BF} during A-NRP is calculated as:
$CT_{CSA} = [CT_{diameter}\ cm/2]^2 \times \pi$
$CT_{BF/s}$ ml/second = CT_{CSA} $cm^2 \times CT_{VTI}$ cm with VTI calculated over 1 second
CT_{BF} ml/min = $CT_{BF/S}$ ml x 60

Use for transesophageal ultrasound to measure CT_{BF}. A. CT visualized in long axis through colour doppler as the first branch arising from the abdominal aorta; $CT_{diameter}$ is measured. B. VTI of the CT continuous blood flow during A-NRP. A-NRP, abdominal normothermic regional perfusion; CT_{BF}, blood flow through the celiac trunk per minute; $CT_{BF/s}$, blood flow through the celiac trunk per second. CT, celiac trunk ; CT_{CSA}, celiac trunk cross sectional area; $CT_{diameter}$, celiac trunk diameter; VTI, velocity time integral.

Donor BSA m^2	CT Antemortem Diameter cm	CT Antemortem VTI_{CT} cm	CT Antemortem CT_{BF} L/min	CT Post Mortem Diameter cm	Measurements during NRP: Blood Flow 40% CI set EBF LPM	VTI_{CT} cm	CT_{BF} ml/min	Blood Flow 60% CI set EBF LPM	VTI_{CT} cm	CT_{BF} ml/min	Blood Flow 80% CI set EBF LPM	VTI_{CT} cm	CT_{BF} ml/min
1.60	0.5	20	451	0.6	1.5	24	407	2.3	40	678	3.1	52	882
1.71	0.6	23	617	0.6	1.7	29	498	2.5	39	661	3.3	45	763
1.86	0.6	18	417	0.6	1.8	15	254	2.7	26	441	3.6	39	661
2.00	0.6	53	694	0.6	1.9	15	271	2.9	28	475	3.8	30	509
2.10	0.8	23	693	0.8	2.0	14	422	3.0	20	603	4.0	24	723
2.46	0.8	41	1009	0.7	2.3	26	600	3.4	35	808	4.6	50	1154
Percentage of measurements equal to/greater than antemortem CT_{BF}							0			50			83.3

NRP CT_{BF} measurements lower than antemortem CT_{BF} are highlighted in red; CT_{BF} measurements equal to/greater than antemortem CT_{BF} are highlighted in green. BSA, body surface area; CI, cardiac index, calculated as 2.4 L/min/m^2 of BSA (according to Du Bois formula); CT, celiac trunk; CT_{BF}, celiac trunk blood flow; EBF, extracorporeal blood flow; LPM; lier per minute; NRP, normothermic regional perfusion; VTI, velocity-time integral; VTI_{CT}, celiac trunk velocity-time integral.

BOS_08_04 OUTCOMES OF NORMOTHERMIC REGIONAL PERFUSION VS. SEQUENTIAL HYPO- AND NORMOTHERMIC MACHINE PERFUSION

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Background: To address the donor shortage, extended criteria donors after circulatory death (ECD-DCD), are increasingly used. However, ECD-DCD livers bear higher risk of primary non-function and biliary complications. Two main perfusion techniques exist to asses liver function: in-situ abdominal normothermic regional perfusion (aNRP), and ex-situ normothermic machine perfusion, in our center combined with dual hypothermic oxygenated perfusion and controlled oxygenated rewarming (DHOPE-COR-NMP; DCN). This study presents a single center comparison of aNRP and DCN of clinical outcomes of ECD-DCD livers.

Methods: Liver grafts from ECD-DCD donors between October 2018 and the end of December 2023 were included, with a minimum follow-up of 1 year post-transplantation. Livers were categorised as ECD based on factors such as elevated donor laboratory values, or age above 61 years. When the donor was located in the local procurement region, aNRP was performed, otherwise DCN was performed. The primary outcome was death-censored graft survival. Secondary outcomes included acceptance rate, patient survival and post-transplant biliary complications.

Results: In total, 48 aNRP and 37 DCN procedures were performed, which resulted in 36 (75%) and 26 (70%) liver transplantations. At one year, death-censored graft survival and overall patient survival rates were 97% and 100% in aNRP and 92% and 84% for DCN (not significant for death censored graft survival, p=0,02 for patient survival). One year cumulative incidences of non-anastomotic strictures (NAS), anastomotic strictures, and bile leakage were 3%, 20% and 8% in aNRP and 12%, 20% and 16% in DCN. Complications resulting in a Clavien Dindo score of 3 or higher were observed in 53% of aNRP and 69% of DCN. All these differences were not statistically significant.

Conclusions: The results in this cohort confirm that both aNRP and DCN allow for safe transplantation of ECD-DCD livers with excellent death-censored graft survival and patient survival. There was no difference in the risk of post-transplant biliary complications. In comparison with the NAS occurrence in controls from historical cohorts without machine perfusion, we have shown excellent results.

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Challenges and breakthroughs in liver transplantation

BOS_08_05 NORUDCA REDUCES APOPTOSIS AND ENHANCES VIABILITY DURING NORMOTHERMIC MACHINE PERFUSION OF TRANSPLANT-DECLINED LIVERS

Laurin Rauter[1], Jule Dingfelder[2], David Pereyra[3], Sertac Kacar[4], Moriz Riha[4], Nikolaus Becker[4], Tina Saffarian Zadeh[5], Konstantinos Mengrelis[4], Markus Wahrmann[6], Andreas Salat[5], Gerd Silberhumer[4], Thomas Soliman[7], Dagmar Kollmann[8], Gabriela A. Berlakovich[9], Georg Gyoeri[10]

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Background: Normothermic machine perfusion (NMP) provides a platform for ex vivo therapeutic interventions. NorUrsodeoxycholic acid (norUDCA), a bile acid with anti-inflammatory and anti-fibrotic properties, has been studied for treating cholestatic and metabolic liver diseases. This study explores norUDCA therapy during NMP in declined extended criteria donor (ECD) livers.

Methods: 18 livers underwent NMP, with 9 receiving norUDCA treatment after 2 hours. Bile and perfusate composition were analyzed to assess liver viability. Biopsies were collected pre- and post-NMP for mRNA and miRNA sequencing. Apoptosis markers were measured in perfusate samples using a Luminex-based human apoptosis panel. Donor variability was addressed by analyzing relative dynamic changes following norUDCA treatment for each graft.

Results: NorUDCA treatment during NMP enhanced miRNA (32 vs. 8) and mRNA (554 vs. 245) differential expression and mRNA-miRNA interactions (206 vs. 36). Gene set enrichment analysis highlighted apoptotic processes as strongly regulated. Apoptosis markers in the perfusate rose within the first two hours of NMP, but norUDCA treatment at two hours significantly reduced cleaved PARP levels after six hours (p=0.014) and p53 levels (6h: p=0.010; 12h p=0.040). Delta 2-6h values for active caspase-3 (p=0.018), Bcl-2 (p=0.040), cleaved PARP (p=0.024), and Cytochrome c (p=0.030) were significantly reduced. NorUDCA also improved biliary viability, with higher bile bicarbonate levels (3h: p=0.026; 4h: p=0.016; 5h: p=0.030) and lower bile AST (8h: p=0.017) and ALT (8h: p=0.004; 12h: p=0.026) concentrations, although no differences were observed in perfusate transaminases. Treated grafts showed improved viability, evident in more livers meeting transplant criteria after 12 hours (8/9 vs. 3/9, p=0.016).

Conclusions: Our findings demonstrate that norUDCA treatment during NMP improves graft viability in livers initially deemed unsuitable for transplantation, with 8 out of 9 livers meeting transplant criteria compared to 3 out of 9 controls. NorUDCA may also mitigate bile toxicity effects on the ischemia-injured biliary tree and act overall anti-apoptotic. These results highlight the potential of norUDCA as a therapeutic intervention during NMP to improve outcomes in ECD liver grafts.

BOS_08_06 BREAKING THE AGE BARRIER: LIVER TRANSPLANTATION USING OCTOGENARIAN DONORS, A SINGLE CENTRE EXPERIENCE WITH 582 CASES

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Background: Elderly donors belong to extended criteria donors (ECD) category and their use has allowed to expand organs pool for liver transplantation (LT). Herein we report our experience with LT from over 80 years old donors (ED).

Methods: A single-center retrospective analysis was conducted from January 2009 to December 2024, taking into account donor characteristics, pre-, intra- and post-operative data of LT recipients.

Results: 582 LT using organs from ED were performed. Median donor age was 83.5 years and most of them died from cerebrovascular accident (CVA) (81.2%), including 8 donors after cardiac death (1.3%). Recipients' median age was 57.04 years and 70% were males. Most frequent indication for LT was hepatocellular carcinoma (HCC) (43%). The median MELD Na score prior to transplantation was 11. Mean cold ischemia time was 430 minutes and machine perfusion (MP) was for 23 grafts (3.9%). Overall patients survival was 92.5%, 88.7% and 85.5% at 12, 36 and 60 months respectively, whereas graft survival was 89.4%, 85% and 81.8%. We also observed following conditions: early allograft disfunction 23 (3.9%), hepatic artery thrombosis 11 (2%), ITBL 37 (6.3%). Additionally, 32 recipients (5.4%) underwent early or late re-LT.

Conclusions: Use of ED for LT has been accepted and justified given the favorable outcomes reported. Our experience highlights its feasibility, especially in terms of graft and patient survival rates. Although it is considered a challenge, benefits of using ED outweigh the risks because they dramatically alleviate the organ shortage crisis, expanding donor pool in an epoch where LT indications expand as well. Our findings support the use of ED for LT, demonstrating that donor age, plus optimized allocation strategies, should not be a contraindication for organ donation anymore.

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Challenges and breakthroughs in liver transplantation

BOS_08_07 CHANGING THE LANDSCAPE OF LIVER TRANSPLANT IN THE US: IMPACT OF NMP IN A SINGLE CENTER

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Background: In 2021, normothermic machine perfusion (NMP) was approved for clinical use for liver transplantation in the United States. Since that time, NMP has been rapidly adopted as a resource to improve access to transplantation. Here we describe our early single-center experience in establishing an NMP program.

Methods: Retrospective analysis was conducted of the first 100 livers undergoing NMP after program implementation in July 2022. Final analysis included 53 donation after brain death (DBD-NMP) and 39 donation after circulatory death (DCD-NMP) grafts. Eight grafts not meeting viability criteria did not proceed to transplant. Propensity-matched historic cohorts (DBD-H and DCD-H) were developed from transplants performed between January 2018 and July 2022. Donor risk index (DRI) score and degree of macrosteatosis (MaS) served as markers of graft risk. Post-operative outcomes assessed include early allograft dysfunction (EAD), primary non-function (PNF), re-operation during index admission, ICU length of stay (LoS), inpatient LoS, biliary and arterial complications, need for renal replacement therapy (RRT), and 1-year survival.

Results: NMP cohorts trended to greater mean DRI scores than historic cohorts. A larger proportion of DBD-NMP grafts had moderate or severe MaS. Patient outcomes were comparable, including rates of EAD, PNF, re-operation, arterial or biliary complications, and survival. Increased ICU LoS (17.17 vs 8.96, p=0.03) and post-operative RRT (27.40 vs 22.77, p=0.18) were noted in the DBD-NMP cohort, although differences in inpatient LoS (27.40 vs 22.77, p=0.18) and prolonged RRT (9.43% vs 3.77%, p=0.44) did not reach significance [Table 1].

Conclusions: This single-center study demonstrates that implementation of NMP can facilitate safe transplantation of marginal grafts in the burgeoning US context. Further analysis is warranted to optimize graft selection for NMP and elucidate the impact of NMP on national donor graft utilization and waitlist times.

Table 1. Donor Characteristics and Recipient Outcomes

Donor	DBD-NMP (n=53)	DBD-H (n=53)	*p*-value	DCD-NMP (n=39)	DCD-H (n=39)	*p*-value
Steatosis, n (%)	(n=36)	(n=38)		(n=24)	(n=29)	
Microsteatosis	1 (2.78%)	1 (2.63%)		0 (0.00%)	2 (6.90%)	
Macrosteatosis						
Minimal (0-5%)	18 (50.00%)	14 (36.84%)	0.18	23 (95.83%)	18 (62.07%)	0.07*
Mild (5-14%)	7 (19.44%)	16 (42.11%)		1 (4.17%)	6 (20.69%)	
Moderate (15-30%)	3 (8.33%)	2 (5.26%)		0 (0.00%)	2 (6.90%)	
Severe (>30%)	6 (16.67%)	2 (5.26%)		0 (0.00%)	1 (3.45%)	
Undefined	1 (2.78%)	3 (7.89%)		0 (0.00%)	0 (0.00%)	
Donor risk index score	(n=50)	(n=53)				
	1.39 (0.27)	1.34 (0.29)	0.20	1.86 (0.24)	1.80 (0.30)	0.37
Recipient						
Early allograft dysfunction	11 (20.75%)	8 (15.09%)	0.61	5 (12.82%)	7 (17.95%)	>0.99
Primary non-function	0 (0.00%)	0 (0.00%)	>0.99	0 (0.00%)	1 (2.56%)	>0.99
Re-operation during index admission	21 (39.62%)	12 (22.64%)	0.09	7 (17.95%)	8 (20.51%)	>0.99
ICU length of stay after OLT	17.17 (30.47)	8.96 (12.47)	**0.03**	6.46 (5.41)	11.18 (13.56)	0.11
Inpatient length of stay after OLT (days)	27.40 (30.77)	22.77 (27.50)	0.18	17.64 (18.33)	23.67 (21.23)	0.13
Biliary complications	10 (18.87%)	8 (15.09%)	0.80	14 (35.90%)	10 (41.67%)	0.46
Arterial complications	3 (5.66%)	2 (3.77%)	>0.99	5 (12.82%)	2 (5.13%)	0.43
Post-operative renal replacement therapy	22 (41.51%)	11 (20.75%)	**0.04**	9 (23.07%)	16 (41.03%)	0.15
Post-operative renal replacement therapy >14 days	5 (9.43%)	2 (3.77%)	0.44	3 (7.69%)	7 (17.95%)	0.31
1-year patient survival	49 (92.45%)	47 (88.68%)	0.74	37 (94.87%)	34 (87.18%)	>0.99

Bold values are statistically significant $p<0.05$

*Criteria for chi square test not met due to small number in certain categories

Analysis performed in GraphPad Prism

BOS_08_08 LIVER GRAFT STEATOSIS PREDICTION FROM SMARTPHONE PICTURES AI-BASED ANALYSIS DURING PROCUREMENT

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Background: Assessing precisely graft hepatic-steatosis (HS) in the time-sensitive environment of liver transplant is necessary to lowering liver-dysfunction risks after transplantation or to transplant marginal livers. Yet, histopathological analysis of biopsied liver remains the gold-standard for assessing HS, despite being invasive and time consuming. Previous works were published on the use of artificial intelligence (AI) to assess HS levels through pictures. Through this study we evaluated a machine learning based algorithm on a high number of smartphone pictures to predict liver graft steatosis during procurement.

Methods: Eight French liver teams from tertiary transplant centers collected pictures and biopsies of livers pre-clamping during procurement. A segmentation model was developed to only keep the liver from the pictures, and finetuned to keep the edges of the graft fully visible. The segmented pictures were used to train different image recognition architecture, and eventually Auto-Machine Learning (Auto-ML) provided the best results. Three different types of models were trained: 2 classes with a threshold at 30%; 3 classes with 30% and 60% as thresholds; 4 classes with thresholds at 5%, 30% and 60% HS.

Results: A total of 627 pictures were recorded and correlated with graft biopsies. The analysed population was imbalanced with 396 (63,16%) under 5% of HS, 131 (20,89%) between 5% and 30% of HS, 76 (12.12%) between 30% and 60% of HS and 24 (3.82%) above 60% of HS. Of the 627 data points, 126 and 124 were used for model validation and testing respectively. To manage data imbalance, data augmentation, stratified sampling, and randomized undersampling were used on the data. Our results showed an accuracy and recall of 93%-93%, 86,4%-86,4% and 78,9%-78% for the 2 classes, 3 classes and 4 classes models respectively.

Conclusions: These results comfort our hypothesis that image recognition AI can be used to evaluate steatosis levels precisely. Given the low number of testing data concerning high HS livers, our results need to be confirmed with additional HS livers.

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Challenges and breakthroughs in liver transplantation

BOS_08_09 TRANSCRIPTOMIC ANALYSIS OF PROLONGED HYPOTHERMIC MACHINE PERFUSION IN HUMAN DONOR LIVERS

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Background: Liver transplantation is traditionally performed around the clock to minimize cold ischemia time. While normothermic machine perfusion can extend preservation to bridge the night, it induces profound molecular alterations due to active liver metabolism at 35-37°C. In contrast, hypothermic machine perfusion (DHOPE) at 8-12°C maintains a low metabolic rate (~10%) while providing oxygen to restore mitochondrial energy debt. In a previous clinical trial, prolonging DHOPE up to 24 hours (DHOPE-PRO) enabled safe daytime transplantation. In this study we analyzed the molecular effects of prolonged versus short DHOPE during perfusion and after reperfusion.

Methods: This post-hoc analysis utilized liver tissue samples from the DHOPE-PRO trial. Donor livers were categorized into prolonged (PRO; >4h) and conventional (CON; 2h) DHOPE groups. Liver biopsies were obtained at three timepoints: before and after DHOPE, and after reperfusion in the recipient. Transcriptomic changes were analyzed through bulk RNA sequencing using the Smart-3SEQ protocol.

Results: The median total DHOPE time was 9.3h (IQR, 8.0-10.1) in the PRO group (n=12) and 2.2h (IQR, 2.0-2.4) in the CON group (n=12; p=0.01). A total of 59,251 transcripts were identified. Differential gene expression analysis revealed no significant differences between groups prior to DHOPE. By the end of DHOPE, 18 transcripts showed statistically significant changes (p<0.05, >2-fold change). Upon reperfusion in the recipient, minimal transcriptomic changes were observed, with only 31 differentially expressed transcripts between groups. Functional enrichment analysis identified no significant Gene Ontology biological processes at any timepoint.

Conclusions: Prolonged DHOPE prior to liver transplantation induces minimal transcriptomic changes compared to conventional short-duration DHOPE. These findings further support the safety and feasibility of prolonging cold preservation duration with DHOPE to enable daytime transplantation.

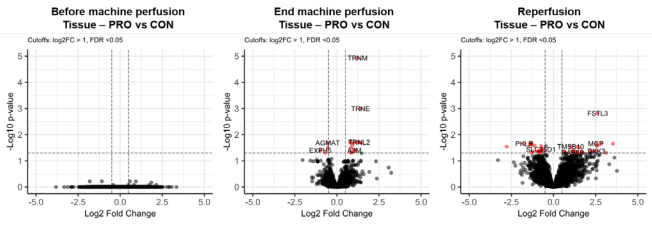

Figure 1. Differential gene expression of prolonged versus conventional (D)HOPE

BOS_08_10 EXTERNAL VALIDATION OF THE UK DCD RISK SCORE IN THE SWISS COHORT: A RETROSPECTIVE MULTICENTER COHORT STUDY

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Background: Donation-after-circulatory death (DCD) liver transplants are a growing source of organs. However, there is a need for careful selection due to the reported higher risk of graft loss. The aim of this study was to externally validate the performance of the UK DCD Risk Score developed to predict transplant futility.

Methods: We conducted a national multicentric retrospective cohort study including all DCD liver transplants between January 2012 and December 2023. The primary outcome was the same as in the model development study, which was a binary outcome of graft loss or death within the first-year post-transplant. The secondary outcome was time to graft loss or death, whatever occurred first, during a 10 year time period. We fitted the primary outcome using a logistic model with the UK DCD Risk Score as the predictor variable. We also tested the effect of the organ preservation technique.

Results: We analyzed data from N=252 DCD liver transplants. 53 graft losses or deaths occurred within the first year (primary outcome) and 75 events altogether (secondary outcome). The UK DCD Risk Score was not predictive in our cohort. The odds ratio for the interquartile difference for a change from 7 to 11 points in the UK DCD Score was 1.03 (95%-CI 0.73−1.4; p=0.98). The discrimination performance was at a chance level; the AUC was 0.50 (95% CI 0.41−0.59). The two-year survival probabilities (95% CI) for the low-risk, high-risk, and futile groups according to the UK DCD Risk Score were 0.76 (0.59–0.86), 0.72 (0.60–0.80), and 0.72 (0.63–0.80); without a different survival probability between the three risk groups (p=0.82). Nevertheless, we observed that the low-risk group had no events 2 years post-transplant. Regarding preservation, static cold storage only (n=19) had 5 (26.3%) graft losses, hypothermic oxygenated machine perfusion (HOPE) (n=195) had 45 (23.1%), and normothermic regional perfusion (NRP) (n=38) had 3 (7.9%). NRP had an odds ratio of 0.23 (95%-CI 0.07 to 0.81) versus HOPE as the reference, showing weak evidence of a benefit of NRP (p=0.07; overall effect of preservation).

Conclusions: At the time of preservation techniques, the UK DCD Risk Score was not able to predict futility in the Swiss cohort and shouldn't be the sole criteria to discard an organ. We found a trend towards better outcomes after NRP compared to HOPE.

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BOS_08_11 MESENCHYMAL STROLL CELLS-DERIVED EXTRACELLULAR VESICLES RECOVER ENERGETIC STRESS IN RAT LIVER NORMOTHERMIC PERFUSION

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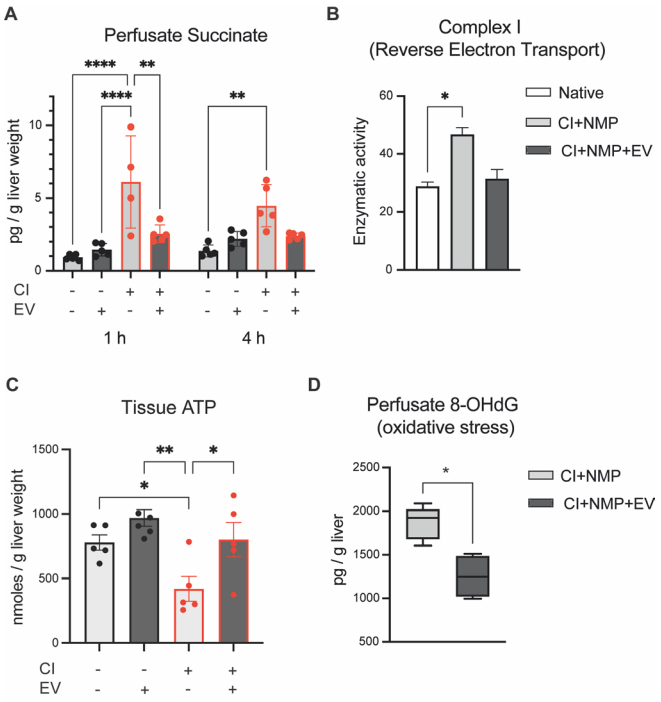
Background: Ischemia-reperfusion injury (IRI) still represents a critical challenge in liver transplantation, even in the era of machine perfusion (MP). Cellular energetic stress and mitochondrial dysfunction are key drivers of injury exacerbation. This study explores the therapeutic potential of mesenchymal stromal cells-derived extracellular vesicles (EVs) to preserve energetic homeostasis and mitochondrial function in rat livers subjected to normothermic MP (NMP).

Methods: An established rat model of NMP was used. After procurement, livers were either immediately perfused for 4h (n=10) or exposed to 30min-cold ischemia (CI) and then to 4h-NMP (n=10). EVs (NMP+EVs and CI+NMP+EVs, n=5 each) or an equal volume of saline (NMP and CI+NMP, n=5 each) were directly added to the perfusion fluid. Perfusate samples were collected throughout the procedure, biopsies were taken at the end of NMP. Liver specimens collected from rats in resting conditions were used as reference samples (Native, n=5).

Results: Consistent with previous data, ischemic livers exhibited succinate accumulation, flavin mononucleotide (FMN) release, activation of reverse electron transport (RET), and severe ATP depletion. EV treatment effectively reversed such ischemia-induced deleterious effects, by restoring a condition comparable to livers not exposed to CI. Moreover, EVs were associated with improved AMP/ATP ratios and prevention of AMP-activated protein kinase activation, a key regulator of response to energy depletion. Decreased concentrations of oxidative stress markers, cell death factors, and pro-inflammatory cytokines were likewise observed in EVs-treated livers compared to the CI+NMP group.

Conclusions: These findings support the potential of EVs as a tool to preserve mitochondrial function and promote energy recovery, while mitigating inflammatory imbalances. These positive actions could significantly contribute to enhance organ viability and function in marginal livers during NMP.



BOS_08_12 FERROPTOSIS INHIBITION IN A PRECLINICAL MODEL OF LIVER TRANSPLANTATION AFTER CIRCULATORY DEATH

Lene Devos[1], Nicholas Gilbo[2], Joris Blondeel[3], Tom Vanden Berghe[4], Jacques Pirenne[5], Diethard Monbaliu[6], Ina Jochmans[7]

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Background: Ferroptosis, a regulated form of cell death, promotes inflammation post-transplantation through the activation of both innate and adaptive immune cells. The clinical significance of ferroptosis in solid organ transplantation is increasingly recognized. Modulating ferroptosis emerges as a potentially viable strategy to mitigate complications following liver transplantation. We hypothesized that flushing warm ischemically damaged porcine livers with a cold preservation solution supplemented with a ferroptosis inhibitor (UAMC-3203) may reduce ischemia reperfusion injury (IRI) and improve liver function in our validated isolated liver perfusion model.

Methods: Ten porcine livers were exposed to 60 minutes of warm ischemia, procured and flushed with 1L IGL-1® containing 10 mg/kg UAMC-3203 (n=5) or no treatment (controls, n=5), prior to 4 hours of static cold storage in the same conditions, and followed by 6 hours of whole blood normothermic reperfusion (as a surrogate for liver transplantation). Perfusate and bile samples were taken every hour during reperfusion and were analysed to assess IRI severity [aspartate transaminase (AST)], liver function (bile production), markers of lipid peroxidation/ferroptosis [malondialdehyde (MDA)] and inflammation (IL-1β, IL-6, TNF-α, IL-8, IL-10).

Results: UAMC-3203 treatment significantly reduced perfusate AST concentrations during reperfusion (Figure 1A), whilst bile production increased compared to controls (Figure 1B). MDA concentrations in perfusate were significantly lower in treated livers (Figure 1C). Pro-inflammatory cytokines (IL-1β, IL-6, TNF-α, IL-8) in perfusate were upregulated in both groups (data not shown). However, increased levels of IL-10, an anti-inflammatory cytokine, were observed after UAMC-3203 treatment (Figure 1D).

Conclusions: Ferroptosis inhibition with UAMC-3203 reduces IRI and improves liver function. Changes in ferroptosis and anti-inflammatory markers confirm therapeutic efficacy of UAMC-3203 against IRI. These findings support the therapeutic potential of ferroptosis inhibition early on in the transplantation process. Supplementation of preservation solutions with ferroptosis inhibitors warrants further investigation in both static and dynamic preservation settings.

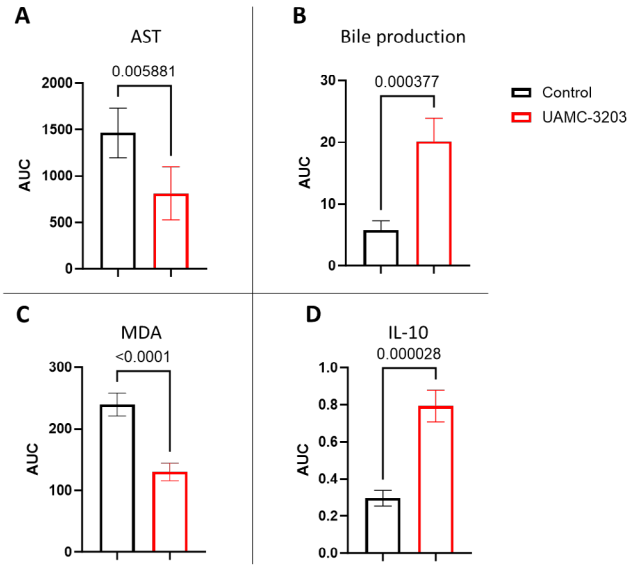

Figure 1.

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Challenges and breakthroughs in liver transplantation

BOS_08_13 PREDICTIVE VALUE OF MICRORNAS DURING EX SITU NORMOTHERMIC MACHINE PERFUSION OF HUMAN LIVERS

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Background: Normothermic machine perfusion (NMP) allows for the evaluation of liver graft functionality prior to transplantation. However, standardized and certified biomarkers remain unavailable. Circulating microRNAs (miRNAs) have emerged as sensitive indicators of tissue injury and cell function. This study investigated the dynamics of perfusate miRNAs during liver NMP and their association with clinical and biochemical parameters.

Methods: Human livers (N=44) underwent NMP for up to 24 hours (h). Serial perfusate samples were collected at 1h, 4h, 6h, 12h, and at the end of NMP for routine lab work. The hepatomiR® kit (TAmiRNA) was utilized to measure perfusate levels of miR-151a-5p, miR-122-5p, and miR-192-5p. Outcome of transplanted livers were assessed based on the occurrence of early allograft dysfunction (EAD).

Results: During the discovery phase, a total of 120 perfusate samples from 24 individual liver perfusions revealed significant differences in miRNA levels between transplanted and non-transplanted livers at all time-points. Notably, these differences were evident as early as 1h of NMP for all analyzed miRNAs (miR-151a-5p: p=0.0002; miR-122-5p: p=0.0003; miR-192-5p: p<0.0001). These trends were confirmed in the performance analysis of the validation cohort (N=20), with significantly elevated levels of miR-151a-5p (p=0.0075), miR-122-5p (p=0.0202) and miR-192-5p (p=0.0191) in non-transplanted livers at 1h NMP, compared to transplanted livers. Moreover, miR-122-5p levels at the end of NMP corresponded with posttransplant EAD (p=0.0165).

Conclusions: Measurement of perfusate miRNAs using the hepatomiR® kit during NMP represents a reliable tool for evaluating liver quality and predicting early graft function posttransplant. Importantly, significant differences in miRNA levels were detectable as early as 1h of NMP.

BOS_08_14 MITOCHONDRIAL TRANSPLANTATION REDUCES INURY AND IMPROVES FUNCTION IN A PORCINE MODEL OF HEPATIC ISCHEMIA/REPERFUSION

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Background: We hypothesized that mitochondrial transplantation (MitoTx) via portal vein infusion during reperfusion would be hepatoprotective in a survival porcine model of liver ischemia/reperfusion (I/R).

Methods: Male Yorkshire pigs (38±1kg) were subjected to 2 hours of ischemia in the left hemi-liver (left portal-triad clamping), and at the beginning of reperfusion (marked as t=0h), animals were randomized to receive a 1-hour infusion of mitochondria (Mitos, 6.71x109/kg) or saline (controls) via the portal vein. Mitos were autologous, isolated from Rectus abdominis muscle (10g). Mitos viability was assured by membrane potential measurement using JC-1. Follow-up ended at t=24h. Liver tissue oxygen saturation (SO2) was assessed by photoacoustic imaging. Two-way ANOVAs with Tukey's tests were used, and hazard ratios (HR [95% CI]) were computed with Cox models.

Results: Twelve pigs (6 MitoTx vs. 6 controls) underwent 2-hour left hemi-liver I/R. All pigs recovered and were ambulatory at t=6h. MitoTx reduced peak AST levels at t=2h reperfusion compared to controls (300±47 vs. 879±255 U/L; p=0.049). At t=24h, MitoTx pigs had lowered necrosis area percentage (4±2 vs. 17±7%, p=0.08) in left lobes, compared to controls– all right lobes had 0% necrotic area. MitoTx pigs had shorter prothrombin time, plateauing around t=8h (12.9±0.3 vs. 14.1±0.1s; p=0.003), faster lactate clearance (<2 mmol/L) from the blood (HR: 1.3, [1.1, 1.7]; p=0.003) and from the bile (HR: 1.4, [1.1, 1.7]; p=0.009) compared to controls. At t=6h, MitoTx pigs had decreased IL-6 (304±71 vs. 686±87 pg/mL; p=0.009) and a trend toward increased IL-10 at t=2h (22.1±7.7 vs. 6.4±4.4 pg/mL; p=0.113) in plasma, compared to controls. Photoacoustic imaging showed a reduction in SO2 in the left lobe in both groups after clamping, with a better SO2 recovery after clamp release in MitoTx pigs than in controls. Fluorescent imaging revealed that deep-red-labeled mitochondria were sequestered in the liver and kidney with no signal in the spleen or lungs (t=0-6h). At t=24h, no surgical or MitoTx-related adverse events were observed.

Conclusion: MitoTx reduces I/R injury and improves liver function after prolonged porcine hemi-liver I/R, showing promise in liver transplantation with the emergence of donation after circulatory death and machine perfusion.

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BOS_08_15 CHARACTERIZING THE PERFUSATE METABOLOME OF DONOR LIVERS UNDERGOING MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) has rapidly come into practice as a platform to assess donor liver function. However, existing viability markers poorly identify graft dysfunction, and the *ex vivo* metabolome is poorly understood. We performed a metabolomic analysis of livers during NMP to characterize the signatures of livers donated after brain death (DBD) and circulatory death (DCD).

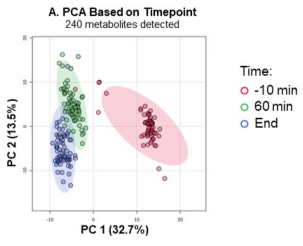
Methods: A total of 195 perfusate samples were collected at baseline (T-10), 1 hour (T60), and end of NMP (TEnd) from 68 donor livers perfused with the OrganOx *metra*. The mean NMP duration was 10.99 hours (SD = 3.02). Metabolomics analysis was performed using Orbitrap IQ-X Tribrid coupled with HILIC Amide separation with both targeted and untargeted approaches. Statistical analysis was performed with MetaboAnalyst 6.0 and GraphPad Prism 10.3.1.

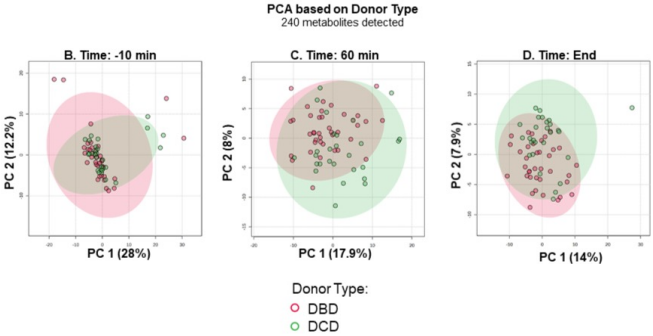
Results: Perfusate showed distinct clustering per timepoint and clear temporal changes (Fig. 1A). Perfusate by donation type was similar and further homogenized as NMP progressed (Fig. 1 B-D). Specific metabolites varied significantly in DCD vs. DBD perfusate at T60 and TEnd (Fig. E-G). N6-Acetyl-L-Lysine was greater in DCD livers at T60 and TEnd (Fig. 1H). Arginosuccinic acid was greater in steatotic livers at T60 (Fig. 1I).

Conclusions: As we seek to maximize utilization of donor organs, metabolic analysis could guide rigorous and safe evaluation during machine perfusion and even direct study into functional differences. The characterized trend towards metabolic equilibrium during perfusion could inform liver viability assessment timing, perhaps supporting stronger consideration of marginal livers that may "equalize" after some duration of NMP. Our novel results also show dysregulation of acetylated compounds, including N6-Acetyl-L-Lysine, within DCD and/or steatotic grafts. Already implicated in fatty livers, the acetylation pathway could be studied as a possible biomarker or therapeutic target during perfusion. In addition, steatotic livers, which present greater risk for reperfusion injury, showed elevated arginosuccinic acid. This compound is broken down during removal of ammonia, and its accumulation is a sign of dysfunction. Understanding the molecular underpinnings of perfusion could refine transplantation practices to improve patient outcomes.

Donor type	N=
DCD	29
DBD	39
Macrosteatosis grade	**N=**
Mild (<10%)	53
Moderate (10-30%)	4
Severe (>30%)	7

Table 1: Donor liver characteristics.





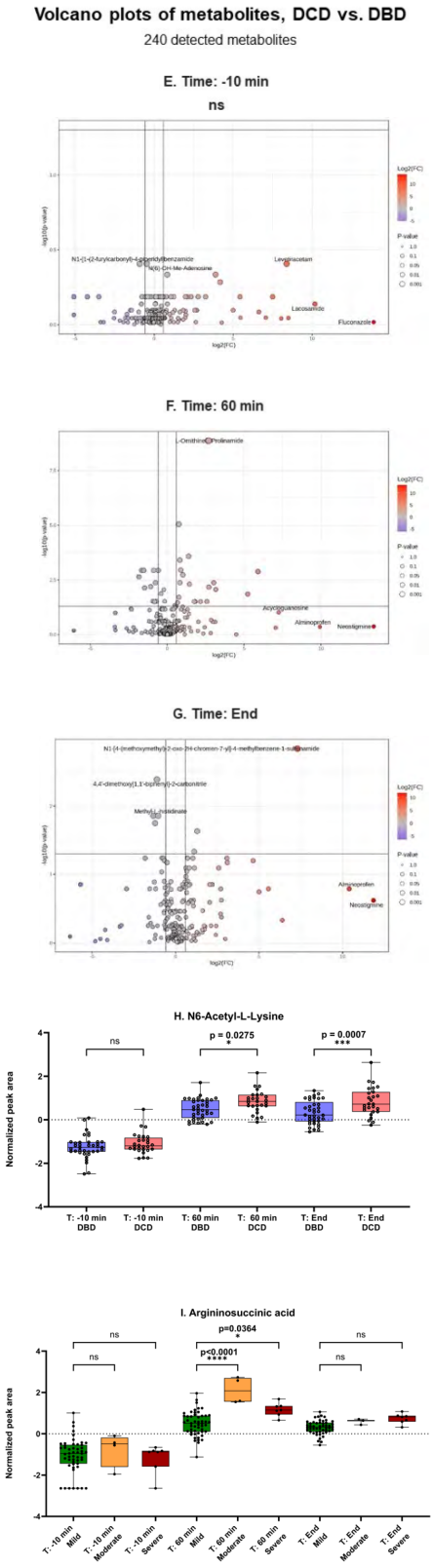


Figure 1: Metabolic signature of donor liver perfusate samples. **A:** Principal component analysis (PCA) of perfusate by timepoint (n=195). **B, C, D:** PCA of samples stratified by donation type at T-10 (n=65), T60 (n=66), and TEnd (n=64), respectively. **E, F, G:** Volcano plots of metabolites in DCD vs. DBD livers at T-10, T60, and TEnd, respectively. **I:** Quantification of N6-Acetyl-L-Lysine in perfusate by donation type (n=195). **H:** Quantification of argininosuccinic acid in perfusate by macrosteatosis grade (n=195). * = p<0.05, *** = p<0.001, **** = p<0.0001.

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Experimental and innovative immunotherapy

BOS_09_01 IGURATIMOD UPREGULATED PTPN22 AND INHIBITED B CELLS ACTIVATION IN ABMR AFTER RENAL TRANSPLANT

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Background: Iguratimod, a novel small molecule anti-rheumatic drug, has demonstrated potential immunosuppressive effects in clinical applications for rheumatoid arthritis. Our previous research in renal transplant recipients has indicated that Iguratimod may effectively decrease de novo donor-specific antibody (DSA) levels, alongside population response antibody (PRA) levels, leading to a notable reduction in kidney allograft rejection with a favorable safety profile.

Methods: A mouse model of acute antibody-mediated rejection (ABMR) was established to investigate the protective effects of Iguratimod through allograft survival analysis and pathology. Flow cytometry was employed to assess changes in donor-specific antibodies (DSA) and T/B cell subtypes in peripheral blood, spleen, and kidney allograft following Iguratimod administration. Kidney allografts and B cells from the spleens of transplanted mice were isolated using magnetic beads and subjected to RNA sequencing. Notably, gene PTPN22 (Protein Tyrosine Phosphatase Non-receptor 22) emerged and then we constructed adeno-associated virus vector of CD19 specific promoter of PTPN22 shRNA to infect ABMR model mice to validate the mechanism of Iguratimod.

Results: Iguratimod exhibited the ability to reduce DSA levels, significantly mitigate pathological injuries, and extend allograft survival in a mouse acute ABMR model. Flow cytometry analysis revealed a decrease in the CD4/CD8 ratio in peripheral blood, a reduction in activated B cells in the spleen, and a decline in plasma cells in peripheral blood following Iguratimod administration. Transcript sequencing suggested that Iguratimod might exert a pronounced effect by upregulating PTPN22. Finally, mice infected with an adeno-associated virus vector containing the CD19-specific promoter for PTPN22 shRNA confirmed the potential mechanism of Iguratimod, highlighting its ability to inhibit PI3K/AKT/mTOR.

Conclusions: Iguratimod could mitigate acute antibody-mediated rejection and extend renal graft survival by upregulating PTPN22, subsequently inhibiting B cell activation in a mouse kidney transplant model through the suppression of the PI3K/AKT/mTOR signaling pathway.

BOS_09_02 LIBERATE STUDY: ENGINEERED REGULATORY T CELLS AND RATG CONDITIONING TO INDUCE TOLERANCE IN LIVER TRANSPLANTATION

Alberto Sanchez-Fueyo[1], Marc Martinez-Llordella[2], Alison Taylor[3], James Sun[3], Jie Wang-Jairaj[2], Rupert Kenefeck[2], Kourosh Saeb-Parsy[4], Jacques Pirenne[5], Jake Demetris[6], Andrew Lesniak[6], Natalie Belmonte[2], Aaron Vernon[2], Peter Cooper[2], Gareth Wright[2], Annie Woodburne[2], Laurie Baylor-Curtis[2], Luke Devey[2]

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Background: LIBERATE (NCT05234190) is an ongoing phase I/IIa, single-arm, open-label, multi-centre study to investigate the safety of QEL-001, an autologous Chimeric Antigen Receptor (CAR) regulatory T (Treg) cell therapy, and its potential to induce allograft tolerance post liver transplantation. QEL-001 expresses an HLA-A2 specific CAR, a FOXP3 phenotype lock, and an inducible safety switch. The Safety Cohort of the study has been completed (N=3) and shown QEL-001 was well tolerated, trafficked to and engrafted in the transplanted livers.

Methods: The Expansion Cohort is being conducted in the UK and EU. Eligible subjects were aged 18-75 years and underwent liver transplantation 1-5 years prior to enrolment. Low dose rATG (rabbit anti-thymocyte globulin) was administered for lymphodepletion before QEL-001 infusion. A Data Safety Monitoring Board (DSMB) performed periodic independent reviews of the data.

Results: Low dose rATG administration prior to QEL-001 infusion resulted in mild to moderate AEs were reported, in line with product label. rATG mediated a significant reduction in CD4 and CD8 T-cell frequencies, while other immune populations were mostly unaffected. Active rATG was cleared from circulation approximately 3 weeks post administration. QEL-001 CAR-Treg engraftment and detection in circulation was significantly higher in rATG-treated patients than what we observed in the Safety Cohort (without rATG conditioning). Furthermore, dPCR analysis of liver biopsies post QEL-001 infusion showed that CAR-Tregs were able to migrate and accumulate in the allograft. Clinical batches produced for all subjects were within the pre-defined product specifications, and without CD8 impurities. Characterization of circulating and liver infiltrating CAR-Treg showed phenotypic stability of the QEL-001 cell products.

Conclusions: QEL-001 infusion after rATG conditioning was well tolerated in patients treated to date. Specific T-cell lymphodepletion was apparent post ATG which subsequently enhanced QEL-001 engraftment and durability in circulation compared with previous data in the safety cohort.

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BOS_09_03 ENHANCING THE FUNCTIONALITY OF REGULATORY T CELL THERAPIES BY AFFINITY-TUNING THEIR CHIMERIC ANTIGEN RECEPTORS

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Background: Regulatory T cells (Tregs), known for their potent immunomodulatory properties, can be genetically engineered using chimeric antigen receptor (CAR) technology to target organ-specific antigens. The safety and tolerance-promoting properties of autologous anti-HLA-A2 CAR-Tregs are currently being evaluated in clinical liver transplantation. As compared to T cell receptors, CARs exhibit supraphysiological affinity to their target antigens. The impact of modifying the binding affinity of the CAR's single-chain variable fragment (scFv) on CAR-Treg functionality remains unexplored. In this study, we aimed to evaluate the functional properties of affinity-tuned human anti-HLA-A2 CAR-Tregs.

Methods: Three second-generation anti-HLA-A2 CAR constructs expressing low-affinity (LA), moderate-affinity (MA) and high-affinity (HA) scFvs were designed. Human HLA-A2 negative $CD4^+CD25^+CD127^-$ Tregs were FACS sorted and transduced using lentiviral vectors. The antigen-specific activation and suppressive function of CAR-Tregs expressing different CARs were assessed in vitro using cell lines and precision-cut liver slices (PCLS). Therapeutic efficacy was evaluated in an in vivo xeno graft-versus-host disease (GvHD) by infusing CAR-Tregs together with HLA-$A2^+$ PBMCs into irradiated NSG mice. Mechanistic studies focused on CAR avidity, internalization and recycling using dextramer tracking.

Results: When cultured together with HLA-A2 expressing cells, LA CAR-Tregs exhibited the highest proportion of activated alloantigen-specific cells and suppressive effects. Furthermore, when cultured with PCLS, they showed greater tissue infiltration than other cells. In vivo, LA CAR-Tregs exhibited improved persistence, delayed GvHD onset, and prolonged recipient survival. Mechanistically, HA CAR-Tregs exhibited higher avidity for their target antigen but underwent rapid CAR internalization, and reduced dextramer expression when stimulated with physiological antigen levels, suggesting CAR downregulation.

Conclusions: Affinity-tuning the CAR of anti-HLA-A2 CAR-Tregs significantly alters their functionality, both in vitro and in vivo, which has implications for the design of engineered Treg therapies for clinical use.

BOS_09_04 OPTIMAL TIMING OF ANTI-CD3F(AB')2 TREATMENT IN SENSITIZED MODEL OF HEART TRANSPLANTATION

Takuji Ota[1], Ryoichi Goto[2], Takuya Harada[1], Agustina Forgioni[1], Norio Kawamura[1], Masaaki Watanabe[3], Tsuyoshi Shimamura[4], Akinobu Taketomi[5]

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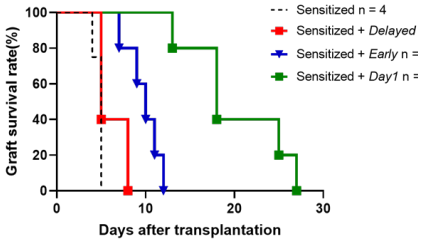
Background: Previous studies have demonstrated a unique effect of the non-Fc binding anti-CD3 antibody ($aCD3F(ab')_2$), where *delayed* timing of treatment effectively promotes transplant tolerance in a mouse model. With the recent clinical use of humanized Fc-engineered CD3 antibodies, determining the optimal treatment strategy, including appropriate timing of use, has become crucial for organ transplantation.

Methods: C57BL/6 mice were sensitized with BALB/c tail skin grafts, followed by BALB/c heart transplantation 8-12 weeks later. Three $aCD3F(ab')_2$ treatment protocols (50µg daily for 5 consecutive days) were as follows: *early* (day-1 to day 3 post-transplantation), *delayed* (day 3 to day 7), revised *delayed* (day 1 to day 5). Intragraft lymphocytes were assessed by flow cytometry.

Results: The *early* treatment protocol of $aCD3F(ab')_2$ significantly prolonged graft survival in the BALB/c to C57BL/6 heart transplant model (n=5, MST =38 days). Notably, the *delayed* protocol promoted long-term graft acceptance (MST >100 days). A significantly higher percentage of $ly108^+$ $TCF1^{high}$ $PD\text{-}1^+$ $CD8^+$ T cells was observed in the graft treated with the *delayed* protocol. However, in a sensitized situation, the *delayed* protocol failed to prevent rejection (MST=5 days), with an increase in intragraft granzyme B^+ $CD8^+$ T cells by day 3. The revised *delayed* protocol, starting from day 1 post-transplantation, significantly prolonged graft survival (MST=18 days, p=0.0018 vs. MST=10 days in *early* protocol) even under sensitized situation (Figure. A). Additionally, significantly higher percentages of $Foxp3^+$ $CD25^+$ $CD4^+$ T cell and $ly108^+$ $TCF1^{high}$ $PD\text{-}1^+$ $CD8^+$ T cell were observed in the graft treated with the revised *delayed* protocol (Figure. B).

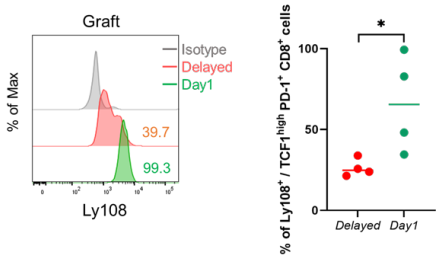
Conclusions: Optimal timing of $aCD3F(ab')_2$ treatment is critical in sensitized situation. $Ly108^+$ $TCF1^{high}$ $PD\text{-}1^+$ $CD8^+$ T cells play a key role in maintaining immune balance within the graft.

Figure. A : Heart allograft survival rates in skin-sensitized recipient mice treated with anti-CD3F(ab')2.



5 independent experiments

Figure. B : The percentage of $Ly108^+$ $TCF\text{-}1^{high}$ $PD\text{-}1^+$ $CD8^+$ T cells in the sensitized group treated with aCD3F(ab')2.



4 independent experiments

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Experimental and innovative immunotherapy

BOS_09_05 INTERLEUKIN-2 IMMUNE COMPLEX THERAPY SYNERGIZES WITH TRADITIONAL IMMUNOSUPPRESSION FOR LONG-TERM GRAFT SURVIVAL

Ikbale El-Ayachi[1], Rachael Teodorescu[2], Ken Washburn[3], Mark Rubinstein[2], *Austin Schenk*[1]

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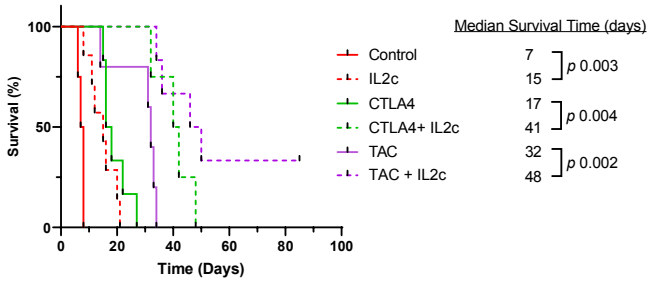
Background: Immune complexes of interleukin-2 and anti-IL-2 monoclonal antibodies (IL-2c) selectively provide IL-2 to CD25+ T cells and IL-2c therapy can be used to expand endogenous CD25+ regulatory T cells (Treg) in the context of transplantation. We tested the capacity of IL-2c therapy, alone and in combination with traditional immunosuppressants, to prolong murine cardiac allograft survival.

Methods: Wild-type C57BL/6 mice were treated prior to transplant with IL-2c and then received fully-MHC mismatched BALB/c (H-2d) heterotopic cardiac allografts with or without peri-transplant tacrolimus or CTLA4-Ig. Graft survival, anti-donor T cell priming, and donor-specific antibody production were measured. High-dimensional flow cytometry and transcriptomic analyses were used to characterize IL-2c induced modulation of the alloimmune response.

Results: IL-2c therapy alone significantly prolonged allograft survival vs. control (15 days vs. 7, p 0.003). A single 250 ug dose of CTLA-4-Ig on the day of transplant prolonged survival to 15 days, and CTLA4-Ig + IL-2c prolonged survival to 41 days (p 0.004). Three weeks of peri-transplant tacrolimus therapy prolonged survival to 32 days, and peri-transplant tacrolimus + IL-2c prolonged graft survival to 48 days with one-third of the cohort surviving indefinitely (p 0.002). Mechanistic analyses reveal Treg activity at both the priming and effector sites and markedly reduced myeloid activity within the allografts.

Conclusions: IL-2c therapy synergizes well with existing immunosuppressants. Pre-transplant expansion of Tregs with IL-2c and short-course peri-transplant tacrolimus synergize to produce long-term allograft survival in the absence of ongoing immunosuppression. Further modulations of these regimens may enable meaningful tolerance induction.



BOS_09_06 USE OF A HEPATOCYTE-SPECIFIC CHIMERIC ANTIGEN RECEPTOR ENHANCES RECRUITMENT OF REGULATORY T CELLS TO LIVER

***Ada Kurt*[1], Elisavet Kodela[2], Emmanuelle Landmann[1], Paula Ruiz[1], Marwa Elgosbi[1], Maegen Fleming[1], Louisa Tang[3], Anna Koi[3], Eva Bugallo Blanco[3], Sim Tung[3], Daniela Penston[3], Marc Martinez-Llordella[3], Alberto Sanchez-Fueyo[4]**

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Background: Regulatory T cells (Tregs), known for their powerful immunomodulatory properties, are being evaluated as a therapeutic strategy to ameliorate immunopathology and re-establish immunological tolerance in autoimmunity and transplantation. Treg activation requires T cell receptor (TCR)-mediated cognate antigen engagement. In pre-clinical studies, Tregs with specificity for antigens expressed at the site of inflammation preferentially traffic and persist in these sites, resulting in more powerful compartmentalized immunosuppression. The antigen specificity of Tregs can be artificially modified using the synthetic chimeric antigen receptors (CARs) technology. We hypothesized that by engineering Tregs to express a CAR recognizing a hepatocyte-specific antigen, we would promote their selective migration to the liver.

Methods: We designed and synthesized several second-generation CAR constructs incorporating single-chain antibody fragments recognizing asialoglycoprotein receptor 1 (ASGPR) and different transmembrane and hinge domains. Initial screening for specificity and functionality was performed using a Jurkat NFAT-reporter cell line stimulated with recombinant proteins and/or ASGPR-expressing cells. Human $CD4^+CD25^+CD127^-$ Tregs were then transduced, using lentiviral vectors, and their specificity and functionality was assessed through activation, proliferation, and suppression in vitro assays. The tissue homing and persistence of liver-specific CAR-Tregs were evaluated *in vivo* in immunocompromised NSG mice under homeostatic conditions.

Results: CARs were selected based on their specificity for ASGPR and activation profile following antigen recognition. As compared to untransduced polyclonal Tregs, ASGPR-specific CAR-Tregs exhibited enhanced activation, proliferation and suppressive function *in vitro*. Following infusion into NSG mice, CAR-Tregs preferentially homed and persisted in the liver.

Conclusions: Organ-specific CAR targeting is a promising strategy to improve outcomes in transplantation and inflammatory liver diseases by enhancing Treg recruitment to the target organ.

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Experimental and innovative immunotherapy

BOS_09_07 DEVELOPMENT OF A CYTOTOXIC FUSION PROTEIN TO SPECIFICALLY TARGET ANTI-HLA MEMORY B LYMPHOCYTES

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Background: The development of new desensitization strategies for highly sensitized patients awaiting transplantation is a priority. In these patients, memory B lymphocytes (B cells) are considered the main source of donor-specific anti-HLA antibodies (DSAs) post-transplantation. Anti-CD20 antibodies are currently used to deplete these cells before transplantation, but they are ineffective against subpopulations with low CD20 expression and increase the risk of infection by targeting all B cells regardless of antigen specificity.

Methods: To specifically target anti-HLA memory B cells, the researchers developed a dimeric fusion protein consisting of two HLA-A2 molecules linked by the constant fragment of a cytotoxic immunoglobulin. This protein has been further ameliorated with the insertion of different mutations that enhance the cytotoxicity and protect the molecules from IdeS-dependent cleavage. As control, a second version of the protein presenting the Ovalbumin as antigen instead of HLA-A2 was also generated. The fusion protein has been used to specifically target anti-HLAA2 producing hybridoma cell line and to treat mice immunized against the two antigens.

Results: In vitro: The HLA-A2-Ig dimers selectively destroyed hybridomas producing anti-HLA-A2 antibodies in the presence of complement. In vivo: memory B cells specific to HLA-A2 and ovalbumin were transferred into wild-type mice. These mice were treated with the dimers alongside Belatacept to prevent cellular responses against the dimers. After stimulation with HLA-A2 and ovalbumin antigens, mice treated with HLA-A2-Ig dimers did not produce anti-HLA-A2 antibodies but did produce anti-ovalbumin antibodies. Conversely, mice treated with ovalbumin-Ig dimers showed the opposite response. This effect is maintained several weeks after re-stimulation with the antigens.

Conclusions: This approach demonstrates potential for more effective and safer desensitization strategies for highly sensitized patients waiting for transplantation.

BOS_09_08 COMBINATION OF TCR-DEFICIENT CAR-TREGS AND NON-MITOGENIC ANTI-CD3 TO PROMOTE TRANSPLANT TOLERANCE

***Tifanie Blein*[1], Soeli Charbonnier[2], Nicolas Ayas[2], Baptiste Lamarthée[3], Herman Waldmann[4], Lucienne Chatenoud[5], Isabelle André[6], Julien Zuber[7]**

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Background: CAR-regulatory T cells (Treg) therapy holds promises for inducing long-term transplant tolerance while getting rid of immunosuppressive drugs. Our strategy aims to enhance the proportion of donor-specific CAR-Tregs and selectively deplete alloreactive T cells. We hypothesize that TCR-deficient (TCR-) CAR-Tregs will act synergistically with anti-CD3 therapy to achieve these goals.

Methods: Human TCR-deficient HLA-A2-targeted CAR-Tregs were generated via lentiviral transduction and CRISPR-Cas9 gene editing. In a first *in vivo* model, NSG mice received HLA-A2+ PBMC along with either TCR+ or TCR- CAR-Tregs. In a second model, a mixture of TCR+ CAR-T and TCR- CAR-Tregs, expressing CBG or Firefly luciferase, respectively, was adoptively transferred into murine hosts bearing HLA-A2+ skin grafts. Selective depletion of TCR+ cells by anti-CD3 therapy was assessed by *in vivo* bioluminescence imaging and flow cytometry.

Results: TCR-deficient CAR-Tregs, despite the absence of the TCR/CD3 complex, could still be activated in a HLA-A2-specific manner. These cells retained key phenotypic and epigenetic Treg markers. Transcriptomic analysis revealed that gene editing predominantly affected *TRAC*-related genes, with minimal impact on other pathways. TCR+ CAR-Tregs, in contrast to their TCR- counterparts, were selectively eliminated from blood and lymphoid organs following anti-CD3 treatment. Similarly, anti-CD3 therapy induced selective depletion of TCR+ CAR-T infiltrating HLA-A2+ skin allograft, while TCR-deficient CAR-Tregs were preserved and persisted within the allografts (Figure 1). Ongoing transcriptomic profiling and imaging mass cytometry analysis of skin allografts are being conducted to further evaluate the effectiveness of this combination strategy and to map the location of graft-resident CAR-Tregs.

Conclusions: Our data demonstrate that anti-CD3 therapy can selectively advantage TCR-deficient CAR-Treg cells over resident TCR+ T cells *in vivo*. This approach enhances the therapeutic potential of CAR-Tregs, while reducing the number of cells required, thereby improving the clinical applicability of CAR-Treg-based therapies.

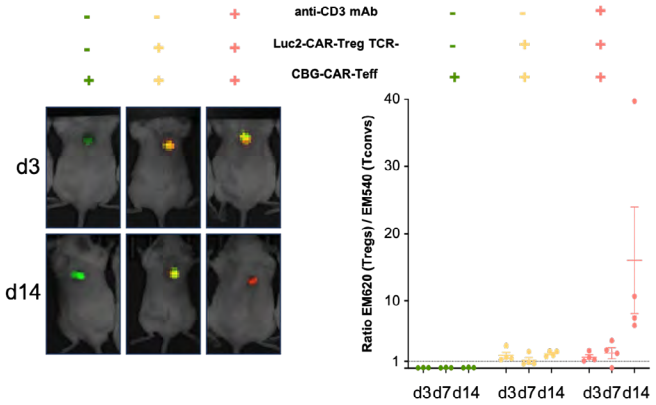

Figure 1: TCR- CAR-Tregs Luc2+ and CAR-T CBG+ tracking by bioluminescence live imaging in an allogenic HLA-A2 skin graft model.

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BOS_09_09 CHIMERIC HLA ANTIBODY RECEPTOR (CHAR) NK CELLS TARGET CLASS II HLA-SPECIFIC B CELLS IN SOLID ORGAN TRANSPLANTATION

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Background: Antibody-mediated rejection (ABMR) is a major complication after transplantation that is associated with poor graft prognosis. The presence of donor-specific anti-HLA antibodies (DSA) increases the risk of rejection. Current therapies are aimed at controlling the immune response, but there is no specific therapy to selectively reduce the generation of DSA. Chimeric HLA antibody receptor (CHAR) T cells are a promising therapy for targeting HLA-specific B cells in sensitized patients, who have developed antibodies and B cells against HLA. Previous research demonstrated that CHAR T cells can eliminate class I HLA-specific B cells with exceptional specificity. However, the immunosuppressive treatments could reduce the efficacy of CHAR-Tc. The objective was to generate DQ7-CHAR NK cells to specifically eliminate HLA-DQ7-specific B cells.

Methods: Lentiviral vectors were designed encoding HLA-DQ CHARs composed of HLA-DQA1*05:01 with HLA-DQB1*03:01 (DQ7) and the CLIP peptide combined with intracellular costimulatory and signaling domains. NK92 and primary NK cells were transduced to express the CHAR molecules and enriched when necessary. Furthermore, B cell lines were generated that express HLA-DQ7-specific human recombinant B cell receptors.

Results: Engineered CHAR-NK cells, which expressed HLA-DQ7 CHAR molecules, were successfully generated. Notably, these cells were capable of specifically eliminating HLA-DQ7-specific B cells in a manner that did not affect other antibody-producing B cells.

Conclusions: The potential applications of this therapy include the desensitization of sensitized renal transplant patients and the treatment of ABMR in solid organ transplantation.

BOS_09_10 DONOR-SPECIFIC BLOOD TRANSFUSION DELAYS REJECTION DEVELOPMENT IN A MICE LUNG TRANSPLANTATION MODEL

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Background: Lung transplantation (LTx) is still hindered by a high rate of chronic rejection, necessitating profound immunosuppression with associated complications. Donor-specific blood transfusion (DSBT) is a pre-transplant strategy aimed at improving graft acceptance. Limited attention has been given to its application in LTx, and the precise mechanisms underlying DSBT-induced tolerance remain incompletely understood. This study aimed to establish the first DSBT animal model for LTx and evaluate its safety and efficacy in improving lung allograft rejection.

Methods: Aim 1: The blood donor mice were BALB/c (DSBT, n=6) or C57BL/6N [iso-transfusion control (ICON), n=6], and the recipient mice were all C57BL/6N. 0.2 ml of heparinized whole blood was collected from the donor's inferior caval vein and injected within one hour through the recipient's tail vein. Data from non-transfused C57BL/6N mice (NCON, n=6) were recorded as the baseline. Complete blood counts were conducted using hematology analyzer, along with microCT scans on D1, 3 and 7. All mice were sacrificed on D7 for left lung Hematoxylin and Eosin staining. Aim 2: DSBT (BALB/c to C57BL/6N n=5) was performed approximately 24 hours before LTx. Non-transfused allograft transplantation mice [BALB/c to C57BL/6N (ACON) n=5] were set as the control group. MicroCT scan was conducted on D7, 14 and 35. All mice were sacrificed on D35 for left lung Masson's Trichrome staining.

Results: Aim 1 (Fig 1): All mice maintained stable weight after transfusion. No signs of transfusion-related hemolysis, histological injury or organ dysfunction were observed in any group. White blood cell counts, primarily lymphocytes, decreased significantly on D1 and began to recover on D3. On D7, lymphocyte and monocyte counts stabilized in the DSBT group but decreased in the ICON group. Lymphocyte percentages (Lym%) decreased following allo-transfusion. Aim 2 (Fig 2): More left lung airways remained open in the DSBT group compared to the ACON group until D14. However, the rejection level was comparable between the DSBT and ACON groups by D35.

Conclusions: DSBT was feasible and safe in the mice LTx model. Lymphocytes and monocytes evolved differently following allo- or iso-transfusion. DSBT delayed rejection development in the short term but did not improve long-term outcomes after LTx.

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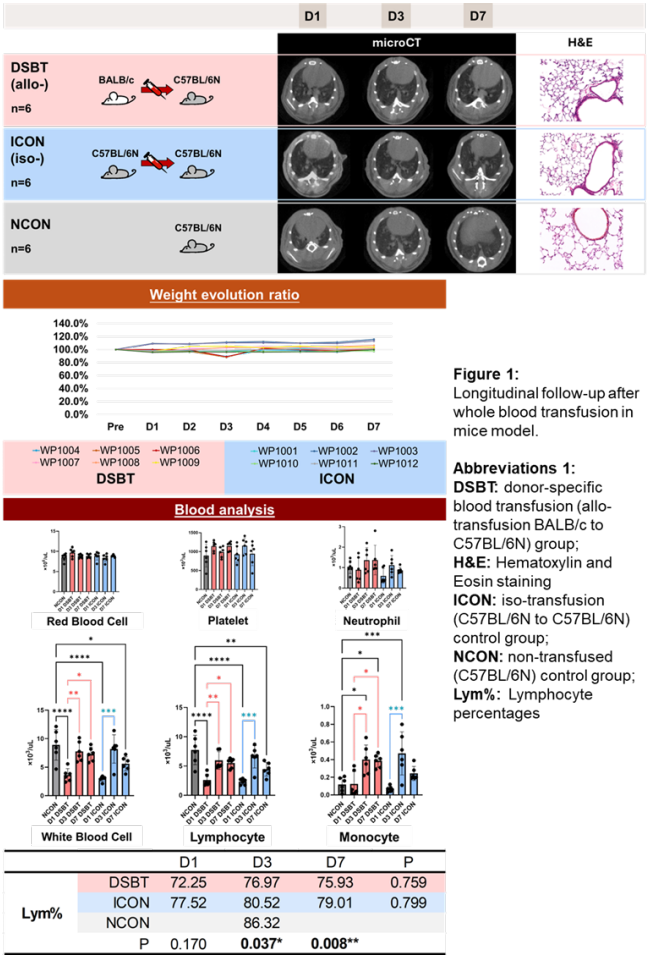

		D1	D3	D7	P
Lym%	DSBT	72.25	76.97	75.93	0.759
	ICON	77.52	80.52	79.01	0.799
	NCON		86.32		
	P	0.170	**0.037***	**0.008****	

Figure 1:
Longitudinal follow-up after whole blood transfusion in mice model.

Abbreviations 1:
DSBT: donor-specific blood transfusion (allo-transfusion BALB/c to C57BL/6N) group;
H&E: Hematoxylin and Eosin staining
ICON: iso-transfusion (C57BL/6N to C57BL/6N) control group;
NCON: non-transfused (C57BL/6N) control group;
Lym%: Lymphocyte percentages

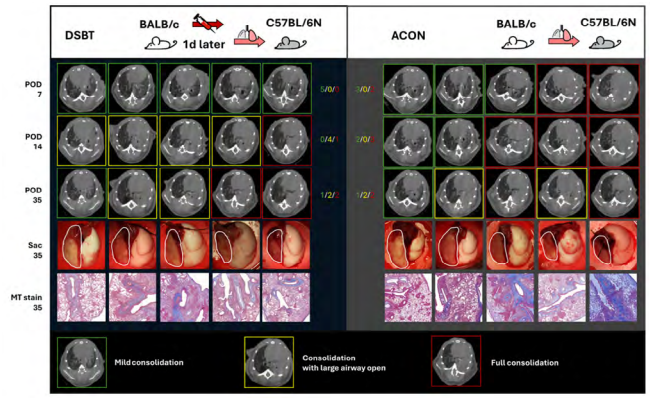

Figure 2:
Longitudinal follow-up after allograft (BALB/c to C57BL/6N) lung transplantation in mice model.

Abbreviations 2:
ACON: non-transfused allograft control group; **DSBT:** donor-specific blood transfused allograft group; **MT:** Masson's Trichrome; **POD:** postoperative day; **Sac:** macroscopic photo of heart-lung bloc after sacrifice. The left lung graft is indicated in the white frame.

BOS_09_11 LAWSONE INDUCE CARDIAC ALLOGRAFT TOLERANCE BY SUPPRESSING TH1 DIFFERENTIATION IN MICE

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Background: Lawsone a natural compound demonstrates diverse biological properties. However, the potential of lawsone in organ transplant remains unknown. We aim to evaluate the application of lawsone in fully MHC-mismatched murine cardiac transplantation.

Methods: Hearts from donor C57 mice were heterotopically transplanted to the abdomen of recipient C3H mice. Lawsone was administered intragastrically to recipients. The allografts were used to observe the survival, pathological changes and immune cells infiltration. CFSE-labeled T cells were treated with lawsone or vehicle, and the proliferation was measured by flow cytometry. Bone marrow cells were isolated, induced to differentiate into bone marrow-derived dendritic cells(BMDCs), and subsequently co-cultured with T cells in the presence of lawsone or vehicle control. Th1 cell differentiation was induced by culturing naïve CD4+ T cells with lawsone or vehicle. Additionally, inflammatory cytokines were detected via ELISA, while RNA-seq and WB were used to investigate the underl

Results: Lawsone resulted in long-term graft survival in the transplant model(-median survival time >100 days). Notably, recipients exhibited reduced T cells in both grafts and spleens 7 days post operation. Similarly, lawsone suppressed the proliferation of CD4+ and CD8+ T cells in vitro, and inhibited the antigen-presenting capability of BMDCs by suppressing their maturation. The levels of the pro-inflammatory cytokine IFN-γ were lower and the levels of the anti-inflammatory cytokine IL-10 were higher in the serum of lawsone-treated groups. Lawsone-treated group demonstrated declined expression of IFN-γ both in vitro and in vivo, indicating lawsone suppressed Th1 cells differentiation. GO and KEGG pathway enrichment revealed a correlation between lawsone treatment and T cell-related pathways, and STAT signaling pathways. Western blot analysis demonstrated down-regulated levels of phosphorylated STAT3 in the lawsone-treated Th1 cells.

Conclusions: We revealed the protective effect of lawsone in murine transplant model. In vitro experiments revealed lawsone against rejection presumably via suppressing IFN-γ/p-STAT3 signaling. Our data suggest that lawsone could be a novel therapeutic approach in solid organ transplantation.

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Experimental and innovative immunotherapy

BOS_09_12 IRE1A-XBP1 INHIBITORS: A PROMISING APPROACH TO TREAT CHRONIC VASCULAR REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Chronic vascular rejection (CVR) is the leading cause of graft loss following organ transplantation. Natural Killer (NK) cells play a pivotal role in CVR, being activated through two main mechanisms: missing-self (MS) recognition, which detects the absence of self-HLA molecules, and antibody-dependent cellular cytotoxicity (ADCC) in the presence of donor-specific antibodies (DSA). NK cell activation requires an initial "priming" signal, commonly provided by cytokines such as interleukin 15 (IL-15). Recent studies have shown that IL-15 activation induces the IRE1α-XBP1 pathway in NK cells, which regulates their effector functions and survival. This study aimed to confirm the involvement of the IRE1α-XBP1 pathway in NK activation during CVR and explore whether blocking this pathway could be a potential therapeutic approach.

Methods & results: We first analyzed single-cell RNA sequencing data from biopsies of CVR patients and found that most intragraft NK cells highly expressed XBP1s. In vitro, we confirmed that IL-15 priming significantly increased XBP1s expression, validating the activation of the IRE1α-XBP1 pathway in NK cells. Furthermore, we demonstrated that IL-15 priming was essential for NK cell activation through both MS recognition and ADCC mechanisms. Only IL-15-primed NK cells were capable of degranulation and IFN-γ production in response to DSA or MS when co-cultured with allogeneic endothelial cells. Notably, two distinct IRE1α inhibitors effectively blocked NK cell activation by both mechanisms involved in CVR. Ongoing experiments in murine in vivo models will further validate these findings.

Conclusions: These results underscore the critical role of the IRE1α-XBP1 pathway in NK cell activation during chronic vascular rejection. Targeting this pathway with specific inhibitors may provide a novel therapeutic strategy for managing chronic vascular rejection in transplant recipients

BOS_09_13 TACROLIMUS VARIABILITY, PREDICTIVE FACTORS AND ITS IMPACT ON KIDNEY GRAFT FUNCTION

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Background: Aim of this study was to evaluate association of tacrolimus(TAC) variable pharmacokinetics with graft function and survival in the one-year follow-up period, also to identify factors that influence variability.

Methods: A prospective study was conducted in 32 kidney transplanted patients. Intra-individual variability of CV>30% was defined as high. Due to concentration/dose ratio (Co/D) patients were divided into slow and fast metabolizers. The clinical outcome on graft function was estimated as change in the eGFR in the 1-year follow up period. Demographic, laboratory, and clinical factors were included in the variability predictive analysis. An analysis for prevalence and influence of the genetic polymorphisms of CYP3A5 gene on tacrolimus variable pharmacokinetics was performed.

Results: TAC blood concentration ranged between 5.28 and 9.37 with median value of 6.79ng/ml, with higher variability demonstrated through standard deviation 0.73-4.01. CV > 30% was found in 12.5% and low Co/D in 15.6% of patients. Both fast metabolizers and high IPV group patients showed higher creatinine after 6 and 12 months and lower eGFR, but the difference didn't reach statistical significance (135.11 ± 50.89 vs. 158.29 ± 68.33, p=0.499; 126.36 ± 45.60 vs.150.80 ± 58.60, p=0.322) (p=0.582, 0.703, 0,547, 0.652), respectively. The reduction ratio of eGFR ranged from -64 to +40%, mean -1.26 ± 20.60%. In the predictive model age remained the sole factor of tacrolimus variability (β=1.18, CI:1.015-1.379, p=0.031), indicating persistence of other predictive factors that need to be investigated. Preliminary results regarding genetic analysis of CYP3A5*3 (6746A>G) polymorphism revealed 4 patients heterozygotes for AG allele, 3 (75%) of them with C0/D<1.05.

Conclusions: Further follow up is needed on tacrolimus variability and kidney graft function. Evaluation of persistence of one or more genetic polymorphisms and their influence of TAC variability is of essential need.

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Experimental and innovative immunotherapy

BOS_09_14 EXPLORING THE IMPACT OF EXTRACORPOREAL PHOTOPHERESIS ON SOLUBLE SERUM FACTORS IN LUNG TRANSPLANT RECIPIENTS

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Background: Chronic lung allograft dysfunction (CLAD) limits lung transplant success. While extracorporeal photopheresis (ECP) shows promise in reducing CLAD risk, its mechanisms remain unclear. As part of a comprehensive ongoing investigation, we employed diverse analytical approaches to assess the impact of ECP on soluble factors in serum with the eventual goal of identifying relevant immune pathways.

Methods: In a prospective, randomized, controlled single-center trial, lung transplant patients received standard immunosuppression (n=30 per group). The intervention group additionally underwent 8 ECP cycles within three months post-transplant, while the control group did not. Serum samples were collected before transplantation and three months afterward. A broad array of soluble, immunologically relevant factors was measured in these serum samples using a 65-plex Luminex-based immunoassay. Immune patterns were identified via FlowSOM unsupervised clustering, and feature importance was determined using Random Forest. Temporal dynamics were assessed with log2 fold change, and group differences were analyzed using the Mann-Whitney U test. PLS-DA was used to differentiate identified factors between groups, and KEGG pathway analysis identified related immune pathways.

Results: FlowSOM analysis identified VEGF-A, Eotaxin-2, and MMP-1 as key factors influencing cluster distinctions in the ECP group. Temporal dynamics analysis showed that IL-16 was reduced in both groups at 3 months, with a significantly smaller reduction in the ECP group. PLS-DA of the five factors with the lowest p-values from the Mann-Whitney U test (BLC, IFN-γ, TNF-α, MIP-1β and IL-16), revealed group differentiation. KEGG analysis highlighted 'allograft rejection' and 'graft versus host disease' pathways.

Conclusions: The identified factors potentially play a role in the mechanisms through which ECP modulates alloreactivity and warrant further investigation and confirmation.

BOS_09_15 EXTRACORPOREAL PHOTOPHERESIS IN LUNG TRANSPLANTATION: FIRST INSIGHTS OF A MULTICENTRIC CASE CONTROL STUDY

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Background: Chronic lung allograft dysfunction (CLAD) is the main limitation for long term survival post lung transplantation. Previous studies have suggested extracorporeal photopheresis (ECP) to be able to prevent and stabilize CLAD. We describe here the first insights of a multicentric, case control study evaluating ECP efficacy.

Methods: This is a retrospective multicentric case control study based on the COLT (Cohort Lung Transplantation) database. All recipients who had undergone ECP were included. CLAD phenotypes were determined at the time of ECP initiation by adjudication committee. We also defined a preCLAD phenotype by persistent decline of more than 10% but less than 20% from baseline FEV1.

Results: From 2009 to 2021, 131 recipients were found to have benefited from ECP (ECP +). Mean age at transplant was 42.8 ± 14 years, there were 56 women (43%) and 75 men (57%). Most common underlying diseases were cystic fibrosis (40 patients, 30%), chronic obstructive pulmonary disease (40 patients, 30%), interstitial lung disease (19 patients, 15%), group I pulmonary hypertension (18 patients, 14%) and other aetiologies (14 patients, 11%). CLAD was identified in 110 patients whose phenotype at the start of ECP was bronchiolitis obliterans syndrome (BOS) in 79 patients, restrictive allograft syndrome (RAS) in 8 patients, mixed in 8 patients and undefined in 15 patients. We identified 12 preCLAD patients and 11 recipients were neither CLAD nor pre-CLAD. The median duration of ECP was 9.5 months $_{IQR}$[3 -23], with a mean survival time of 4.7 ± 2.8 years for the whole cohort. Analysis of the FEV1 evolution show a trend to stabilization of lung function after ECP start in CLAD recipients and a moderate increase in the preCLAD group. We have also started the identification of COLT control recipients with a CLAD or preCLAD diagnosis and who did not benefit from ECP (ECP -). We will match ECP + with ECP – recipients for age at transplant, gender, underlying disease, CLAD stage and phenotype.

Conclusions: The main phenotype treated with ECP was BOS but more than 40% of ECP-treated recipients were for other phenotypes including preCLAD recipients who seem to have a stronger lung function benefit from treatment. Analysis are on-going to perform a comparison of FEV1 evolution between ECP + and ECP – recipients.

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BOS_10_1 IMPACT OF DELAYED GRAFT FUNCTION ON CARDIOVASCULAR OUTCOMES IN KIDNEY TRANSPLANTATION

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Background: Acute kidney injury (AKI) increases long-term cardiovascular risk in non-transplanted patients. Delayed graft function (DGF) mimics AKI in kidney transplant recipients, yet its impact on their cardiovascular risk remains unclear.

Methods: We investigated the impact of DGF on cardiovascular morbidity and mortality in kidney transplant recipients using data from patients across 17 French centres from the Astre and Divat cohorts. Included patients were aged 18 years or older, transplanted between 2008 and 2022, with follow-up until 31/03/2023. DGF was defined as the need for hemodialysis within the first week following renal transplantation. The primary outcome was the impact of DGF on the occurrence of a cardiovascular event (composite endpoint including cardiovascular death, coronary artery disease, stroke, heart failure), adjusted for conventional and specific cardiovascular risk factors. Analyses were performed using univariate and multivariate Cox models.

Results: Among the 18,149 patients transplanted during the inclusion period, 4,182 experienced DGF (23.0%). In the multivariate Cox model, DGF was independently associated with cardiovascular risk (adjusted Hazard Ratio [HR] = 1.24, p<0.0001). especially with coronary artery disease, heart failure, and cardiovascular death, but not stroke. The effect of DGF was more prominent in low-risk populations such as women, non-diabetic and cardiovascular disease-free recipients. DGF was also linked to a higher 10-year probability of graft failure (13.7% vs. 9.9%) and non-cardiovascular death (23.9% vs. 16.9%).

Conclusions: DGF is an independent risk factor for the occurrence of cardiovascular events in kidney transplant recipients. Strategies aimed at minimizing DGF could potentially reduce cardiovascular complications in these patients.

BOS_10_2 GLP-1/GLUCAGON RECEPTOR DUAL AGONISM REDUCES KIDNEY ALLOGRAFT FIBROSIS BY IMPROVING LIPID METABOLISM

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Background: Kidney allograft fibrosis accelerates the progression of chronic kidney disease (CKD), leads to allograft failure, and increases patient mortality. Emerging evidence suggests that metabolic syndrome in transplant recipients is associated with fibrosis development. However, it remains unclear whether targeting metabolic pathways can mitigate allograft fibrosis. This study aimed to explore the potential of targeting metabolic pathways using the GLP-1R/GCGR dual agonist TB001 for the treatment of kidney allograft fibrosis.

Methods: Kidney allograft fibrosis was induced in rat kidney transplant models. Histological analysis, transcriptome sequencing, and in vitro experiments were performed to investigate the efficacy of TB001 and its underlying mechanisms.

Results: Compared with the control group, TB001-treated recipients had significantly improved kidney allograft function, as evidenced by lower creatinine and 24-hour urine protein levels. Moreover, TB001 treatment decreased the body weight and serum total cholesterol, LDL-cholesterol, and TNF-α levels in transplant recipients, indicating metabolic improvements. Pathological analysis demonstrated that TB001 treatment reduced inflammatory cell infiltration and downregulated the expression of fibrosis markers, including TGF-β1, α-SMA, COL1A1, and Vimentin. Further transcriptome sequencing of kidney grafts revealed that TB001-treated group had a gene expression pattern similar to that of the syngeneic control group and showed significant enhancement of lipid metabolism-related pathways, particularly the PPAR pathway. In vivo and in vitro experiments further demonstrated that TB001 upregulated the expression of CPT1A, a key molecule involved in lipid metabolism, and inhibited TGF-β1/Smad2/3/Twist and PKC-α/PKC-β pathways.

Conclusions: Targeting metabolic pathways using the GLP-1R/GCGR dual agonist TB001 shows potential for managing kidney allograft fibrosis.

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BOS_10_3 PILOT EXPERIENCE OF ESAXERENONE IN HYPERTENSIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: Hypertension is a prevalent and critical risk factor for cardiovascular disease and allograft loss among kidney transplant recipients (KTRs). Despite the efficacy of renin–angiotensin system (RAS) inhibitors, their monotherapy often fails to achieve adequate blood pressure (BP) control due to enhanced mineralocorticoid receptor (MR) activity. Esaxerenone, a novel non-steroidal MR blocker, demonstrates potent selectivity and minimal renal clearance, making it potentially suitable for KTRs. This study evaluated the efficacy and safety of esaxerenone as an add-on therapy to RAS inhibitors in hypertensive KTRs

Methods: This retrospective observational study included 23 KTRs with uncontrolled hypertension or significant albuminuria despite RAS inhibitor therapy. Inclusion criteria were estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m² and post-transplant duration ≥3 months. Esaxerenone was initiated at 1.25–2.5 mg/day, with dose adjustments based on BP and serum potassium levels, over a 180-day observation period. Clinical parameters, including BP, eGFR, urinary albumin excretion (UAE), and liver-type fatty acid-binding protein (L-FABP), were monitored.

Results: The administration of esaxerenone was discontinued due to adverse events in 5 patients (21.7%). Eighteen patients completed the study. Esaxerenone significantly reduced systolic BP from 134.4 ± 11.8 mmHg at baseline to 123.1 ± 7.4 mmHg at 6 months ($p < 0.05$). Diastolic BP also decreased from 77.7 ± 8.3 mmHg to 71.9 ± 7.5 mmHg ($p < 0.05$). UAE and L-FABP levels decreased by 53.1% and 55.9%, respectively, indicating renoprotective effects.

Conclusions: This pilot study is the first to demonstrate the effectiveness of esaxerenone in hypertensive KTRs. By augmenting RAS blockade, esaxerenone significantly reduced BP and urinary biomarkers of kidney damage. These findings suggest that esaxerenone may be a promising option for managing post-transplant hypertension and preventing long-term graft dysfunction. Further randomized controlled trials are warranted to confirm these findings and optimize dosing strategies.

BOS_10_4 INCIDENCE, RISK FACTORS AND IMPACT OF CORONARY ARTERY DISEASE AFTER KIDNEY TRANSPLANTATION

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Background: Coronary artery disease is a significant cause of morbidity and mortality among kidney transplant recipients. The epidemiology and impact of coronary events after transplantation remain poorly understood in France. We investigated these aspects using data from 17 French centers, sourced from the Astre and Divat cohorts.

Methods: We included adult kidney allograft recipients transplanted between 2008 and 2022, with follow-up until 03/31/2023. The primary outcome was the incidence of coronary events post-transplantation, defined as the need for coronary angiography with percutaneous transluminal angioplasty. We also studied risk factors and the impact of early events on patient and graft survival (<1 month post-transplantation) using univariate and then multivariate Cox models.

Results: Among the 19,837 kidney transplant recipients included, 764 experienced a coronary event (3.9%), with an incidence of 0.77 per 100 person-years, particularly high in the first month (12.8 per 100 person-years). The majority of these events (n=505, 66.1%) occurred in patients without known coronary artery disease. In multivariate analysis, risk factors for post-transplant coronary artery disease included age, cardiovascular history, diabetes, smoking, depleting induction therapy, dialysis duration, and delayed graft function. Early coronary events were associated with all-cause mortality (Hazard ratio 1.77) and a lower GFR at 3 months (44.7 ml/min vs 48.9 ml/min in the case of coronary events, $p = 0.023$).

Conclusions: Post-transplant coronary events are frequent, particularly in the first month, and can occur in patients without history of coronary artery disease. They are a significant cause of morbidity and mortality and are associated with an early decline in graft function.

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BOS_10_5 EXPLORING THE EVOLUTION OF CIRCULATING PROTEIN BIOMARKERS IN LT SETTING FOR MASH, ALD AND METALD

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Background: There is a significant lack of data on the utility of peripheral biomarkers (e.g. cytokines, chemokines, adipokines, and inflammatory or tissue remodeling mediators) in the non-invasive assessment of MASLD in the post-LT setting. This study aimed to explore whether circulating levels of selected plasma proteins could associate with graft fibrosis after LT for MASH, ALD and MetALD.

Methods: This prospective cohort study included 61 adults transplanted for cirrhosis due to MASH (n=20), ALD (n=20), or MetALD (n=21) between Jan 2019 and Feb 2023 in 2 LT centers in Spain. Plasma levels of IL-1α, IL-1ß, IL-6, IL-8, IL-10, IL-12p70, IL-18, MCP-1, TNFα, adiponectin, resistin, tPAI-1, sIL-1RI, sIL-2Rα, CHI3L1, CK-18 M30, CK-18 M65, IGF-1, leptin, M2BPGi and TIMP-1 were measured before LT and at 6, 12, 24 and 36 months after LT by Luminex multiplex assay or ELISA, as appropriate. The 6-month post-LT measurement was assumed as the baseline timepoint after LT without graft fibrosis. FibroScan was carried out at least 1 year after LT and LSM values <8 kPa were used to rule out significant/advanced graft fibrosis.

Results: In the pre-LT setting, all patients, regardless of the etiology, had similar levels of the biomarkers tested (p>0.05), except for resistin (p<0.001) and tPAI-1 (p<0.022). When comparing pre-LT vs 6-month post-LT time-points, all biomarkers "normalized" after LT (p<0.05), except for IL-1α, IL-1ß, resistin, sIL-1RI, and TNFα. When categorizing by etiology, only IL-6, IL-8, tPAI-1, CHI3L1, CK-18 M30, M2BPGi and TIMP-1 "normalized" in the 3 groups (p<0.05). Regarding the FibroScan outcomes, 14 patients (23%) had LSM values >8 kPa (30% MASH, n=6; 20% ALD, n=4; and 19% MetALD, n=4; p=0.657). Patients with significant/advanced fibrosis (LSM values >8 kPa*) had significantly higher levels of CK-18 M30 (p=0.047) and CK-18 M65 (0.049) at the last elastographic evaluation. In addition, this former group also presented increased levels of CK-18 M30 (p=0.011) and CK-18 M65 (p=0.013) at 6, 12, 24 and 36 months after LT.

Conclusions: The evolution of the circulating biomarker profile among transplanted MASH, ALD or MetALD patients may serve as a potential non-invasive tool to assess/predict graft fibrosis. However, the causal associations between specific protein biomarkers and MASLD remain elusive.

*PMID: 39225307

BOS_10_6 CARDIAC FUNCTION IN LIVER TRANSPLANT RECIPIENTS BEFORE AND AFTER TRANSPLANTATION

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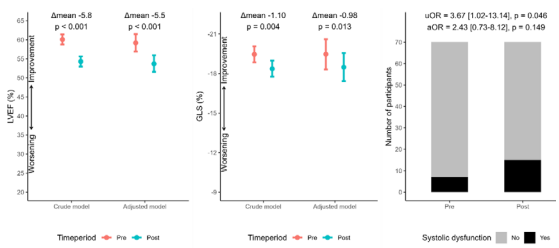
Background: Cardiovascular disease in liver transplant recipients contributes to post-transplant mortality and morbidity. This may result from transplantation-related hemodynamic stress, pre-existing cardiac conditions, and immunosuppressives causing diabetes, hypertension, and dyslipidemia. Modern echocardiographic techniques, like global longitudinal strain (GLS), enable early detection of cardiac dysfunction, even when conventional measures are normal. This study aimed to investigate changes in systolic function before and after transplantation using transthoracic echocardiography (TTE) and identify associated risk factors.

Methods: The Danish Comorbidity in Liver Transplant Recipients (DACOLT) Study examined recipients aged 20 or older with TTE. Pre-transplant TTEs were analyzed retrospectively, while post-transplant TTEs were performed as part of the DACOLT Study. Systolic dysfunction was defined as left ventricular function (LVEF) <50% and/or GLS ≤ -16%. Changes in systolic function were evaluated using linear and generalized linear mixed models, adjusted for risk factors and heart rate at both timepoints.

Results: Seventy recipients with TTEs both within one year before and after transplantation were included (Table 1). Significant decreases in LVEF (mean difference unadjusted: -5.8% [95% CI: -7.1 to -4.3], *P* < 0.001; adjusted -5.5% [-6.90 to -4.11], 0.001), and GLS (mean difference unadjusted: -1.1% [-1.8 to -0.4], 0.004, adjusted: -0.98% [-1.75 to -0.21], 0.013) were observed post-transplantation. The prevalence of systolic dysfunction increased from 10% to 21%. The unadjusted odds ratio (uOR) for systolic dysfunction was significantly higher post-transplantation (uOR 3.67 [1.02 to 13.14], 0.046, but the adjusted odds ratio (aOR) was not significant (aOR 2.43, [0.73 to 8.12], 0.149) (Figure 1). No risk factors were found to be associated with changes in LVEF, GLS, or systolic dysfunction.

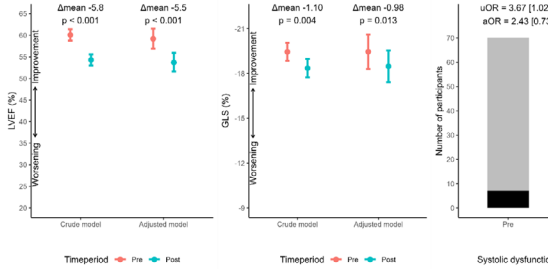
Conclusions: In this study, cardiac systolic function decreased significantly, and the prevalence of systolic dysfunction more than doubled after liver transplantation. Further prospective studies are needed to investigate clinical implications, potential progression of cardiac dysfunction, and the risk of symptomatic heart failure in liver transplant recipients.

FIGURE 1: Changes in Left Ventricular Function, Global Longitudinal Strain, and recipients with systolic dysfunction before and after liver transplantation.



Δmean refers to mean differences in LVEF and GLS after liver transplantation. uOR and aOR refers to = unadjusted and adjusted odds ratio for systolic dysfunction after liver transplantation. All models are adjusted for age, sex, heart rate, current smoking status, hypertension, diabetes before and after liver transplantation, and cirrhosis at the time of transplantation.

FIGURE 1: Changes in Left Ventricular Function, Global Longitudinal Strain, and recipients with dysfunction before and after liver transplantation.



Δmean refers to mean differences in LVEF and GLS after liver transplantation. uOR and aOR refers to = and adjusted odds ratio for systolic dysfunction after liver transplantation. All models are adjusted for a rate, current smoking status, hypertension, diabetes before and after liver transplantation, and cirrhosis transplantation.

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BOS_10_7 CARDIOVASCULAR OUTCOMES OF KINEY TRANSPLANTATION IN ELDERLY PATIENTS: A NATIONWIDE COHORT STUDY FROM SOUTH KOREA

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Background: Cardiovascular outcomes of kidney transplantation (KT) in elderly individuals have not been established. This study investigated the incidence and predictors of cardiovascular events (CVE) after KT.

Methods: Data were obtained from the Korea Organ Transplantation Registry, a nationwide cohort study of KT recipients (KTRs). A total of 619 elderly KTRs (age < 65 years) who underwent KT between May 2014 and June 2021 were included. The cumulative incidence and risk factors for CVE were evaluated using the Kaplan-Meier method and Cox proportional hazard model.

Results: A total of 51 CVE cases were identified for 1513.39 person-years (median, 2.00 years). The cumulative 5-year incidence of CVE was 12.50%. KTRs who developed CVE had lower patient survival rate than those without CVE (P < 0.001), while graft survival did not differ. At baseline, a history of cardiovascular disease was a significant predictor for CVE (hazard ratio [HR], 3.407; 95% confidence interval [CI], 1.154–10.061; P = 0.027), while age did not affect the development of CVE. At post-KT 6 months, higher levels of glucose (HR, 1.013; 95% CI, 1.004–1.022; P = 0.004) and triglycerides (HR, 1.010; 95% CI, 1.002–1.017; P = 0.012), and lower hemoglobin (HR, 0.630; 95% CI, 0.430–0.924; P = 0.018) were associated with a higher risk of CVE. A subgroup analysis showed a significant increase in CVE incidence who developed posttransplant diabetes mellitus (PTDM) by log-rank test (p = 0.022), and time-varying Cox regression analysis showed PTDM was significantly associated with CVE (HR, 3.45; 95% CI, 1.101 – 10.805; P = 0.034).

Conclusions: In elderly KTRs, CVE was associated with lower patient survival. A history of cardiovascular disease, and post-KT factors including high glucose and triglycerides levels and low hemoglobin may be responsible for CVE. Additionally, patients with PTDM were at higher risk of developing CVEs.

BOS_10_8 ELECTRONIC NOSE FOR DETECTING IMPAIRED GLUCOSE METABOLISM IN HEART TRANSPLANT RECIPIENTS

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Background: Post-transplant diabetes mellitus (PTDM) affects 34% of heart transplant recipients (HTR) within 5 years and increases the risk of adverse outcomes. While the oral glucose tolerance test (OGTT) is the preferred screening method for prediabetes and diabetes, it is time-intensive and burdensome. We evaluated the diagnostic accuracy of exhaled breath analysis using an electronic nose (eNose) as a potential alternative to detect impaired glucose tolerance (IGT).

Methods: HTR >1 year post-transplant who underwent OGTT screening were included, along with a positive control group of fasting diabetic HTR. Exhaled breath analysis was performed using an eNose (SpiroNose) pre-glucose loading. eNose parameters were combined with clinically relevant parameters for PTDM (time after HTx (years), fasting glucose level (mmol/L), Prednisolon use, weight (kg)) in a multivariate logistic regression model to assess the accuracy in assessing IGT.

Results: A total of 76 HTR were included (29% female, median age 56 [range 19–77] years, median post-transplant time 7.8 [1.5–26.5] years). Among them, 18 had normal glucose tolerance (fasting glucose 5.3 [4.3–5.8] mmol/L, HbA1c 35 [29–39] mmol/mol), 33 prediabetes (fasting glucose 5.9 [4.6–7] mmol/L, HbA1c 40 [32–50] mmol/mol), and 25 PTDM (fasting glucose 7.8 [4.4–17] mmol/L, HbA1c 58 [35–96] mmol/mol). Overall, 58 (76%) exhibited IGT. Pre-glucose loading eNose distinguished normal from IGT with AUROC 0.70 (95% CI 0.57–0.83; Fig 1), 68% accuracy, 69% sensitivity, 67% specificity, 40% negative predictive value (NPV), and 87% positive predictive value (PPV). Adding clinical parameters improved AUROC to 0.88 (95% CI 0.81–0.96; Fig 1), 78% accuracy, 71% sensitivity, 100% specificity, 51% NPV, and 100% PPV.

Conclusions: Impaired glucose metabolism is a frequent finding in HTR. Exhaled breath analysis using eNose technology has the potential to non-invasively monitor and identify patients at risk for IGT in addition to clinical parameters and may serve as alternative for OGTT given its high PPV and specificity. Additionally, eNose technology's rapid point-of-care application allows for subsequent OGTT testing if its results are inconclusive. However, further validation in larger cohorts is necessary to confirm its effectiveness as a replacement screening tool for OGTT.

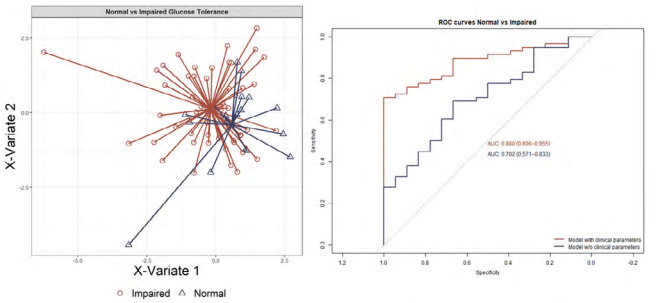

Figure 1: Discrimination between HTR with normal and impaired glucose tolerance using the SpiroNose. On the left, discrimination between normal and impaired glucose tolerance using the SpiroNose, using the first two latent variables obtained by PLS-DA is shown. Each point is a measured patient. In short, PLS-DA is a modelling technique for data reduction, creating new latent variables containing as much information as possible of the complete dataset. On the right, the corresponding ROC curves for both the eNose only and eNose with clinical parameters model are shown.

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BOS_10_9 EFFECT OF FERRIC CARBOXYMALTOSE ON EXERCISE CAPACITY AFTER KIDNEY TRANSPLANTATION: A RANDOMIZED CONTROLLED TRIAL

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Background: Iron deficiency (ID) affects ±30% of kidney transplant recipients (KTR) and has been associated with adverse functional outcomes. In chronic heart failure, ID correction improves exercise capacity and quality of life; whether these effects also occur in KTR is unknown. The main objective of this trial was to address whether intravenous iron improves exercise capacity in iron-deficient KTR.

Methods: We performed a 24-week, double-blind, multicenter, randomized, placebo-controlled trial evaluating the efficacy of ferric carboxymaltose (FCM) in stable KTR with ID (plasma ferritin <100 µg/L or ferritin 100-299 µg/L with transferrin saturation (TSAT) <20%). Participants were assigned to four doses of FCM (500 mg Fe3+/dose) or placebo, with six-week intervals. The primary end point was change in six-minute-walk-test (6MWT) between baseline and week 24. Secondary outcomes included changes in hemoglobin and iron status, muscle mass and strength, kidney function, total fibroblast growth factor 23 (FGF23), cardiac structure and function, cognitive performance and quality of life.

Results: We included 148 iron-deficient KTR (age 57 (interquartile range (IQR) 47-66) y, 68% male, median time since transplant 2 (1-7) y, hemoglobin 13.2±1.3 g/dL, ferritin 47 (27-71) µg/L, TSAT 20±10%, eGFR 61±18 mL/min/1.73 m2). The 6MWT distance improved both in the FCM arm (+21±53 m vs. baseline) and the placebo arm (+19±50 m, P=0.42 between groups, **Fig 1A**). FCM increased hemoglobin and ferritin (**Fig 1B-C**) and improved the Timed Up-and-Go test (**Fig 1D**), a measure of functional muscle strength, but not other parameters of muscle mass or strength. FCM treatment also improved kidney function (**Fig 1E**) and reduced FGF23 levels (**Fig 1F**), but did not affect cardiac structure and function, cognitive performance or quality of life.

Conclusions: ID correction with FCM resulted in a small but significant increase in kidney function and functional muscle strength and a significant reduction in total FGF23 level. However, FCM did not improve exercise capacity, cardiac structure and function, cognitive function or quality of life.

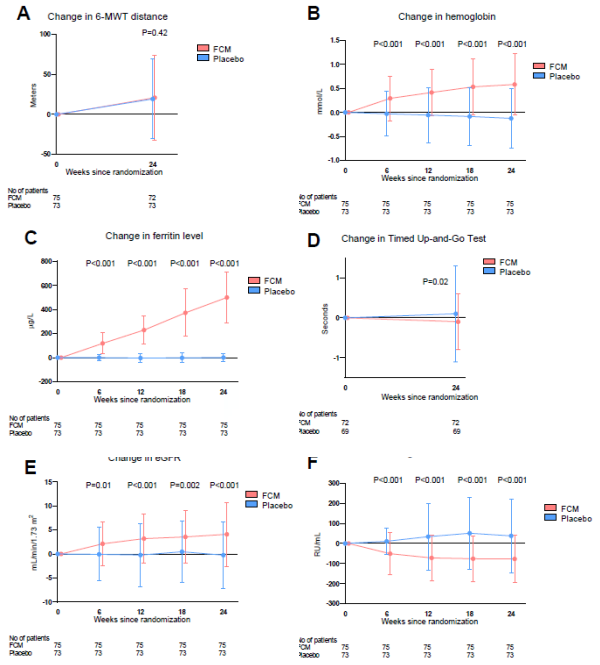

Figure 1

BOS_10_10 GLUCAGON LIKE PEPTIDE1 RECEPTOR AGONISTS AND RENAL OUTCOMES IN KIDNEY TRANSPLANTS WITH DIABETES

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Background: Glucagon-like peptide-1 receptor agonists (GLP1-RAs) have shown renal protective effects in type 2 diabetes mellitus, but data for post-transplant diabetes is limited. We aimed to assess the impact of GLP1-RAs impact on renal outcomes in kidney transplant recipients (KTR) with diabetes.

Methods: Retrospective cohort study. Adult (>18 years) KTR diagnosed with diabetes mellitus either before or after transplantation and treated with GLP1-RAs were matched with those on other anti-hyperglycemic agents. Cumulative risks for study outcomes were estimated using Kaplan-Meier analysis. Cox proportional hazards regression analysis was used to calculate hazard ratios (HR) and 95% confidence intervals (CI).

Results: The study included 272 patients (69% male, mean age 58.3 ± 11.0 years) with a median follow-up of 3.1 years. GLP1-RA treatment was associated with a reduced incidence of composite renal outcomes (first occurrence of graft rejection, dialysis initiation, re-transplantation, or mortality) after adjusting for risk factors (114 vs. 68 events per 1000 patient-years in controls vs. GLP1-RA users, HR 0.49, 95% CI 0.27-0.88). GLP1-RA users also exhibited improvements in glycemic control, lipid profile, and reductions in BMI. Treatment was safe, with no increase in genitourinary infections or biliopancreatic events.

Conclusions: GLP1-RAs effectively improved renal outcomes and metabolic control in diabetic KTR, suggesting renoprotective benefits in this vulnerable population. Prospective studies are needed due to exclusion of KTR from large trials.

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BOS_10_11 EXERCISE AND PREDIABETES AFTER RENAL TRANSPLANTATION: EXPRED II

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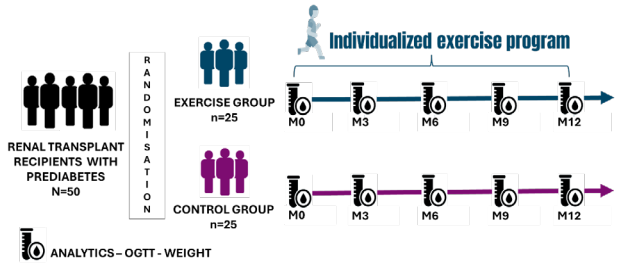
Background: Post-transplant diabetes mellitus (PTDM) observed beyond 12 months after transplantation develop mainly in cases with prediabetes. Thus, treating patients with prediabetes might help preventing PTDM. In the general population, exercise prevents the evolution from prediabetes to diabetes. However, the evidence in renal transplantation is limited. In an exploratory study, the Exercise and Prediabetes after Renal Transplantation (EXPRED-I; doi:10.1186/s40798-023-00574-8), we showed that exercise reverted 60% of the cases with prediabetes. Hereby, we design the EXPRED-II, a clinical trial to evaluate the efficacy of exercise in reverting prediabetes, as a first step to prevent PTDM.

Methods: 50 patients with prediabetes beyond 12 months post-transplant with capacity to perform exercise will be randomized to standard life-style recommendations (control group, n=25) or to a training intervention (exercise group, n=25). Prediabetes will be diagnosed based on fasting glucose levels and an Oral Glucose Tolerance Test (OGTT). Patients on exercise will complete a survey of physical capacity and then will start with aerobic exercise (walking, swimming, or cycling) 5 times/week, 30 min/day for 12 months. The training will be gradually increased to 80 min/day and combined with strength exercise. An adherence plan will be implemented, including weekly calls, monthly visits and an activity tracker. The reversibility/persistence/relapse of prediabetes will be evaluated with fasting glucose and OGTT every 3 months. Hereby, we present the preliminary data of 19 patients at 6 months.

Results: 19 patients achieved 6 months of follow-up (exercise group n=8 vs control group n=11). In the exercise group, 5 patients (63%) reverted to normal glucose levels both at fasting (<100 mg/dL) and after an OGTT (<140 mg/dL) vs 2 patients (18%) of the control group (p=0.048). The exercise group also reduced weight (from 75 ± 15 kg to 70 ± 15 kg, p=0.012) and triglycerides levels (from 131 ± 62 mg/dL to 101 ± 34 mg/dL, p=0.028). The control group showed no changes in these variables. Adherence to exercise was 76%. No adverse events were observed.

Conclusions: exercise seems to be effective and safe in reverting prediabetes in renal transplant patients at risk of PTDM.



1. Study design. Months (M); Oral Glucose Tolerance Test (OGTT)

BOS_10_12 UNDERUTILIZING OF LIPID-LOWERING AGENTS IN SOLID ORGAN TRANSPLANT RECIPIENTS: A CALL FOR IMPROVEMENT

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Background: Dyslipidemia affects 40-60% of solid organ transplant (SOT) recipients and is a key risk factor for cardiovascular disease (CVD), the leading cause of mortality post-transplant. Kidney transplant recipients face a 5-10 times higher CVD risk, while liver recipients have nearly double the risk compared to the general population. Effective lipid management is crucial but may be underutilized, as suggested by studies outside the field of transplantation. In this study, we evaluated the adequacy of lipid management one year after SOT and compared practices across SOT programs (heart, liver, lung, and kidney).

Methods: Cross-sectional data from SOT recipients one year post-transplantation were obtained from the TransplantLines biobank an cohort study (NCT03272841) for analysis. A LDL-cholesterol concentration of ≥2.6mmol/L was defined as dyslipidemia, based on Dutch cardiovascular risk management and SOT program guidelines. The number of lipid-lowering agents prescribed to each patient was recorded.

Results: We analyzed 942 SOT recipients (23 heart, 113 liver, 131 lung, and 675 kidney transplant recipients), of whom 582 (62%) males, with a mean age of 57 ±13 years. Adequate LDL targets (<2.6 mmol/L) were achieved in 48% of heart, 42% of liver, 28% of lung, and 51% of kidney transplant recipients (p<0.001; **Fig 1A**). Lipid-lowering agent use varied significantly between groups, with 13% of heart, 47% of liver, 60% of lung, and 23% of kidney transplant recipients with dyslipidemia (LDL ≥2.6mmol/L) being untreated and 35% of heart, 9% of liver, 12% of lung, and 23% of kidney transplant recipients with dyslipidemia (LDL ≥2.6mmol/L) using only one lipid lowering agent (p<0.001; **Fig 1B**).

Conclusions: With only 28-51% of recipients meeting LDL targets across SOT groups, dyslipidemia treatment needs improvement and represents a promising opportunity for improving cardiovascular risk and mortality. Management between programs and the use of lipid-lowering agents varied notably between SOT groups. Opportunities lie in treating recipients with dyslipidemia who remain untreated, and optimizing treatment regimens for those already on therapy.

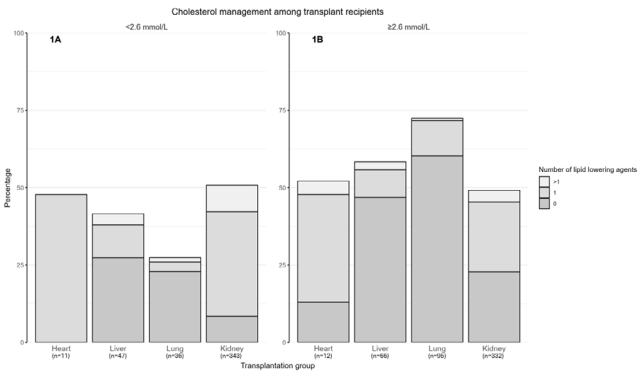

Figure 1: Cholesterol management among heart-, liver-, lung- and kidney transplantation recipients showing the distribution of the use of lipid lowering agents within different LDL-cholesterol categories (1A: <2.6mmol/L and 1B: ≥2.6 mmol/L).

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BOS_10_13 CORONARY ARTERY DISEASE RISK ASSESSMENT IN LT CANDIDATES: A MODIFIED CAD-LT ALGORITHM INTEGRATED WITH CCTA

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Background: Epidemiological changes in liver transplant (LT) candidates have increased the prevalence of coronary artery disease (CAD) risk factors. The CAD-LT algorithm, validated in the U.S. for guiding cardiac evaluation in LT candidates, relies on invasive tests like coronary angiography (ICA). Coronary artery calcium scoring (CACS) and coronary computed tomography angiography (CCTA) demonstrate high negative predictive value for clinically significant CAD in the general population. This study investigates a modified CAD-LT (mCAD-LT) algorithm integrating CACS and CCTA to improve CAD risk stratification in LT candidates.

Methods: This prospective, single-center study enrolled LT candidates between August 2022 and October 2024. The mCAD-LT algorithm incorporated obesity and metabolic-associated fatty liver disease (MAFLD) as risk factors and redefined cardiovascular risk as low (<7), intermediate (7–10), or high (>10). Intermediate- and high-risk patients underwent CACS, with scores <400 prompting CCTA and scores >400 leading to stress testing or ICA based on risk stratification.

Results: Among 177 candidates (mean age 59 ± 9 years; 74% male), metabolic alcohol-associated liver disease (MetALD) was the most common etiology, with MAFLD present in 12% and obesity in 25% (mean BMI 26.9 ±4.5 kg/m²). Twenty-seven patients (15%) were low risk and required no further evaluation. Of 150 intermediate- and high-risk patients, 100 had CACS <400, with 13 showing significant stenosis on CCTA; ICA confirmed stenosis in 3 cases. Among 46 patients with CACS >400, 28 underwent ICA, identifying stenosis in 7. Eighteen intermediate-risk patients underwent stress testing; 5 were referred to ICA, confirming stenosis in 2. Overall, 46 ICAs (26%) were performed, identifying significant stenosis in 12 patients. Ten underwent percutaneous coronary intervention (PCI); 2 were excluded from LT due to contraindications for short-term dual antiplatelet therapy (DAPT).

Conclusions: The mCAD-LT algorithm reduced ICA use by over 50% compared to the original CAD-LT algorithm. Among 116 patients transplanted, one acute myocardial infarction occurred (<1%), successfully managed with repeat PCI. These findings support mCAD-LT as a less invasive and effective strategy for CAD risk stratification in LT candidates.

BOS_10_14 PREVALENCE AND RISK FACTORS OF FRAILTY AND SARCOPENIA IN LONG-TERM KIDNEY TRANSPLANT SURVIVORS

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Background: Frailty and sarcopenia are common among kidney transplant recipients and are associated with adverse outcomes. While initial improvements in physical function are observed post-transplantation, data on frailty and muscle function during long-term follow-up remain scarce.

Methods: This prospective cross-sectional study evaluated frailty, muscle strength, and physical performance in stable long-term kidney transplant recipients between November 2022 and January 2024. Frailty was assessed using the Fried phenotype score, with frailty defined as a score of ≥2. Muscle strength was measured using handgrip strength, and physical performance was evaluated using the short physical performance battery, which includes gait speed, chair stand, and balance tests.

Results: A total of 567 kidney transplant recipients were included (median age: 60 years, IQR: 55–65 years; median post-transplant follow-up: 91 months, IQR: 50–155 months). The overall prevalence of frailty was 12.0% (68/567), with rates increasing over time: 9.2% within 1–5 years, 10.3% at 5–10 years, and 15.7% beyond 10 years post-transplantation. Frailty was strongly associated with muscle weakness and impaired physical performance. Multivariate analysis identified older age, higher waist circumference, longer post-transplant duration, and low hemoglobin levels as independent risk factors for frailty. In contrast, regular exercise and the use of mechanistic target of rapamycin inhibitor demonstrated a protective effect against frailty.

Conclusions: Frailty is closely associated with muscle weakness and impaired physical performance in stable long-term kidney transplant recipients. Addressing modifiable risk factors, such as exercise and optimized immunosuppressive regimens, may help mitigate frailty and improve outcomes.

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Optimizing cardiovascular health

BOS_10_15 INADEQUATE BLOOD PRESSURE MANAGEMENT AFTER SOLID ORGAN TRANSPLANTATION: OPPORTUNITIES FOR OPTIMIZING CARE

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Background: Hypertension affects 50-80% of solid organ transplant (SOT) recipients and requires adequate management to prevent complications such as cardiovascular disease (CVD), the leading cause of mortality after SOT, and to improve patient survival. However, studies in non-transplant populations suggest antihypertensives are often underutilized. We investigated the adequacy of blood pressure management one year after SOT and determined whether management differs across SOT programs (heart, liver, lung, kidney).

Methods: Cross-sectional data from SOT recipients one year post-transplantation were obtained from the TransplantLines biobank and cohort study (NCT03272841) for analysis. Hypertension was defined as systolic blood pressure (SBP) >130 mmHg or diastolic blood pressure (DBP) >80 mmHg, based on Dutch guidelines for cardiovascular risk management and SOT program guidelines. The number of antihypertensive agents prescribed to each patient was recorded.

Results: We analyzed 975 SOT recipients (23 heart, 108 liver, 140 lung, and 704 kidney transplant recipients), of whom 601 (62%) males, with a mean age of 57 ±13 years. Adequate blood pressure targets (≤130/80 mmHg) were achieved in 30% of heart, 40% of liver, 42% of lung, and 33% of kidney transplant recipients (p=0.12; **Fig 1A**). Antihypertensive agent use varied significantly between groups, with 22% of heart, 31% of liver, 30% of lung, and 8% of kidney transplant recipients with hypertension (blood pressure > 130/80 mmHg) untreated and 26% heart, 20% liver, 20% lung and 20% kidney transplant recipients with hypertension (blood pressure > 130/80 mmHg) using only one antihypertensive (p<0.001; **Fig 1B**).

Conclusions: With only 30-42% of recipients meeting blood pressure targets across SOT groups, hypertension treatment needs improvement and represents a promising opportunity for improving cardiovascular risk and mortality. The number of prescribed antihypertensive agents varied notably between SOT groups. Opportunities lie in treating recipients with hypertension who remain untreated, and optimizing treatment regimens for those already on therapy.

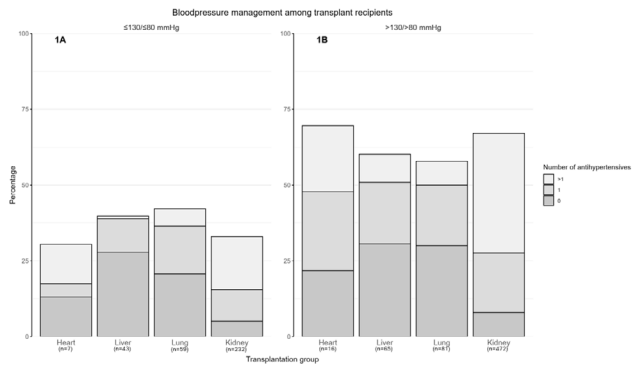

Figure 1: Blood pressure management among heart-, liver-, lung- and kidney transplantation recipients showing the distribution of antihypertensive use within different blood pressure categories (1A: ≤130/80 mmHg and 1B: >130/80 mmHg).

Advancing value based outcomes in transplantation

BOS_11_1 ULTRA-LONG-TERM OUTCOME OF LIVER TRANSPLANTATION IN THE NETHERLANDS: A 40-YEAR OBSERVATIONAL COHORT STUDY

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Background: Over the past 60 years, liver transplantation (LT) has evolved from an experimental procedure into the standard treatment for patients with end-stage or otherwise untreatable liver disease. In the Netherlands, LT has been performed since 1979. In this study we evaluated four decades of LT practice and assessed long-term patient survival.

Methods: This multicenter observational cohort study included primary adult LT performed between 1979 and 2021. Data were obtained from the Dutch Organ Transplant Registry (NOTR) and individual medical records. To identify trends, data were grouped into three consecutive periods: before 2000, 2000-2009, and the current era (2010 onward). A landmark analysis was conducted, excluding deaths and graft failures within the first year, followed by a time-to-event analysis. The primary outcome was patient survival.

Results: A total of 1778 LTs were included: 395 (22.2%) performed before 2000; 537 (30.2%) between 2000-2009, and 846 (47.6%) between 2010-2021 (p < 0.001). Median patient survival was 8.92 years (range 1.01-42.1 years). The 10-year patient survival rates were across the eras: 75.2% before 2000, 73.9% between 2000-2009, and 70.5% between 2010-2021 (p = 0.94; Figure 1A), despite significantly increasing median donor age (35.0, 48.0, 55.0 years, p < 0.001) and recipient age (46.0, 52.0, 55.0 years, p < 0.001) over time. No significant difference in survival was found between donation after brain death (DBD) and donation after circulatory death (DCD) donors, with 15-year survival rates of 65.4% and 63.2%, respectively (p = 0.07; Figure 1B). Females showed significantly better 15-year survival compared to males: 60.0% vs 71.2% (p < 0.001; Figure 1C).

Conclusions: Long-term patient survival after LT remained consistent across eras, provided that the patient and graft survive the first year. Donor type seemed to have no impact on long-term survival, while female recipients showed significantly better long-term survival compared to males.

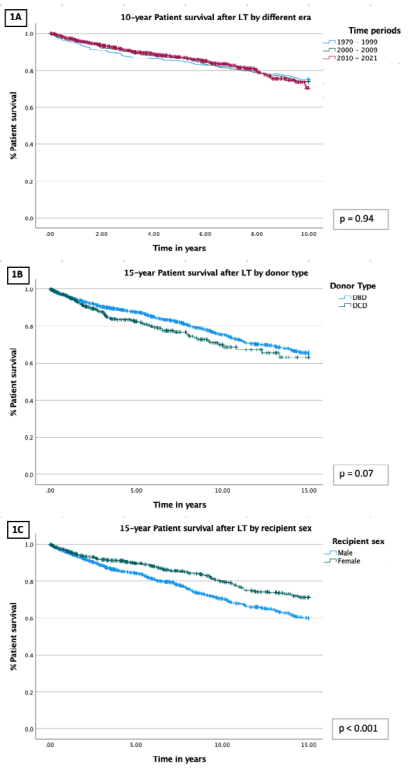

Figure 1. Patient survival after Liver Transplantation

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BOS_11_2 BETA-CELL REPLACEMENT AFTER PANCREAS TRANSPLANT FAILURE: A SYSTEMATIC REVIEW

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Background: Pancreas transplantation (PT), typically performed simultaneously with kidney transplantation (SPK), restores euglycaemia for patients with complicated type 1 diabetes mellitus (T1DM). However, SPK is associated with morbidity and occasional pancreatic graft loss. We review the evidence on treatment options available (further PT (pancreas after pancreas; PAP), islet transplantation (IAP) or best medical therapy (BMTAP)) for glycaemic control after pancreas graft loss.

Methods: A systematic literature review using PRISMA methodology analysed MedLINE, EMBASE and Cochrane databases from 2000-2024. Employed MeSH terms included ('Islet transplantation' AND 'pancreas transplantation' AND 'type 1 diabetes' AND 'graft failure') OR 'Pancreas retransplantation' OR ('Type 1 diabetes' AND (insulin pump OR diabetes technology OR insulin therapy OR automated insulin delivery) AND graft failure).

Results: Across the 16 studies included, 1393 patients received PAP, 14 patients received IAP and six patients received BMTAP. Mean age of recipients was 38.3, 48.6 and 43.0 years respectively. 31.4% of PAP recipients experienced Clavien-Dindo grade >II complications, with 1-Year graft survival of 37.2-100%. IAP induced a decrease in HbA1c by 8-32 mmol/mol across 3 studies with mean daily exogenous insulin between 0.21-0.37 units/kg. Mean daily insulin dose with BMTAP reduced from 0.53-0.41 units/kg. There was no difference in frequency of severe hypoglycaemic episodes (SHE) before or after commencement of BMTAP. One patient experienced SHE after IAP. PAP and IAP preserved renal function more than standard insulin regimes.

Conclusions: PAP provides excellent outcomes but is associated with morbidity and early graft loss. IAP offers improvements in glycaemic control, typically with supplemental exogenous insulin, suitable for recipients with reduced cardiorespiratory reserve. BMTAP with diabetes technology has limited data in setting of severe complicated T1DM or PT failure but may become an important viable alternative or adjunct with the improvement in technologies available.

BOS_11_3 NON-RETRIEVAL AND NON-UTILISATION OF DECEASED DONOR KIDNEYS FOR TRANSPLANTATION: AN AUSTRALIAN COHORT STUDY

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Background: An efficient organ procurement program must maximise utility of retrieval team activity. We aimed to quantify non-retrieval and non-utilisation rates of deceased donor kidneys.

Methods: Cohort study of deceased kidney donors in Australia 2014-2021 using ANZOD data. Outcomes were non-retrieval (kidneys not retrieved after surgical incision) and non-utilisation (kidneys retrieved but not transplanted). We compared non-retrieval and non-utilisation rates using logistic regression by donor factors (age, sex, blood-group, ethnicity, BMI, smoking, socio-economic disadvantage, remoteness, year, cause of death, resuscitation, pathway, KDPI, side, dual-allocation/*en-bloc*), and system factors (state/territory of donor hospital, retrieval team, and intended recipient's hospital).

Results: Among 7,211 kidneys (3,683 donors) accepted for retrieval, 675 (9%) were non-retrieved and 430 (7%) were non-utilised. Crude non-retrieval rates doubled from 5% to 10% between 2014-2021 (p=0.01) while non-utilisation remained around 7% (p=0.1). After adjustment, non-retrieval was greater among donors with KDPI≥75 (OR 4.28, 95%CI: 2.08–8.81, p<0.001), diabetes (OR 1.74, 95%CI: 1.25–2.43, p=0.001), and in recent years (annual OR 1.08, 95%CI: 1.03–1.55, p=0.002), and lower for ECD DCDD (OR 0.46, 95%CI: 0.26-0.81, p=0.01). Non-utilisation was greater for SCD DCDD (OR 1.90, 95%CI: 1.28-2.82, p<0.001), blood group AB (OR 2.05, 95%CI: 1.16-3.64, p=0.03) and in recent years (annual OR 1.08, 95%CI: 1.02-1.15, p=0.01), and lower in Tasmania (OR 0.28, 95%CI: 0.08-0.97) and Queensland (OR 0.57, 95%CI: 0.36-0.92, p=0.03). Documented reasons for non-utilisation lacked transparency but included poor perfusion (17%).

Conclusions: Efforts to maximise transplantation of donor kidneys could focus on improving utilisation of higher KDPI kidneys and perfusion techniques.

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BOS_11_4 FACILITATING THE ADOPTION OF ENHANCED RECOVERY AFTER SURGERY (ERAS) IN TRANSPLANTATION ACROSS THE UK

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Background: Enhanced recovery after surgery (ERAS) is mainstay in most surgical specialties, known to reduce the risk of post-operative complications, empower patients, reduce hospital stay and improve resource utilisation. Despite this, adoption by the transplant community has been slow. We aimed to draw from centres with existing ERAS experience, alongside experts in transplantation, to provide a repository of evidence-based resources and encourage and facilitate the adoption of ERAS in UK kidney transplant centres.

Methods: An ERAS in Transplantation (ERAS in Tx) steering group was comprised of specialists from across the UK, including surgeons, physicians, anesthetists, physiotherapists, patients, and lay representatives. Three workstreams were created: 1) Core and Desirable pathway components; 2) Educational Resources; 3) Evaluation and Measurements. This model was designed to be adaptable for other transplant specialties. A panel of expert patients contributed to the co-production of patient-facing resources, including both web-based and downloadable content.

Results: An on-line ERAS in Tx clinical 'toolkit' is now published, including a link leading to core and desirable criteria, specific to the adult kidney transplant recipient. Criteria are organised into pre, peri and post-operative sections which link to supporting evidence and downloadable resources for transplant centres to tailor to their specific needs. Evaluation criteria are provided to measure centre-specific performance against each domain. Additionally, existing patient-facing information was updated to include an explanation of ERAS in transplantation.

Conclusions: The ERAS in Tx initiative has increased community engagement with enhanced recovery in kidney transplantation. Providing a transferable model for other transplant specialties, this has also fostered broader engagement within the transplant community. Current workstreams for completion in 2025, include Adult Liver transplant and Living Kidney Donor, with interest from the lung, pancreas, and paediatric kidney transplant communities. It is anticipated that widespread implementation and evaluation of ERAS in transplantation, will continue to empower patients, improving both their experience and clinical outcomes

BOS_11_5 EFFECT OF SYSTEMIC VASCULAR RESISTANCE ON ANALGESIA NOCICEPTION INDEX AND SURGICAL PLETH INDEX DURING LT

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Background: The Analgesia nociception index (ANI) and Surgical Pleth Index (SPI) are proposed as means to assess the balance between noxious stimulation and the anti-nociceptive effects of anesthesia. While ANI is a heart rate variability-based index derived from electrocardiography, SPI relies on a balanced sum of normalized heartbeat intervals (HBIs) and plethysmographic pulse wave amplitudes derived from a photoplethysmographic sensor. Systemic vascular resistance (SVR) may affect the pulse wave amplitude. In the present study, we compared ANI and SPI during liver transplantation, where systemic vascular resistance changes significantly.

Methods: Forty-seven adult recipients were included in the present study. SPI from photoplethysmographic sensor at the index finger and ANI from two electrodes in V1 and V5 were collected at 5-minute intervals during the surgery. The primary outcome was the agreement of degree of pain by ANI and SPI under situations of different systemic vascular resistance. The secondary outcome was to compare the ability of delta ANI and delta SPI to detect the standard noxious stimulation.

Results: Total 1,318 pairs of data were collected during surgery. The percentage agreement indicating the same analgesic level between ANI and SPI was 32.4%, and weighted Cohen's kappa coefficient [95% Confidence interval (CI)] was 0.03 [0 to 0.05]. The weighted kappa coefficient indicated slight agreement between ANI and SPI. As shown in table 1, the agreement between ANI and SPI was better when SVR was higher (weighted Cohen's kappa coefficient [95% CI], 0.05 [0.04, 0.08]). For SPI, 71 out of 484 pairs (14.7%), 67 out of 554 pairs (12.1%), and 28 out of 280 pairs (10.0%) showed higher analgesic level than the analgesic level measured by ANI in low SVR, normal SVR, and high SVR, respectively. Also, the ability of ANI to detect standard noxious stimulation was fair with an area under the curve (AUC) of 0.748 [0.6-0.863] (Figure 1). But SPI showed insignificant predictability (AUC=0.569 [0.417-0.713]; *P*=0.662).

Conclusions: We found that ANI and SPI cannot be used interchangeably to assess the degree of pain during liver transplantation. However, ANI predicted standard noxious stimulation during surgery more successfully and may be a more appropriate index compared to SPI under such conditions.

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BOS_11_6 OVERCOMING PAIN AFTER BILATERAL LUNG TRANSPLANTATION: PILOT STUDY ON INTERCOSTAL NERVE CRYOABLATION

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Background: Suboptimal postoperative pain control in lung transplantation can significantly increase complication rates. Intraoperative intercostal nerve cryoablation (CRYO) has emerged as a promising analgesic technique, but its application in lung transplantation has not been thoroughly examined. This pilot study aimed to assess the feasibility, safety, and efficacy of CRYO for pain management in patients undergoing bilateral lung transplantation.

Methods: A consecutive series of eighteen patients undergoing bilateral lung transplantation were prospectively enrolled and 1:1 randomly assigned to either the CRYO group or the standard pain management group. In the CRYO group, cryoablation was performed bilaterally from the third to the seventh intercostal space. Key data points included total surgical time, complications, and postoperative analgesic consumption. Analgesics were converted to morphine equivalents (ME): Morphine (1:1), Tramadol (10:1), Ketorolac (6:1), and Paracetamol (520:1). The first 21 postoperative days were analyzed.

Results: Cryoablation was successfully performed in all nine patients in the intervention group. The mean operative time was 592.9 minutes [95% CI: 533.9–651.9] in the CRYO group and 619.0 minutes [95% CI: 507.7–730.3] in the control group. No early or delayed CRYO-related complications were noted. Patients in the CRYO group consumed a mean of 101.9 ME per patient [95% CI: 51.1–152.7], whereas the control group received a mean of 219.9 ME per patient [95% CI: 101.6–338.2]. Daily analgesic consumption was 5.5 ME/day [95% CI: 2.7–8.3] in the CRYO group, compared to 13.8 ME/day [95% CI: 6.2–21.4] in the control group.

Conclusions: Intraoperative intercostal nerve cryoablation during bilateral lung transplantation is a safe, fast and straightforward technique without specific complications. This pilot study suggests it may significantly reduce postoperative analgesic requirements. These findings support the need for a larger, more comprehensive trial to confirm CRYO's benefits in this population.

BOS_11_7 ASSOCIATION OF PERIOPERATIVE MYOCARDIAL INJURY WITH INTRAOPERATIVE HEMODYNAMICS IN LT PTS ACCORDING TO CAD-LT SCORE

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Background: Perioperative cardiovascular complications are the leading cause of non-graft-related mortality in liver transplant (LT) patients. Among patients undergoing noncardiac surgery, the occurrence of perioperative myocardial injury (PMI) was demonstrated to increase 30-day mortality. Risk stratification for LT patients is crucial even though no standardization is available. Among others, Coronary Artery Disease in LT (CAD-LT) score has been used. However, the profound hemodynamic instability occurring intraoperatively could play a further role in affecting perioperative outcomes. Our study aims to evaluate the association between the occurrence of PMI and intraoperative hemodynamics among patients undergoing LT stratified using CAD-LT.

Methods: This is a retrospective study including patients undergoing LT with CAD-LT scores available. Patients were admitted to Niguarda Hospital from February 2022 to September 2024. Patients' characteristics were described according to CAD-LT risk classes: low (-2-3), intermediate (4-8), high (9-25). The primary outcome was the occurrence of PMI defined as postoperative high-sensitivity Troponin T (hs-TnT) >65 ng/L, within 72 hours from LT surgery. We built a multivariate regression model with PMI as dependent variable and the following as independent: intraoperative hypotension (mean arterial pressure <90 mmHg for at least 10 minutes), vasoactive inotropic score (VIS), peak of serum lactate, lowest time-weighted hemoglobin and blood transfusions, and CAD-LT score.

Results: We included 57 patients undergoing LT, and PMI occurs in 35 (61%). The occurrence of PMI was associated with peak lactate level (OR 1.6, 95% CI 1.10–2.67, p = 0.03) and maximum VIS (OR 1.03, 95% CI 1.002–1.06, p = 0.04). Instead, it was not associated with CAD-LT score. As post-hoc analysis, we found that PMI was associated with the occurrence of postoperative AKI (p = 0.02) and longer ICU stay (median 16 [IQR 13, 19] *vs.* 41 [23, 64] days for patients with PMI).

Conclusions: Intraoperative hemodynamics is independently associated with the occurrence of PMI. The lack of association with CAD-LT score may suggest effective risk reduction through preoperative cardiac optimization. Further studies are needed to confirm our findings

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BOS_11_8 PREDICTORS OF PROLONGED HOSPITAL STAY FOLLOWING LIVER TRANSPLANTATION: A 10-YEAR RETROSPECTIVE ANALYSIS

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Background: Liver transplantation (LT) is a life-saving procedure for end-stage liver disease, but prolonged hospital stays post-transplantation increases the risk of complications and healthcare costs. Identifying predictors of extended hospitalisation is critical for improving patient outcomes and optimising health-care resource use.

Methods: A retrospective cohort study was conducted using data from consecutive 1710 adult LT recipients at a single centre over a 10-year period (2014–2023). Prolonged length of stay (LOS) was defined as ≥16 days post-transplant, based on median data and statistical prediction. Data on recipient demographics, clinical characteristics, transplant indications, and post-operative complications were collected. Univariate and multivariate binary logistic regression analyses were performed to identify independent predictors of prolonged LOS.

Results: Prolonged LOS was observed in 45.5% of recipients. Independent predictors included recipient age >65 years (OR = 1.54, p = 0.049), acute liver failure (OR = 2.90, p = 0.001), cryptogenic cirrhosis (OR = 3.44, p = 0.04), autoimmune hepatitis (OR = 1.42, p = 0.01), and post-operative bile leaks (OR = 9.95, p < 0.001). Additionally, a poor performance status (OR = 3.23, p = 0.023), the need for pre-transplant renal support (OR = 5.725, p = 0.002), and increased stay in the Intensive Therapy Unit (OR = 1.31, p < 0.001) were significant predictors.

Conclusions: This study highlights several key factors associated with prolonged LOS after liver transplantation, emphasising the need for enhanced pre-operative and post-operative care for high-risk patients. Further multicentre research is warranted to validate these findings and develop strategies to reduce hospitalisation and improve outcomes.

BOS_11_9 INNOVATIVE APPROACH IN IMPLEMENTING PROMS FOR SOLID ORGAN TRANSPLANTATION: LESSONS LEARNED

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Background: In our transplant center, a comprehensive approach has been chosen to implement value-based healthcare (VBHC), meaning that all organ transplantation departments are collaborating. This approach is unique and has not been implemented in this way before. The VBHC dashboard is integrated into de electronic patient file. The aim of this study was to measure the extent to which VBHC has been integrated into the outpatient clinic.

Methods: Patient Reported Outcome Measures (PROMs) was implemented, post-transplant, in phases from July 2023 to October 2024 starting with kidneys and lung transplant recipients, followed by liver and heart transplant recipients. Questionnaires used were the Patient Reported Outcomes Measurement Information System and the Basel Assessment of Adherence to Immunosuppresive Medication Scale (PROMIS and BAASIS). The PROMIS measures physical health (e.g. fatigue, pain), mental health (e.g. anxiety), social health (e.g. activities). In addition, participants had the possibility to respond to an open question on which topics they wanted to discuss with their healthcare provider (HCP).

Results: Overall, PROMIS response rate was 78% (n= 1594), and BAASIS response rate was 77% (n= 1577). Of the responders 58% were men with a mean age of 57 years. Per department, for kidney the response rate (BAASIS and PROMIS) was 64% (n = 868), lung 87% (n = 323), liver 72% (n = 379), heart 76% (n = 206). The number of questionnaires opened by the HCP during the consultation ranged between 5% to 15%. Open questions were completed by 1558 participants, and topics they wanted to discuss were related to medication, fatigue and pain.

Conclusions: VBHC changes the way we interact with patients to a person-centered approach. Therefore, effective communication and information-sharing by the HCP are crucial. However, a low percentage of HCP open the questionnaires during the consultation. By discussing the outcomes of a questionnaire during the consultation, problems can be promptly addressed to optimize care which is in line with the goal of VBHC. To do that HCP need to adapt the way they run their outpatient clinic. By combining our efforts, we can further optimize the quality of care.

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BOS_11_10 DEPRESSION AND ANXIETY IN A NATIONAL COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: Depression and anxiety are prevalent conditions that cause substantial morbidity and all-cause mortality. The risk of these mental health conditions in kidney transplant (KT) recipients has not yet been described in a large national cohort.

Methods: Patients 11+ years old who received a kidney transplant prior to 12/31/2022 were identified in EPIC Cosmos electronic health records (EHR) data (N=170,983). Using a Poisson framework, we identified risk factors associated with new diagnoses of depression and, separately, anxiety in the 2 years post-transplant. We stratified models by adolescents (11-21 years old) and adults. Diagnoses were identified based on Clinical Classifications Software (CCS) criteria.

Results: Among adult kidney recipients, 3.0% were newly diagnosed with depression and 3.5% with anxiety in the 2 years post-transplant. 3.3% and 3.4% of adolescents were diagnosed with depression or anxiety, respectively. Relative to White patients, Black patients had a 23% lower risk of being diagnosed with depression and a 19% lower risk of being diagnosed with anxiety. Asians had a 49% and 36% lower risk of being diagnosed with depression and anxiety, respectively. Females had a 39-41% higher risk than males. Adolescents had a 30% higher risk of depression and 14% higher risk of anxiety relative to 22–40-year-old KT recipients. Recipients aged 70 years or older were at greatest risk (RRs: 1.67 and 1.50 for depression and anxiety). Receipt from a living donor was associated with 34% lower risk of depression and 30% lower risk of anxiety. Hispanic ethnicity and Social Vulnerability Index (SVI) were not statistically significant risk factors.

Conclusions: The study found significant variations in the risk of depression and anxiety among KT recipients based on demographic and clinical factors. White, female, older, and deceased donor KT recipients may be at higher risk of developing depression and anxiety post-transplant.

	Adult (22+ years old) (N=163,595)			Adolescent (11-21 years old) (N=7,388)		
	Pre-Transplant	De Novo Diagnoses Post-Transplant	Either time frame	Pre-Transplant	De Novo Diagnoses Post-Transplant	Either time frame
Substance use disorder	9,692 (5.9%)	2,749 (1.7%)	12,441 (7.6%)	83 (1.1%)	76 (1.0%)	159 (2.2%)
Schizophrenia spectrum and other psychotic disorders	854 (0.5%)	759 (0.5%)	1,613 (1.0%)	21 (0.3%)	12 (0.2%)	33 (0.4%)
Bipolar and related disorders	969 (0.6%)	312 (0.2%)	1,281 (0.8%)	<11	<11	17 (0.2%)
Depressive and other mood disorders	10,121 (6.2%)	4,918 (3.0%)	15,039 (9.2%)	314 (4.3%)	245 (3.3%)	559 (7.6%)
Anxiety, trauma, and stress-related disorders	12,025 (7.4%)	5,731 (3.5%)	17,756 (11.0%)	673 (9.1%)	254 (3.4%)	927 (13%)
Suicide attempt or intentional self-harm	306 (0.2%)	315 (0.2%)	621 (0.4%)	41 (0.6%)	43 (0.6%)	84 (1.1%)
Any of the above	22,288 (14%)	3,035 (2.0%)	24,487 (16%)	807 (11%)	21 (0.3%)	833 (12%)

	Depression			Anxiety		
		95% CI			95% CI	
	RR	Lower	Upper	RR	Lower	Upper
Race (ref: White)						
Black	0.77	0.71	0.83	0.81	0.75	0.87
Asian	0.51	0.42	0.61	0.64	0.54	0.74
Other/missing	0.85	0.78	0.93	0.98	0.91	1.06
Age, years (ref: 22-40)						
Adolescent	1.30	1.12	1.50	1.14	0.99	1.31
41-50	1.04	0.95	1.14	1.02	0.94	1.11
51-60	1.24	1.14	1.35	1.10	1.01	1.19
61-70	1.36	1.25	1.49	1.34	1.24	1.45
70+	1.67	1.48	1.88	1.50	1.34	1.67
Female	1.41	1.33	1.49	1.39	1.32	1.47
Ethnicity: Hispanic	1.00	0.91	1.11	1.02	0.93	1.11
Living Donor	0.66	0.61	0.70	0.70	0.66	0.74
SVI Percentile	0.97	0.87	1.08	0.95	0.86	1.05

BOS_11_11 MANAGING DELIRIUM IN CRITICAL CARE AFTER LIVER TRANSPLANTATION IN FRANCE AND FRANCOPHONE COUNTRIES

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Background: The management of delirium in critical care after liver transplantation (LT) requires particular attention due to its prevalence, estimated at around 25% of patients within the first three postoperative days (1).

Methods: A survey conducted in 2024 among 86 critical care physicians across 21 LT centers (16 French ICUs, 1 Canadian, 1 Swiss, and 1 Belgian ICU) assessed current practices.

Results: In most cases, the RASS (79%) and Glasgow (74%) scales are used to assess the neurocognitive status of critically ill patients. Following LT, 57% of physicians use a specific scale to assess delirium, with preferences for the CAM-ICU (33%) and RASS (23%). Only 17% of practitioners consider pharmacological prevention of delirium when risk factors are identified. Haloperidol remains the first-line treatment for 37% of physicians in cases of post-LT delirium, followed by dexmedetomidine (29%), hydroxyzine (13%), and diazepam (6%). However, 6% of physicians do not prescribe any initial medication. Physical restraint is an option for 93% of physicians. The most commonly requested diagnostic tests are a serum ammonia measurement (51%), brain CT scan (47%), and EEG (35%), as first-line assessments, while 16% of physicians do not order any tests initially. Regarding immunosuppressive treatment, 56% of respondents consider replacing tacrolimus, and 29% consider reducing corticosteroids. For patients with a history of hepatic encephalopathy treated before LT, 42% of physicians continue these treatments either routinely or after delirium onset. Ammonia level measurement is prescribed by 57% of practitioners after LT, systematically or in cases of post-LT delirium.

Conclusions: This survey highlights the variability in practices for managing delirium after LT. A prospective multicenter study would help better understand the underlying mechanisms and refine management strategies, considering anesthetic and critical care factors.

(1) Cardoso FS, Kok B, Dong V, Kim M, Karvellas CJ. Post liver transplantation delirium assessment using the CAM-ICU-7 scale: A cohort analysis. Can Liver J. 2023 Jul;6(2):261–8.

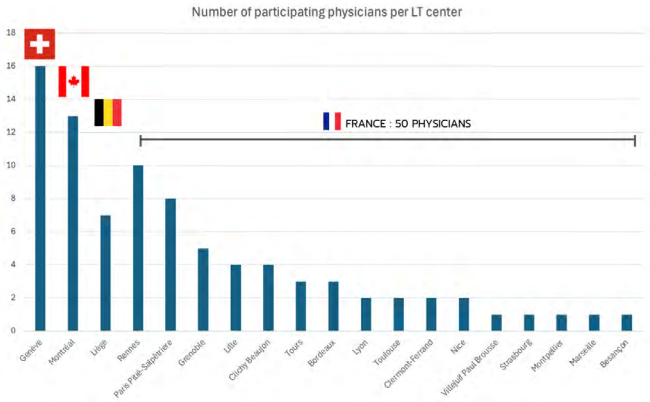

Figure: number of participating physicians per LT center

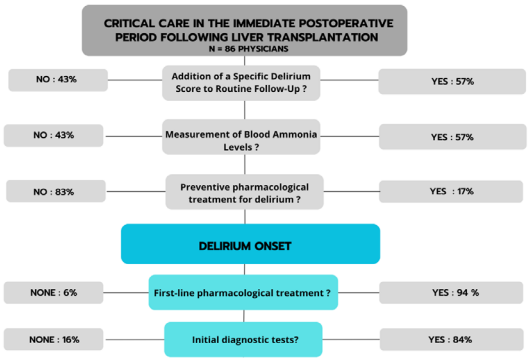

Table: main results of the survey

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BOS_11_12 RIGHT SPLIT LIVER GRAFTS: A 15-YEAR SINGLE-CENTER MATCHED-PAIR ANALYSIS OF OUTCOMES, COMPLICATIONS AND SURVIVAL

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Background: While split liver transplantation (SLT) increases organ use, concerns regarding vasculobiliary complications and graft survival remain. Risk stratification, donor-recipient matching, splitting allocation policies, and complication management are crucial for decision-making and outcomes. The study evaluates complications and survival in recipients of ex situ right split liver grafts (RSLG) compared to matched full-size liver grafts (FSLG).

Methods: This retrospective single-center cohort study, conducted at Hannover Medical School, included all RSLG recipients between 2005 and 2020. Forty-two RSLG recipients were matched 1:1 with FSLG recipients based on recipient age, sex, and transplant indication. The primary endpoint was graft and patient survival. Secondary endpoints included postoperative complications, classified using the Comprehensive Complication Index (CCI), as well as hospital and intensive care unit (ICU) stays.

Results: Following matching, 84 patients were included, with a median follow-up of 8.5 years. RSLG recipients had significantly lower lab-MELD scores (14 vs. 25; $p = 0.037$) and more commonly received organs from younger donors (39 vs. 50 years; $p < 0.001$). Cold ischemia time (CIT) was significantly longer in RSLG recipients (13 vs. 10 hours; $p < 0.001$). Vascular complications were more frequent in RSLG recipients (26% vs. 10%; $p = 0.046$). Biliary complications, particularly leakage, occurred more often in RSLGs (36% vs. 19%; $p = 0.087$). Median hospital stays (43 vs. 45 days) and ICU stays (16 vs. 19 days), as well as CCI scores at discharge (53 vs. 55) and 12 months (65 vs. 71), were comparable. One- and five-year graft survival rates were similar between RSLG and FSLG groups (71% vs. 81% at one year, 62% vs. 71% at five years; $p = 0.885$). Patient survival rates at one year were 81% vs. 83% ($p = 0.378$) and at five years 81% vs. 74%.

Conclusions: RSLGs show slightly higher vasculobiliary complications rates but comparable graft and patient survival rates compared to FSLGs. Donor-recipient matching is core for achieving good outcomes. Looking ahead, the integration of machine perfusion technologies to streamline graft splitting and logistics, besides enhanced allocation policies, are vital for establishing sustainable transplantation practices in the Eurotransplant region.

BOS_11_13 TRANSITION TO ADULT CARE THROUGH A JOINT PAEDIATRIC AND ADULT TRANSITION PROGRAM

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Background: Sahlgrenska University Hospital in Gothenburg is the only Transplant Centre in Scandinavia performing all modalities of solid organ transplantation. There is a close collaboration between the adult and paediatric teams at respective hospitals. A dedicated interdisciplinary approach is implemented along with a new program to achieve a smooth and seamless transition from paediatric to adult services. Young adulthood entails challenges for most individuals on their way to become an independent person. Young organ recipients additionally have to deal with adult health care, attaining skills in self-care, develop healthy behaviours, take responsibility for daily medication and live with a constant threat of rejection. Studies have shown that if health care can support and empower the young patients (and their parents), it will lead to a higher rate of self-management and successful adaptations to adulthood.

Methods: Since 2019 we have a shared transition program for young, transplanted patients. Staff from both the paediatric and the adult clinic have completed a university course in “Transition knowledge and Coordination”. Within the framework of our ordinary out-patient clinic we started a special Clinic for Young Adults.

Results: The process starts in the paediatric clinic at the age of 12-14. At the age of 16 the adolescent and their family have a first meeting with the transition nurse from the adult out-patient clinic. The outcome of this first meeting is a transition care plan, focusing on strengths and abilities to be further developed, along with needs, difficulties and fears that should be approached prior to the transit. At the adult services the young adults (age 18-25) are invited to join a special Young Adult Clinic that offers a joint meeting with the transplant physician and transplant nurse. Additionally, lunch lectures together with peers are offered as well as on demand appointments with a physiotherapist, dietitian, or a social worker.

Conclusions: The implementation of this transition program has been highly appreciated by the young adults and their families. Five years experiences reveals that a well-thought-out transition program and a Young Adult Clinic has the potential of being a contributing factor in building sustainability in the transplantation process.

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BOS_11_14 BEST PRACTICES IN CHRONIC KIDNEY DISEASE MANAGEMENT IN PREPARATION FOR TRANSPLANTATION

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Background: Clinical practice in chronic kidney disease management varies greatly across healthcare providers. However, little is known about current practice and how it compares to best practices.

Methods: A survey tool was designed and validated to collect data on chronic kidney disease management clinical practice and patient experience. Survey respondents (253) included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: General practitioners are key healthcare professionals involved in newly diagnosed CKD patients (55%). However, gaps in primary care training and resource allocation hindered their effectiveness, even though there is consensus regarding CKD diagnosis. While patient education on transplant preparation was rated as “very” (49%) to “moderately” (32%) accessible, many patients reported feeling inadequately informed until advanced CKD stages. Emotional preparation for surgery (40%) and support structures for post-surgical recovery (29%) were identified as gaps in patient communication and education. Communication among all specialties for patient monitoring and preparation for kidney transplant was very effective (48%), but communication with primary care was described as inconsistent. Respondents emphasized the urban-rural gap in continuity of care.

Conclusions: Standardized protocols, improved primary care training, clear communication between primary care and specialists, and enhanced, systematic patient education are needed to address gaps in access to equitable care and align practices with best-practice recommendations.

BOS_11_15 INTEGRATING ENHANCED RECOVERY AFTER SURGERY IN RENAL TRANSPLANT PATIENTS:PHYSIOTHERAPY PERSPECTIVE

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Background: The Enhanced Recovery After Surgery (ERAS) pathway aims to optimize post-operative recovery and improve outcomes. Physiotherapy, in the peri-operative phase of a kidney transplant, plays a key role in improving mobility, reducing hospital stays, and enhancing patient outcomes, but remains underutilised and under-funded in most transplant units. **Aims:** • To assess the impact of physiotherapy-led interventions on post-operative time to mobility and functional independence, post operative complications and length of stay. • To identify and address barriers to implementing a comprehensive ERAS pathway.

Methods: **Pre-ERAS:** •Baseline assessment of patient’s mobility using the Manchester Mobility Score (MMS) on post-operative days 1 and 2 performed on 74 patients over 5 months. **Post-ERAS:** • Frailty assessments (DASI, clinical frailty score, and short battery performance test-SBPT) at admission. • Based on SBPT results, individualised ERAS pathway was assigned. Following implementation, we evaluated 130 patients over 10 months. Basic demographics, pre- and post-ERAS implementation comparison outcome data including mobility, days to independence, post op pulmonary complication was captured and analysed.

Results: 74 consecutive patients in pre-ERAS and 130 patients in post ERAS audit were included. Mean age in pre and post ERAS group was 48.1 vs 50.1yrs(p>0.36). Significant improvements in mobility post-ERAS implementation were noticed. On Day 1, 60% of patients mobilized post-ERAS vs 27% pre-ERAS p<0.008), while on Day 2, 82% mobilized post-ERAS vs 62% pre-ERAS (p<0.0005). We noted a significant reduction in days to functional independence (5 vs 3 days; p<0.0001). There was no significant difference in length of stay (9.6 vs 8.7 days; p>0.24). Post ERAS, patients suffered significantly less post-operative pulmonary complications (12% vs 0.8%, p<0.0001). Barriers identified were limited staffing, funding gaps, and cultural challenges related to patient and staff expectations.

Conclusions: The Physiotherapy component of the ERAS pathway significantly improved the outcomes. Sustained investment in renal transplant physiotherapy services and implementation of other components of ERAS is crucial.

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BOS_12_1 HLA EPITOPE ELECTROSTATICS; A NOVEL METHOD TO ASSESS HLA-DQ IMMUNOGENICITY AT THE EPITOPE LEVEL

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Background: A deeper understanding of the immunogenicity and antigenicity of HLA epitopes through structural and physicochemical analyses may improve transplant histocompatibility assessment. We aimed to evolve the Electrostatic Mismatch Score 3D (EMS3D) beyond comparison of electrostatic potential (EP) of the entire HLA molecular surface to enable quantification of EP differences at the HLA epitope level.

Methods: A novel algorithm was developed to compare the EP between specific regions (epitopes) on HLA molecules. The relationship between HLA epitope electrostatics and donor-specific-antibody (DSA) formation (via Luminex) was examined using an experimental, human mode of HLA sensitisation (patients receiving standardised donor lymphocyte injections, total mismatched HLA-DQ n=230). The most polymorphic residues within HLA-DQ extracellular domain were identified (via genotypes from BeTheMatch registry including all major ethnic groups with Shannon Entropy ≥1) to define 9 potential HLA-DQ epitope regions on HLA-DQ, grouping polymorphic residues together by mathematical proximity. Machine learning methods were utilised to identify which epitope Donor-Recipient EP differences were associated with DSA.

Results: HLA Epitope Electrostatics is a novel algorithm implementing EMS3D methodology which can visualise and perform comparative electrostatics on HLA surfaces, enabling tertiary-level EP assessment for regions of interest. There were four HLA-DQ regions/epitopes highly associated with DSA development (AUC:0.75-0.78). The dataset was split into train:test (66%:33%, x10 repeats) and machine learning models (Support Vector Machines, Gaussian Naïve Bayes, Linear Discriminant Analysis, Logistic Regression) identified combinations of EP epitope differences that outperformed whole-molecule scoring (average accuracy: 0.77-0.79).

Conclusions: We describe a novel methodology for quantification of HLA electrostatic potential differences at the epitope level and validate the utility of this approach on HLA-DQ immunogenicity prediction. This approach may inform efforts to identify highly immunogenic, conserved epitopes on multiple HLA molecules.

BOS_12_2 IMPACT OF HLA EVOLUTIONARY DIVERGENCE AND MOLECULAR MISMATCHES ON KIDNEY ALLOGRAFT ANTIBODY-MEDIATED REJECTION

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Background: To assess HLA immunogenicity and stratify immunological risk, several in-silico methods have emerged**,** including HLA molecular mismatches and HLA evolutionary divergence (HED). However, their ability to stratify the risk of antibody-mediated rejection (AMR) beyond standard immunological assessment remains uncertain.

Methods: We included consecutive ABO-compatible kidney transplant patients (2004-2017) from four French centers. HED for Class I/II HLA were calculated using Grantham distance, eplet mismatches with HLAMatchmaker®, and PIRCHE-II scores via PIRCHE-II algorithm based on inferred high-resolution HLA typing. We evaluated at the time of transplant a total of 33 clinical and immunological parameters, including HLA eplet mismatches, PIRCHE-II scores, and HED. We then assessed their associations with the occurrence of AMR using Cox models.

Results: Among 5,159 patients, 1,024 (19.85%) developed AMR. The median follow-up post-transplantation was 7.52 years. The independent immunological determinants of AMR were Class I/II anti-HLA DSA (MFI 500-1400, HR: 1.87; MFI > 1400, HR: 3.84, p<0.001) and HLA Class II eplet mismatches (HR: 1.02, p<0.001). HLA-DQB1-derived PIRCHE-II scores (HR:1.01, p=0.005) and HLA-DRB1-derived PIRCHE-II scores (HR: 1.01, p=0.001) also showed association with AMR, while donor and recipient HED for both class I and II were not associated with AMR. These findings remained consistent across different centers and subpopulations, including non-sensitized patients (n=4137). Sensitivity analyses in 425 patients demonstrated good accuracy of inferred high-resolution HLA typing compared to NGS-based HLA typing across all loci.

Conclusions: In a large, multicentric, well phenotyped kidney transplant cohort, HLA Class II eplet mismatches and HLA Class II derived PIRCHE-II scores showed independent association with AMR. In contrast, HLA evolutionary divergence showed no association with AMR, suggesting limited utility for immune-risk stratification at a population level.

Trial registration: Clinicaltrials.gov NCT06436586.

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BOS_12_3 HUMAN LEUKOCYTE ANTIGEN MISMATCH IMPACT OF GRAFT SURVIVAL IN PANCREAS TRANSPLANTATION ALONE

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Background: In kidney transplantation it has been shown that HLA matching is associated with better outcomes. For pancreas transplantation recipients there is still controversy, with studies done in the 90s showing worse graft survival with higher number of mismatches and more contemporary studies with no difference for HLA A and B matching, but with HLA DR in SPK recipients. There is no such information in the context of pancreas transplantation alone (PTA). The aim of this study is to analyse the effect of molecular HLA mismatch (MM) on graft survival in PTA in a large single centre series.

Methods: A database of pancreas transplant recipients for the period from July 2004 to December 2024 was analysed. The graft failure cohort was compared with functioning grafts for demographic and transplant variables; Kaplan-Meier and Cox regression analyses for graft survival were undertaken. HLA grading according to the UK (NHSBT) mismatch classification was used: Grade 1: 000, Grade 2: [0 DR and 0/1 B] or [1 DR and 0 B], Grade 3: [0 DR and 2 B] or [1 DR and 1 B]; and Grade 4: [1 DR and 2 B] or [2 DR].

Results: During the study period 223 PTA were performed, 20 cases were excluded due to graft loss in the first 30 postoperative days. 203 patients were included in the analysis. The pancreas graft survival observed in stratified HLA MM was significantly lower with higher levels of mismatch (p=0.038) for 5-year (Grade 1 vs Grade 2 vs Grade 3 vs Grade 4: 100% vs 60% vs 84.5% vs 50.0%); 10-year (Grade 2 vs Grade 3 vs Grade 4: 50.4% vs 63.3% vs 41.6%, and 15-year graft survival (Grade 2 vs Grade 3 vs Grade 4: 50.4% vs 44.7% vs 36.6%) (Figure 1). After adjustment for other variables in a Cox regression analysis, the increasing level of HLA MM was independently associated with increased risk of graft loss (p=0.037).

Conclusions: This study on a large cohort of PTAs, highlights the importance of the stratified HLA mismatch on graft survival. The development of new predictive scores for pancreas graft survival in PTA is paramount and should take into account HLA grading.

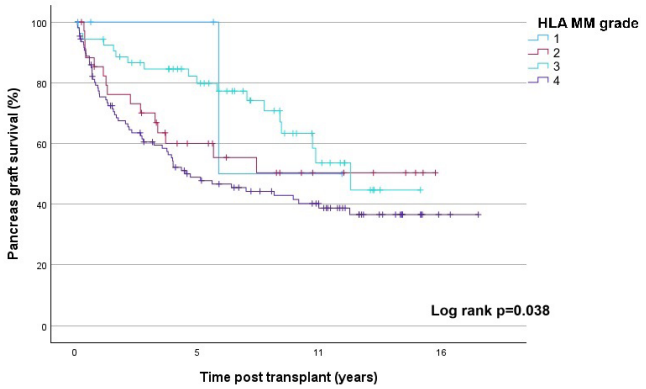

Figure 1. Pancreas graft survival according to HLA mismatch stratification.

BOS_12_4 ESTIMATING A CAUSAL ASSOCIATION BETWEEN PRE-TRANSPLANT BLOOD TRANSFUSION AND ALLOSENSITISATION

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Background: Red blood cell (RBC) transfusion is widely accepted as an alloimmune stimulus but ensuing HLA antibodies are often thought to be transient. The quantitative impact of RBC transfusions on transplant offers and outcomes is unknown. The aim of this study was to estimate the causal effect of receiving an RBC transfusion prior to kidney transplantation on allosensitisation measured by calculated reaction frequency (CRF) at the time of transplant.

Methods: A single centre cohort comprising all deceased donor kidney transplant recipients over a 5-year period was analysed. A potential outcomes framework was used to identify the causal effects. Missing values in key covariates were accounted for using multiple imputation. Inverse Probability of Treatment Weighting was applied on each imputed dataset. The effect was estimated using a zero-and-one inflated beta regression model to account for the U-shaped distribution of CRF.

		Not Transfused (n=481)	Transfused (n=238)	p
Age (mean (SD))		54.5 (12.7)	55.6 (12.8)	0.266
Gender (n(%))	Female	177 (36.8)	77 (32.4)	0.275
	Male	304 (63.2)	161 (67.6)	
Ethnicity (n(%))	Black	83 (18.1)	63 (27.6)	0.002
	Indo-Asian	177 (38.6)	80 (35.1)	
	Other	80 (17.5)	20 (8.8)	
	White	118 (25.8)	65 (28.5)	
Prev. Transplant n(%))	No	436 (90.6)	189 (79.4)	<0.001
	Yes	45 (9.4)	49 (20.6)	

Results: The cohort, described in the table, included 719 patients. Overall, 238 (33.1%) were transfused prior to transplant. The median time from transfusion to transplantation was 2.98 years (IQR 2.2-4.3). The transfusion free survival probabilities for 1-, 3- and 5-years pre-transplant were 96.9%, 84.2% and 71.1% respectively. Patients who received an RBC transfusion were 7% (95% CI 1-13%) less likely to have a CRF of 0% and 6% (95% CI 3-10%) more likely to have a CRF of 100%. The mean CRF was 9% (95% CI 4-14%) higher in those who received an RBC transfusion.

Conclusions: In this study we have provided evidence for a causal association between RBC transfusion and allosensitisation measured by CRF. Patients who received an RBC transfusion had a higher CRF at the time of transplantation after marginalising across the confounding variables. This highlights the importance of good patient blood management in the pre-transplant population, and the potential benefit of HLA-selection of unavoidable RBC transfusions for this population.

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BOS_12_5 VALIDATION OF A 'RECIPIENT AGE AND MOLECULAR MISMATCH SCORE' IN PATIENTS RECEIVING STEROID SPARING IMMUNOSUPPRESSION

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Background: A recent 'de novo DSA risk' score was developed to help inform which kidney transplant recipients may benefit from undergoing DSA monitoring, to help improve the cost-effectiveness of DSA screening. The score was developed in a population receiving predominantly triple immunosuppression. The aim of this study is to investigate the applicability of the score in predicting dnDSA in recipients receiving a steroid sparing protocol.

Methods: 546 kidney transplants were analysed. All donor and recipients were HLA typed by high-resolution NGS using GenDx MX6-1 HLA kits. HLA-Matchmaker was used for the epitope analysis. DR/DQ molecular mismatch (mMM) risk was defined as low (DR:0-6 and DQ:0-8), intermediate (DR:any, DQ:≤14) or high (DR:any, DQ≥15); with a recipient age (RA) of 35 considered discriminatory for final RAMM risk category. DSA screening was performed at 3 and 12 months by Luminex SAB.

Results: 154 (28.2%), 270 (49.5%) and 122 (10.6%) patients were categorised as having a low, intermediate and high RAMM respectively. There were no significant differences in baseline patient characteristics across the at risk categories, but significant differences were seen in ABDR mismatch, total HLA mMM (all epitopes and Antibody verified epitopes). De novo DSA were seen in 9 (5.8%), 34 (12.7%) and 30 (24.4%) patients in the low, intermediate and high risk RAMM groups respectively, p<0.0001 (Figure 1). BPAR episodes were also more likely to occur in the high-risk group, with 11 (7.1%), 25 (9.3%) and 20 (16.3%) BPAR events in low, intermediate and high-risk groups respectively, p=0.023. At the end of follow up there was no difference in death censored or all-cause graft survival.

Conclusions: A combined 'recipient age and HLA-DR/DQ mMM' score predicts risk of dnDSA and rejection in a cohort receiving steroid sparing maintenance immunosuppression. Avoidance of minimalist immunosuppression protocols in patients with a high risk RAMM maybe considered.

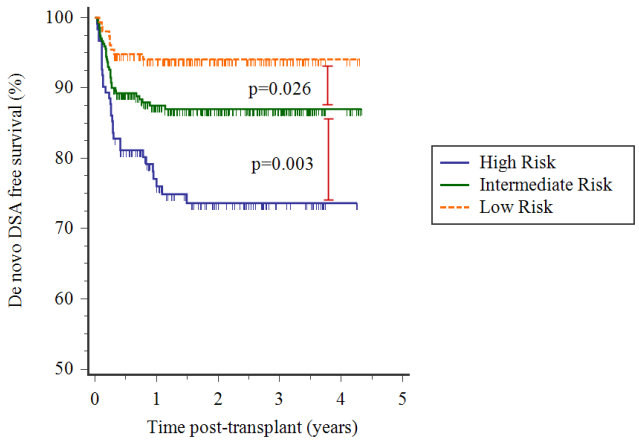

Figure 1. De novo DSA by Recipient Age plus Molecular Mismatch Risk Category

BOS_12_6 NON-CLASSICAL HLA AND MIC VARIATION INFLUENCES THE RISK OF ACUTE REJECTION IN KIDNEY TRANSPLANTATION

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Background: Acute rejection (AR) is a significant complication following kidney transplantation (KT). While classical HLA matching is known to influence AR risk, the roles of other genes within the HLA region are less understood. We investigated the association of allelic variation and matching of *MICA*, *MICB*, and non-classical *HLA-E*, *-F*, and *-G* genes with AR in 1,025 Finnish KT donor-recipient pairs.

Methods: The data were divided temporally into two sets: a discovery cohort (n = 682) consisting of the oldest two-thirds of the data, and a replication cohort (n = 343), consisting of the remaining one-third. A total of 126 non-classical HLA/MIC variables, including imputed allele dosages and allelic mismatching, were tested as predictive variables using multivariate Cox proportional hazards model in the discovery set. Variables showing single associations of p <0.05 were integrated into a sum score to assess the combined effect of non-classical HLA/MIC polymorphisms on AR. This sum score was compared to the effect of HLA-A-B-DRB1 mismatches and HLA class II eplet mismatches. Workflow of the study is presented in Figure 1.

Results: The sum score of the top non-classical HLA/MIC variables was statistically significantly associated with reduced rejection-free survival in both cohorts (Table 1). Decreased survival was observed when the non-classical HLA/MIC score was high regardless of classical HLA matching, indicating an independent effect.

Conclusions: Genetic variation in the non-classical HLA/MIC significantly contributes to the risk of AR in KT. This effect was observed independently of the classical HLA mismatches, highlighting the potential of considering non-classical HLA/MIC in KT compatibility assessments.

	Discovery		Replication	
Variable	**HR [95% CI]**	**P-value**	**HR [95% CI]**	**P-value**
Non-cl HLA/MIC score	1.19 [1.11–1.28]	2.802E-06	1.10 [1.00–1.21]	0.040
Non-cl HLA/MIC score 1st vs 10th decile	4.37 [1.69–11.31]	0.002	14.37 [2.36–87.44]	0.004

Table 1. Results for non-classical HLA/MIC score and its extreme deciles in the Cox proportional hazards models for acute rejection in the discovery and replication cohorts.

CI, confidence interval; HLA, human leukocyte antigen; HR, hazard ratio; MIC, MHC class I polypeptide-related sequence

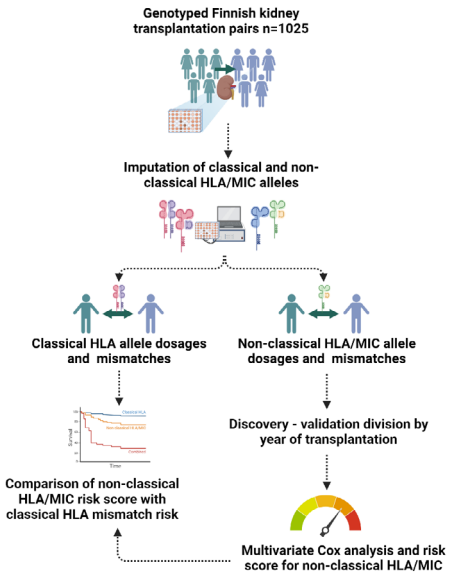

Figure 1. Overall study design and workflow. Created with BioRender.com.

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BOS_12_7 DONOR AND RECIPIENT COMPLEMENT GENETICS ARE ASSOCIATED WITH ACUTE REJECTION RISK AFTER LIVER TRANSPLANTATION

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[1]University Medical Center Groningen, [2]Umcg; Yes; Surgery, [3]University Medical Centre Groningen; University Medical Center Groningen, [4]University Medical Center Groningen; University Medical Center Groningen; Pathology, [5]University Medical Center Groningen; University Medical Center Groningen, [6]Umcg; Nephrology/Surgery, [7]University Medical Center Groningen; Umcg Comprehensive Transplant Center; Hpb Surgery and Liver Transplantation

Background: Despite the liver's tolerogenic properties, 15–25% of liver transplant recipients experience acute T-cell mediated rejection (ACR). Factor H, encoded by CFH, regulates the complement system and impacts alloimmune responses. Humans also possess five Factor H-related proteins (FHR1 to FHR5). Genetic variations in CFH affect Factor H levels and function, with certain haplotypes linked to diseases like atypical hemolytic uremic syndrome and age-related macular degeneration. Given that CFHR3,1 deletion (Δ) is linked to increased ACR risk in kidney transplantation, we hypothesized that CFH haplotypes and CFHR3,1Δ contribute to ACR after liver transplantation.

Methods: ACR was defined as histologically confirmed rejection (grade ≥2). Recipients with grade 1 or biochemically suspected rejection were excluded. Donor and recipient DNA genotypes were imputed against the TOPMed reference panel and phased through SHAPEIT. Associations with ACR were analyzed using Kaplan-Meier survival curves and multivariable Cox regression.

Results: We included 698 donor-recipient pairs, of which 90 (13%) recipients experienced ACR. The donor H2 haplotype, present in 291 (24%) donors, was protective against ACR (HR 0.59, 95%CI 0.37-0.92, p=0.021; Fig. 1A), while the donor H4a haplotype, found in 140 (16%) donors, increased ACR risk (HR 1.60, 95%CI 1.01-2.56, p=0.047; Fig. 1B). Homozygosity for CFHR3,1Δ was observed in 3% (N=22) of both donors and recipients and was associated with a higher ACR risk (donor HR 2.61, 95%CI 1.11-6.11, p=0.027; recipient HR 2.58, 95%CI 1.16-5.74, p=0.021; Fig. 1C,D).

Conclusions: Our study shows that specific donor CFH haplotypes and the CFHR3,1Δ in both donors and recipients are significant predictors of ACR after liver transplantation. The protective effect of the H2 haplotype and the harmful effect of the H4a haplotype align with previous findings in immune-mediated diseases, underscoring the relevance of complement activity in transplant outcomes.

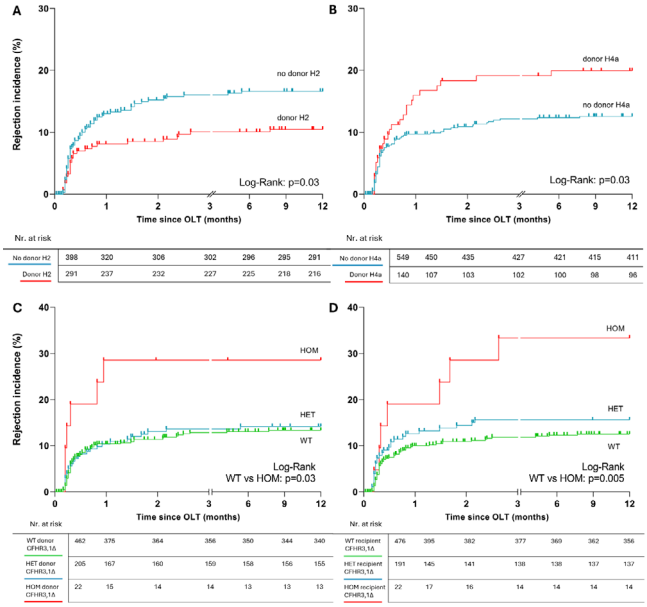

Figure 1. Kaplan Meier curves with log-rank tests depicting ACR incidence across different H2 (A), H4a (B) and CFHR3,1Δ donor (C) and recipient (D) genotypes

ACR, acute T-cell mediated rejection; WT, wildtype; HET, heterozygous; HOM, homozygous

BOS_12_8 INTEGRATING ENHANCED RECOVERY AFTER SURGERY IN RENAL TRANSPLANT PATIENTS:PHYSIOTHERAPY PERSPECTIVE

Thomas Barba[1], Aravind Cherukuri[2], Hou-Ying Cheng[3], Bastien Berger[4], Virginie Mathias[5], Emmanuel Morelon[6], Valérie Dubois[7], Helena Paidassi[8], Fadi Lakkis[9], Olivier Thaunat[10]

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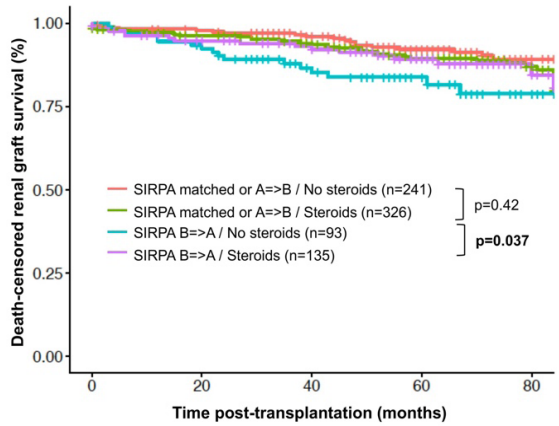
Introduction: Recent studies in mice have shown that monocytes can independently recognize allogeneic non-self through SIRPα, a receptor that binds to CD47. Normally, the SIRPα/CD47 interaction generates inhibitory signals that prevent monocyte activation. However, donor SIRPα polymorphisms with enhanced affinity for recipient CD47 can disrupt this balance, driving monocyte-mediated graft rejection. In humans, the SIRPA gene is also highly polymorphic, and previous research has identified two polymorphism categories: A (low affinity for CD47) and B (high affinity for CD47).

Objectives: This bicentric retrospective study aimed to investigate the clinical impact of SIRPA mismatches on kidney graft failure and explore potential protective factors.

Methods & Results: We genotyped 795 consecutive donor/recipient pairs from two kidney transplant centers (Lyon and Pittsburgh) for SIRPA polymorphisms. Multivariate analysis revealed that several variables were significantly associated with renal graft failure, including: i) deceased donor grafts, ii) low-quality grafts (KDPI), iii) delayed graft function, iv) de novo donor-specific antibodies (dnDSA), and v) B=>A SIRPA mismatches, where a high-affinity donor is transplanted into a low-affinity recipient [HR: 2.93 (1.23–7.01); p=0.016]. Importantly, interaction analyses indicated that while corticosteroids in maintenance immunosuppression did not improve overall graft survival, their use significantly reduced the increased risk associated with B=>A mismatches (**Figure 1**).

Conclusion: This study demonstrates that B→A SIRPA mismatches substantially elevate the risk of kidney graft failure. Importantly, the use of low-dose corticosteroids in maintenance immunosuppression effectively mitigates this risk. Ongoing experimental research seeks to unravel the molecular mechanisms underlying these findings. Furthermore, B→A SIRPA mismatches could serve as a valuable tool to identify patients who would benefit from corticosteroid maintenance.

Figure 1



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BOS_12_9 FIRST GENOME-WIDE ASSOCIATION STUDY OF CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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Background: Lung graft survival remains insufficient with only 50.6% survival at 5 years post-transplantation. The greatest limitation to long-term survival is chronic lung allograft dysfunction (CLAD). Understanding the molecular mechanisms underlying CLAD is critical for improving outcomes. Here, we performed the first genome-wide association study (GWAS) investigating donor and recipient's genetic factors associated with CLAD.

Methods: CLAD is defined by a >=20% decline in measured forced expiratory volume from the baseline level (3 months after transplant in the absence of infection or another identifiable cause). We genotyped a subset of 392 European donor-recipient pairs from the multicentric COLT cohort (Cohort in Lung Transplantation) using the Affymetrix Axiom PRMA microarray. After quality controls and SNP imputation, we tested 7 million SNPs for association with CLAD using multivariate logistic regression models corrected for age, sex, initial disease and genetic ancestry. The GWAS was performed at three levels: (1) donors-only, (2) recipients-only, and (3) donor-recipient mismatches.

Results: We did not observe any significant association between the donors' genotypes or the donor-recipient mismatches and CLAD. However, we identified 13 SNPs from the recipients significantly associated with CLAD ($P<5x10^{-8}$). Our top signals (34% in CLAD vs 66% in non-CLAD recipients, $P=2.18x10^{-9}$, OR=0.39) encompassed the PLXDC2 gene, that encodes a protein previously associated with the risk for bronchopulmonary dysplasia. Importantly, we demonstrated with scRNAseq data from lung explants (n=4) that PLXDC2 was mostly expressed in monocytes and strongly down-regulated in CLAD vs healthy controls ($P=2.22x10^{-16}$).

Conclusions: Here, we unveiled the first GWAS conducted in lung transplantation, displaying a biologically relevant candidate gene from the recipient's genome. Further functional investigations could provide valuable insights into CLAD pathogenesis and potential therapeutic targets. Our study calls for larger genomic initiatives in lung transplantation to increase the power of signal discovery.

BOS_12_10 NON-HLA GENOME-WIDE MISMATCHES INCREASE THE RISK OF COMPLICATIONS IN LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is the standard treatment for end-stage liver disease and acute liver failure. Immunological allograft injury and rejection continue to be significant concerns, especially when efforts are made to reduce immunosuppression. The role of human leukocyte antigen (HLA)-matching in LT remains uncertain. Over the past decade, whole genome-wide incompatibility between recipients and donors has emerged as a potential risk factor in transplantations.

Methods: The study cohort included 666 adult Finnish LT recipient-donor pairs. We calculated genome-wide mismatches of missense variants to identify incompatibilities in various protein groups as well as mismatches in 40 common homozygous deletions. Using a Cox proportional hazards model, we estimated the association of genetic mismatches with time to acute rejection, graft loss, death, and late rejection, adjusting for recipient and donor age, sex, cold-ischemia time, HLA I and II eplet mismatches, year of transplantation, autoimmune liver disease status, and initial calcineurin inhibitor type.

Results: Mismatches in missense variants coding for all proteins were associated with late rejection, with an adjusted hazard ratio (aHR) of 0.998 (95% confidence interval [CI]: 0.996–0.999; *P* = 0.011, false detection rate [FDR] <0.05). Deletion mismatches tagged with rs11985201, rs2342606, rs2174926, and rs1944862 were identified as risk factors for LT outcomes. The cumulative mismatches in deletion variants rs11985201, rs2342606, and rs1944862 was associated with time to acute rejection, with an aHR of 1.377 (95% CI: 1.139–1.664, *P* = 0.001, FDR <0.05).

Conclusions: Genome-wide mismatches have an impact on liver transplantation outcomes. However, to increase detection power and confirm these findings, large-scale studies are essential.

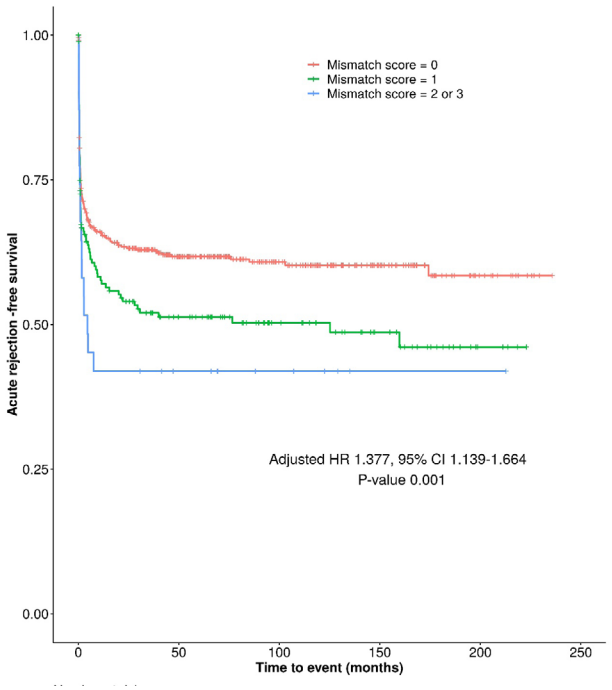

Figure 1. Kaplan–Meier plot displaying the effect of sum of mismatches in deletion-tagging variants rs11985201, rs2342606, and rs1944862 on acute rejection-free survival. Survival curves represent the mismatch score groups 0,1, and combined scores 2 and 3. CI, confidence interval; HR, hazard ratio.

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BOS_12_11 RECIPIENT FCGR3A POLYMORPHISM INFLUENCES THE PROGNOSIS OF AMR AND THE RESPONSE TO IVIG IN RENAL TRANSPLANTATION

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Background: Antibody-mediated rejection (AMR) is the leading cause of kidney graft failure; however, its heterogeneous prognosis complicates both the assessment of graft loss risk and the selection of an appropriate therapeutic strategy at diagnosis. The binding of donor-specific antibodies (DSA) to graft endothelial cells triggers the recruitment of innate immune effectors through their Fcγ receptors, which vary by cell type (FcγR2A, FcγR2B, FcγR2C, FcγR3A, and FcγR3B). Several single-nucleotide polymorphisms (SNPs) have been identified that modulate these receptors' affinity for the Fc portion of IgG. The aim of this translational study was to identify the specific FcγR polymorphism(s) in recipients that are associated with a poor prognosis at the time of AMR diagnosis and to explore their potential therapeutic implications.

Methods & Results: Among 1,682 kidney transplant recipients at Lyon University Hospital who underwent graft biopsy between 2004 and 2017, 135 (8%) were diagnosed with AMR. Of the five functional FcγR polymorphisms described in the literature, only FcγRIIIa*559A>C (rs396991; p = 0.005) was significantly associated with reduced graft survival. Global and single-cell transcriptomic analyses of AMR biopsies revealed that non-classical monocytes and NK cells were the primary innate immune effectors expressing FcγR3A. In vitro co-cultures of these purified innate effectors with allogeneic endothelial cells coated with DSA confirmed that cells with high-affinity FcγR3A: i) exhibited stronger activation and caused greater damage to target cells, and ii) were more effectively controlled by the addition of intravenous immunoglobulin (IVIg) to the culture medium. These in vitro findings were corroborated in our clinical cohort, where the therapeutic benefit of IVIg was observed exclusively in patients with high-affinity FcγR3A binding.

Conclusions: Our study demonstrates that a single functional polymorphism of FcγR3A significantly impacts the severity of AMR. Moreover, patients with the high-affinity FcγR3A polymorphism are those most likely to benefit from IVIg treatment, highlighting the potential for personalized therapy in AMR management.

BOS_12_12 NON-HLA ANTIBODIES ARE ASSOCIATED WITH HUMORAL REJECTION AND MICROVASCULAR INFLAMMATION POST-TRANSPLANTATION

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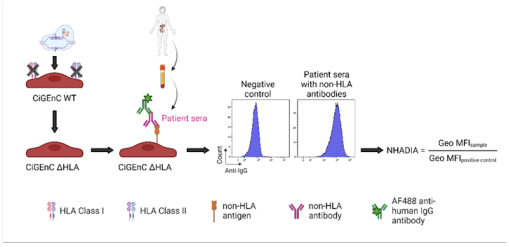
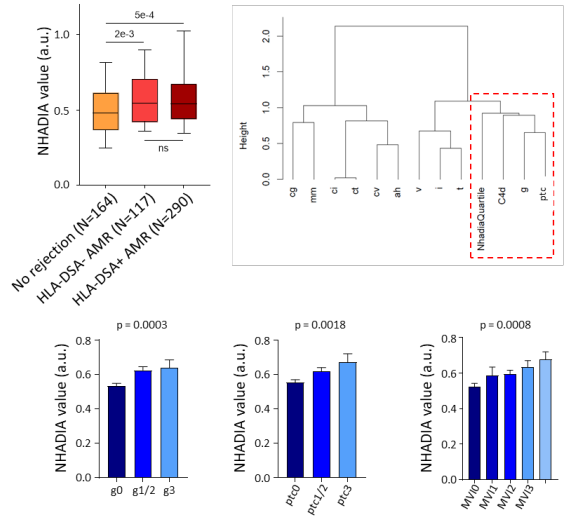
Background: The purpose of this study was to provide evidence that post-transplant circulating non-HLA antibodies identified by our innovative endothelial crossmatch NHADIA (Non-HLA Antibody Detection ImmunoAssay) correlates with microvascular inflammation (MVI) of the renal allograft by taking advantage of a large biological collection of serum samples collected at the time of biopsy showing an antibody-mediated rejection.

Methods: We retrospectively reviewed all consecutive adult patients who received a kidney transplant at Necker Hospital (Paris, France) between January 2009 and October 2021 with available serum collected at time of biopsies post-transplantation and available follow-up at our institution. The last Banff' classification (2022) was applied to select AMR patients with at least one of their biopsies showing MVI with or without HLA-DSA (407 biopsies) and control transplant patients without any sign of MVI or C4d deposition during their follow-up (164 biopsies). Serum samples were tested with the NHADIA using CiGEnCΔHLA cells, capable of specifically detecting non-HLA antibodies even in patients carrying HLA-DSAs.

Results: The NHADIA was performed using the 571 post-transplant serum samples with CiGEnCΔHLA cells as the targets. We observed a significant inter-individual variability of NHADIA results among the total selected population. Although, the NHADIA value was significantly increased in patients with MVI independent of HLA-DSA status. Unsupervised clustering analysis revealed that the NHADIA results preferentially clustered with histological features of MVI. In addition, increasing severity of glomerulitis (p = 0.0003), peritubular capillaritis (p = 0.0018) and MVI (p = 0.0008) were associated with increased NHADIA signals.

Conclusions: Our innovative NHADIA assay is able to detect the significant increase of non-HLA antibodies in MVI patients and its value is associated with the development of histological features of MVI post-transplantation.





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BOS_12_13 THE RELATIONSHIP BETWEEN C1Q POSITIVE DONOR-SPECIFIC ANTIBODIES AND HEART TRANSPLANT OUTCOMES

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Background: De novo donor-specific antibodies (dnDSA) following heart transplantation (HTx) have been associated with worse outcomes including increased incidence of antibody-mediated rejection (AMR), cardiac allograft vasculopathy (CAV), graft dysfunction, and mortality. It is unknown whether complement binding ability on Luminex (C1q+) identifies a more virulent DSA phenotype.

Methods: Between 2010 and 2021, we identified 126 out of 861 HTx recipients who developed dnDSA (14.6%), defined as DSA that were first detected >3 months post-HTx. These patients were divided into C1q+ DSA and C1q- DSA cohorts via the Luminex assay. The primary outcome was all-cause mortality. Secondary outcomes included CAV, AMR (pAMR ≥1), acute cellular rejection (ACR) ≥2R, graft dysfunction (left ventricular ejection fraction (LVEF) ≤40%), and non-fatal major adverse cardiovascular events (NF-MACE) including stroke, coronary revascularization, heart failure, and defibrillator or pacemaker implantation. Baseline characteristics and outcomes were compared utilizing t-tests for continuous variables and chi-square analysis for categorical variables. Logistic regression analysis was used to evaluate for independent associations between C1q status and outcome variables.

Results: There were 40 C1q+ DSA and 86 C1q- DSA patients identified with a mean follow-up of 5.8 years. The mean time to DSA appearance was 2.3 years post-HTx in both cohorts. Mean LVEF at time of DSA identification was lower in the C1q+ vs C1q- cohort (50.8% vs 57.9%, p = <0.001). The primary outcome was higher in the C1q+ cohort (40.0% vs 20.9%, p = 0.025) with a mean time to event of 4 years. AMR was more frequent in the C1q+ cohort (25.0% vs 10.6%, p = 0.036). Causes of cardiovascular mortality in the C1q+ compared to the C1q- group included sudden death (25% vs 11.1%), CAV (18.8% vs 22.2%), acute rejection (25% vs 5.6%), and stroke (6.3% vs 5.6%). There were similar rates of CAV, ACR, graft dysfunction, and NF-MACE between the C1q+ and C1q- cohorts.

Conclusions: C1q+ DSA are associated with increased AMR rates, worse graft function, and higher mortality when compared to C1q- DSA at a mean follow-up of over 5 years. Larger prospective studies are needed to validate those findings and identify potential therapeutic interventions that can improve outcomes.

BOS_12_14 THE PRESENCE OF ANTI-ENOLASE ANTIBODIES PRIOR LUNG TRANSPLANTATION IMPACTS CLAD DEVELOPMENT

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Background: The chronic lung allograft dysfunction (CLAD) is the main cause of graft lost. However, the precise mechanisms underlying its development remain unknown. Among the most well-established causes are prior antibody-mediated rejection (ABMR), patient age, delayed graft function, and ischemia time. Recently, the presence of pre-transplant non-HLA antibodies has been identified as a contributing factor to CLAD. Among non-HLA antibodies, anti-endothelial antibodies have been described as potential contributors to the development of ABMR. This study evaluates the role of anti-Enolase (anti-ENO) antibodies in the development of CLAD.

Methods: A total of 74 lung recipient (LR) transplanted in our institution from 2011 were recruited. Clinical follow-up data were collected at the Pneumology Department. The study of anti-ENO antibodies in pre-transplant sera was performed using Luminex technology (ThermoFisher, One Lambda). The risk of CLAD associated with the presence of pre-transplant anti-ENO antibodies was assessed using Cox regression analysis.

Results: Of the 74 patients included, 11 were misclassified as CLAD due to early loss and were excluded from further analysis. A total of 36 patients developed CLAD following lung transplantation, and 5 out of the remaining 63 had pre-transplant anti-ENO antibodies. Univariate Cox regression analysis showed that the presence of anti-ENO antibodies prior to lung transplantation increased the risk of CLAD (HR = 2.083, p = 0.13). Parameters associated with CLAD development, such as age, ABMR, ischemia time, and primary graft dysfunction, were included in the multivariate analysis. The presence of pre-transplant anti-ENO antibodies was independently associated with CLAD development (HR = 2.793, p = 0.038).

Conclusions: Screening for anti-ENO antibodies prior to lung transplantation could help identify patients on the waiting list who are at risk of developing CLAD. Although larger cohorts are needed to confirm these findings, this study provides further evidence supporting the involvement of non-HLA antibodies in CLAD development.

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Histocompatibility and immunogenetics

BOS_12_15 IN VITRO AND IN VIVO FUNCTIONAL ACTIVITY OF ANTI-ETAR ANTIBODIES IN PEDIATRIC KIDNEY TRANSPLANTATION

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Background: Non-HLA antibodies against specific auto- and allogeneic molecules have been identified as possible triggers of graft damage. Further research is needed to fully understand the effects of antibodies targeting the endothelin-1 type A receptor (ETAR) in pediatric renal transplantation. This research aims to assess the possible functional biological roles of anti-ETAR antibodies in vitro and in vivo.

Methods: Anti-ETAR antibodies were measured in a cohort of pediatric renal transplant recipients (n=170), before and after transplantation for at least 24 months. IgG were purified from the sera of selected patients. In vitro bioactivity of anti-ETAR antibodies was measured in ETAR-transfected CHO cells. In addition, chemotaxis of immune cells following exposure to IgG isolated from the pediatric patients was evaluated. Histological analyses were performed on protocol biopsies at 6 and 24 months after transplantation and immunohistochemical analyses were performed to evaluate the adhesion molecules ICAM and VCAM.

Results: In this cohort of patients, 51% had preformed anti-ETAR antibodies. Throughout the follow-up period, 38% were negative for anti-ETAR antibodies. De novo appearance of anti-ETAR antibodies was evidenced in 11% of transplanted patients. In vitro experiments revealed that IgG purified from pediatric recipients exhibited agonistic activity on ETAR comparable to that of the natural ligand endothelin, within the nanomolar concentration range. Furthermore, IgG isolated from patients with anti-ETAR antibodies were associated with enhanced NK and T cell migration. Strong correlations were found between the levels of anti-ETAR antibodies and the migration of immune cells. Immunohistochemical analyses performed in a limited number of protocol biopsies demonstrated that anti-ETAR antibodies are associated with increased iCAM-1 and VCAM-1 expression in the transplanted kidney.

Conclusions: Anti-ETAR antibodies are often observed in pediatric renal transplant patients. In vitro studies show that these antibodies exhibit a partial agonistic effect on the endothelin receptor. The presence of such non-HLA antibodies may promote recruitment of immune cells and influence their adhesion to the graft.

Next generation kidney preservation

BOS_13_1 NORMOTHERMIC VS HYPOTHERMIC MACHINE PERFUSION IN KIDNEY TRANSPLANTATION; A RANDOMIZED TRIAL

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Background: Currently, hypothermic machine perfusion (HMP) is the gold standard for preservation of deceased donor kidneys. However, for extended criteria donor kidney grafts (ECD-DBD) and kidney grafts that are donated after circulatory death (DCD), the risk of delayed graft function (DGF) remains high and these grafts are subsequently more often discarded. Normothermic machine perfusion (NMP) has emerged as an alternative method of preservation, during which cellular repair processes can initiate during normothermia, without influx of recipient immune cells.The aim of this trial is to compare outcomes of kidney grafts that were preserved on HMP or NMP.

Methods: This is a single-centre, open-label, randomized controlled trial. Patients who received a ECD-DBD or DCD kidney were randomized to receive a kidney that was either preserved on HMP and two hours of end-ischemic NMP (intervention group) or HMP alone (control group). Primary outcome was the incidence of DGF. Secondary outcomes were the incidence of (PNF), biopsy-proven acute rejection (BPAR) and graft and patient survival (APOLLO trial, NCT04882254).

Results: A total of 80 recipients were enrolled, of which 41 received a kidney that was preserved on HMP and NMP and 39 received a graft that was preserved on HMP alone. DGF occurred in 22/38 (57.9%) patients in the NMP group compared to 19/38 (50%) patients in the HMP group (OR: 1.38, 95% CI: 0.56-3.40, p=0.49). PNF occurred in three patients in the NMP group and two patients in the HMP group (OR: 1.46, 95% CI: 0.23-9.25, p=0.69). There was no difference in episodes of BPAR (NMP: 28% vs HMP 16%, p=0.282). There was no difference in death-censored graft (p=0.607) and patient survival (p=0.623) at one year after transplantation.

Conclusions: The addition of two hours end-ischemic NMP does not improve early graft outcomes in kidney transplantation compared to HMP alone. However, this trial does prove that two hours NMP is feasible and safe.

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BOS_13_2 DONOR TIME TO DEATH AND KIDNEY TRANSPLANT OUTCOMES; CAN WE INCREASE GLOBAL ORGAN SUPPLY?

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Background: Lengthening waiting lists for organ transplantation mandate development of strategies to expand the deceased donor pool. Due to concerns regarding organ viability, most organ donation organisations internationally "stand-down" from potential circulatory death donors (DCD) after 1-2 hours, possibly underutilising an important organ source. UK policy mandates a minimum 3-hour stand-down time.

Methods: Population-cohort study (2013-2021) of adult DCD kidney-alone transplants from the prospectively maintained UK Transplant Registry. The impact of time to death (TTD) on post-transplant outcomes was assessed with adjusted regression models. Multiple imputation and restricted cubic splines were employed to deal with missing data and non-linearity.

Results: In 7,183 kidney transplant recipients, median (range) TTD was 15 (0-407) minutes, with 885 and 303 kidneys transplanted from donors with TTD over 1 and 2 hours, respectively. Donor TTD was not associated with 12-month eGFR on adjusted linear regression (change per doubling of TTD = -0.25, 95% CI -0.68 to 0.19, P=0.27), nor with delayed graft function (aOR=1.01; 0.97-1.06, P=0.65) or graft survival (aHR=1.00; 0.95-1.07, P=0.92; Kaplan-Meier in Figure 1A). Results from non-linear modelling with restricted cubic splines confirmed these findings (Figure 1B). In contrast, asystolic time, cold ischaemic time, and reperfusion time independently predicted outcome. Compared to theoretical 1- or 2-hour stand-down times, UK policy (minimum 3-hour wait to stand-down) has led to 14.1% and 4.4% more DCD transplants, respectively.

Conclusions: Donor TTD does not impact on post-transplant outcomes, in contrast to the subsequent asystolic, cold ischaemic and reperfusion times. Altering international transplant policy to mandate minimum 3-hour donor stand-down times would substantially increase the number of kidney transplants performed internationally without compromising outcomes.

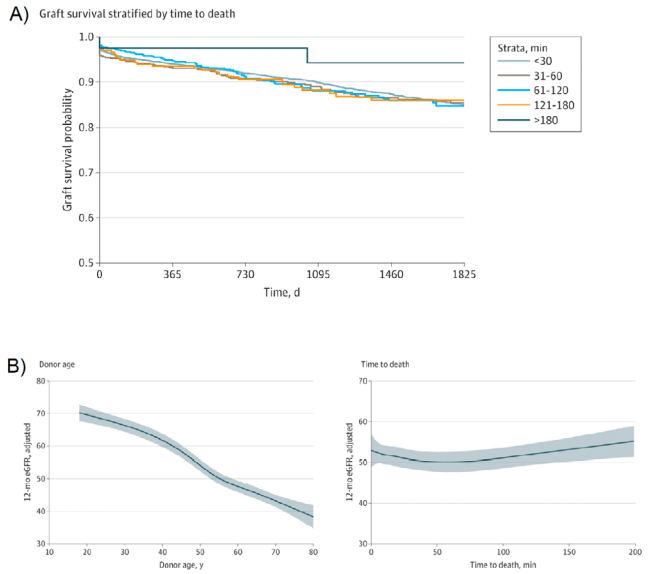

Figure 1 – Impact of donor time to death on kidney transplant outcome. A) Kaplan-Meier plot displaying crude association of Time to Death and Death-Censored Graft Survival. B) Multivariable Restricted Cubic Spline Models for 12-Month Posttransplant Estimated Glomerular Filtration Rate (eGFR), adjusted for a wide range of donor, transplant and recipient factors.

BOS_13_3 RESTORED COAGULATIVE CAPACITY RESOLVES COLD STORAGE INDUCED INJURY IN A KIDNEY NORMOTHERMIC MACHINE PERFUSION MODEL

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Background: Kidney normothermic machine perfusion (NMP) can improve organ preservation and assessment. Non-utilized human kidneys exposed to prolonged cold storage (CS) followed by 48h-NMP with red blood cell (RBC) and albumin-based perfusate exhibited prominent pelvic hematomas while porcine kidneys perfused with autologous leukocyte filtered whole blood (WB) did not. We propose a novel human kidney NMP perfusate composition with coagulative capacity to minimize pelvic hematoma formation after CS.

Methods: Porcine kidneys were perfused for 48 hours with WB or autologous RBCs and albumin, either after 1 hour of CS or after 24h of CS (n=5/group). In a second set of experiments, non-utilized human kidneys were cold stored for 12-24 hours and perfused with RBCs and albumin with: A) antithrombin (AT, n=2), B) AT and fresh frozen plasma (FFP, n=3), C) recombinant tissue plasminogen activator (rtPA, n=2), D) AT, FFP, and rtPA (n=2), E) AT, FFP, and thrombocytes (n=7). Biochemical, histological, and coagulation analyses assessed tissue injury and perfusion quality.

Results: Prolonged CS resulted in severe pelvic hematomas during extended porcine kidney NMP in WB kidneys. Confluent hematomas lead to disruption of the kidney tissue integrity in the ureter and pelvis. This was even more pronounced in RBC-perfused porcine kidneys and consistent with findings in human kidneys. While the addition of AT nor rtPA, AT, FFP and/or rtPA alone did not change the outcome, human kidneys perfused with AT, FFP and thrombocytes (group E) displayed preserved tissue integrity with absence of hematomas and injury after prolonged NMP. Oxygen consumption improved (2.7 mL/min [2.4–2.7]) compared to the baseline (1.6 mL/min [1.1–1.9]), while flow (345 mL/min [150–370]), glucose consumption (1.2 mg/min [1.2–1.4]), and injury marker levels were comparable between groups. The supplementation of AT, FFP, and platelets resulted in physiologic platelet counts (median: 98 G/L [96–109]) extrinsic clotting times (103 s [93–167]) and clot firmness (45 mm [43–46]) in the perfusate.

Conclusions: Prolonged cold storage and reduced coagulative function contribute to pelvic bleeding during extended kidney NMP. Perfusate enrichment with AT, FFP and thrombocytes preserves hemodynamic stability and prevents bleeding in human NMP.

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BOS_13_4 COMPARE: RENAL RESISTANCE DURING HYPOTHERMIC PERFUSION IN DONATION AFTER CIRCULATORY DEATH KIDNEYS

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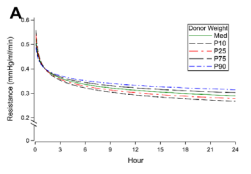
Background: Renal resistance (RR) during hypothermic perfusion is a predictor of delayed graft function (DGF), primary non-function, and graft survival but its accuracy is limited. Despite this, RR is used to assess kidney quality. In 2023, 33% of US-pumped kidneys were discarded, in part due to perceived as poor perfusion parameters. Most studies focus on terminal RR, leaving the RR-trajectory during perfusion unstudied, with unclear links to donor and perfusion factors and post-transplant outcomes.

Methods: We fitted a linear mixed model to the entire RR-trajectory using data from the randomized COMPARE trial. This double-blind, controlled phase 3 trial compared outcomes of kidneys from circulatory death donors ≥50y preserved by hypothermic perfusion with or without oxygen in Belgium, the Netherlands and a part of the UK. We investigated if the RR-trajectory was influenced by donor characteristics and its association with post-transplant outcomes. We also assessed the prognostic value of terminal RR for DGF, given its assumed association.

Results: Perfusion data from 245 kidneys from 159 donors were analyzed, with follow-up data from 194 patients. The RR-trajectory followed an exponential decay model with a multiplicative error, where the intercept relates to initial RR and the slope represents the rate at which RR decreases over time. Donor weight (F=5,32; p=0,005) and cause of death (F=2,91; p=0,008) influenced the RR-trajectory, while oxygenation had no significant effect (F=1,12; p=0,33). The RR-trajectory did not predict DGF (F=1,93; p=0,15), biopsy-proven acute rejection (F=0,41; p=0,66), 1-year kidney function (F=0,61; p=0,54), or 1-year graft survival (F=0,47; p=0,63). Terminal RR was an independent predictor of DGF [OR 1,14 (1,009-1,298), p=0,03), albeit with limited prognostic value [AUC 0.63 (0,55-0,71)].

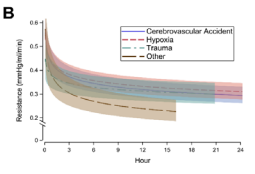
Conclusions: We present a simple, comprehensive model to characterize the RR-trajectory in hypothermically perfused kidneys. The findings suggest that the RR reflects the kidney's intrinsic response to perfusion, which is influenced by donor weight and cause of death. Oxygenation does not seem to affect the RR-trajectory. These results provide the most comprehensive evidence against using RR as a criterion to discard donor kidneys that may function very well after transplantation.



Linear mixed model results

Label	df	F Value	P-value
Effect Donor weight	2	5.32	0.005
Effect on intercept	1	2.43	0.12
Effect on slope	1	10.63	0.001

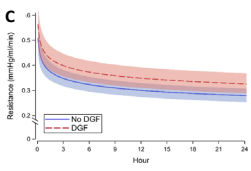
Label	Intercept (95%CI)	Slope (95%CI)
P10 (60 kg)	0.57 (0.50 – 0.66)	0.91 (0.90 – 0.93)
P25 (70 kg)	0.55 (0.50 – 0.62)	0.92 (0.91 – 0.93)
Med (80 kg)	0.53 (0.49 – 0.59)	0.93 (0.92 – 0.94)
P75 (90 kg)	0.51 (0.47 – 0.57)	0.94 (0.93 – 0.95)
P90 (100 kg)	0.50 (0.44 – 0.56)	0.95 (0.93 – 0.96)

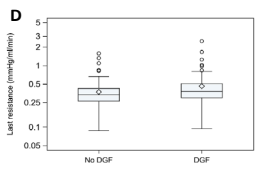


Linear mixed model results

Label	df	F Value	P-value
Effect COD	6	2.91	0.008
Effect on intercept	3	1.13	0.34
Effect on slope	3	3.65	0.01

Label	Estimate (95%CI)	P-value
Difference intercept		
CVA – Hypoxia	1.02 (0.81 – 1.27)	0.89
CVA – Trauma	1.24 (0.96 – 1.16)	0.10
CVA – Other	0.97 (0.70 – 1.35)	0.87
Hypoxia – Trauma	1.22 (0.95 – 1.58)	0.12
Hypoxia – Other	0.96 (0.69 – 1.33)	0.79
Trauma – Other	0.78 (0.55 – 1.11)	0.17
Difference slope		
CVA – Hypoxia	0.99 (0.97 – 1.02)	0.26
CVA – Trauma	0.97 (0.94 – 1.01)	0.09
CVA – Other	1.05 (1.00 – 1.09)	0.03
Hypoxia – Trauma	0.98 (0.95 – 1.01)	0.23
Hypoxia – Other	1.05 (1.01 – 1.10)	0.01
Trauma – Other	1.07 (1.03 – 1.12)	0.001





Linear mixed model results

Label	df	F Value	P-value
Effect DGF	2	1.93	0.15
Effect on intercept		.	.
Effect on slope		.	.

Label	Estimate (95% CI)	P-value
Difference intercept		
No DGF – DGF	1.11 (0.91 – 1.36)	0.31
Difference slope		
No DGF – DGF	1.01 (0.98 – 1.03)	0.59

Last RR*	OR (95%CI)	P-value	AUC (95% CI)
Univariable	1.1 (1.0 – 1.3)	0.04	0.60 (0.52 – 0.69)
Multivariable**	1.1 (1.0 – 1.3)	0.04	0.63 (0.55 – 0.71)

BOS_13_5 ARCHETYPAL ANALYSIS OD DECEASED DONOR KIDNEYS: A MOLECULAR APPROACH FOR POSTTRANSPLANT OUTCOMES

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Background: The quality of donor kidneys significantly impacts transplant outcomes. Traditional procurement biopsies are limited by categorical scoring and observer-dependent variability. Molecular diagnostics offer continuous and objective insights.

Methods: This prospective, single-center study (NCT06171438) included 276 kidneys from 174 deceased donors. Donor procurement biopsies were performed on the backtable and part of the biopsy was stored for future RNA extraction and molecular profiles analysis using Affymetrix microarrays. Three molecular classifiers (the logistic regression model, the Poisson regression and the extreme gradient boosting) with 10-fold cross validation were employed to identify donor categories based on clinical variables (age, BMI, hypertension, marginal kidney) and histological biopsy scores (the vascular fibrous intimal thickening (cv), interstitial fibrosis (ci) and tubular atrophy (ct) and arteriolar hyaline thickening (ah)). Archetypal analysis was applied to determine molecular phenotypes and their association with short- and long-term transplant outcomes.

Results: Three donor molecular archetypes were identified (**Figure 1A**). Archetype 1 ("marginal donors") was characterized by older age (median 68 years), extensive chronic morphological changes (IFTA>0 in 66%, ah>1 in 59%, cv>1 in 36%), and the highest Kidney Donor Risk Index (KDRI). Archetype 2 ("ideal donors") was associated with young age (median 42 years), low KDRI, minimal chronic histological changes (IFTA>0 in 39%, ah>1 in 33%, cv>1 in 13%) and the highest posttransplant eGFR at 12 months (p<0.001, **Figure 1B**). Archetype 3 ("intermediate donors") was associated with older age (median 63 years) however better eGFR despite similar chronic histological changes (IFTA>0 in 73%, ah>1 in 63%, cv>1 in 56%).

Conclusions: Molecular profiling outperforms histology in procurement biopsies and enables the identification of ECD kidneys with better posttransplant kidney allograft function.

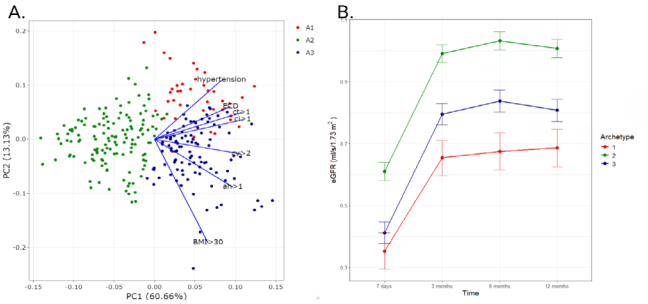

Figure 1. A. Principal component analysis (PCA) of archetypes. For each sample, molecular classifier scores discriminating one of 8 particular groups (donor age >70 years, type of donor (standard criteria vs. extended criteria donors), donor hypertension, donor BMI >30 and histological donor biopsy scores cv>1, ci>0, ct>0 and ah>1) from the rest of patients were calculated as a median of 3 classifiers (logistic regression, Poisson regression a XGBOOST). These data were used as input for PCA. Each donor (dot) is colored by its archetype. The superimposed arrows show the direction and relative magnitudes of the correlations between the 8 input variables and the PC scores. **B. Renal function after transplantation according to donor biopsy archetypes**.

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BOS_13_6 KIDNEY DISCARD ACROSS TWO ERAS IN THE UNITED STATES AND THE ROLE OF HYPOTHERMIC MACHINE PERFUSION

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Background: The supply of kidneys for transplantation remains insufficient for the rising number of waitlisted candidates. This study examines trends in kidney discard rates across allocation eras and the impact of hypothermic machine perfusion ("pumping").

Methods: Deceased donors in the Scientific Registry of Transplant Recipients (SRTR) from December 2014 to March 2024 were analyzed. Kidneys were categorized by allocation era: KAS (12/2014–3/2021) or KAS250 (3/2021–3/2024). Monthly rates of procured, pumped, and discarded kidneys were estimated using linear models with a spline at KAS250 onset. Generalized estimating equations (GEE) estimated the effect of pumping on discard trends.

Results: Of 204,783 kidneys procured from 105,756 donors, 158,521 (77.4%) were transplanted, and 46,262 (22.6%) were discarded. Kidney procurement increased during KAS (+11.5 kidneys/month, p<0.001) and increased at a slightly lower rate after KAS250. Pump utilization increased steadily (+7.5 kidneys/month, p<0.001) across both eras. Discard rates rose during KAS (+3.1 kidneys/month, p<0.001) and further increased after KAS250 (+4.6 kidneys/month, p<0.001) (Fig 1). Early in the study, pumping was associated with a lower discard risk compared to static cold storage (SCS) (RR 0.60, p<0.001). However, this protective effect declined over time (RR 1.09, p <0.001). The risk of discard increased after KAS250 (RR 1.06, p <0.001), coinciding with the discard rates for pumped kidneys surpassing those of SCS kidneys (Fig 2).

Conclusions: Rising discard rates continue to challenge kidney supply. The introduction of KAS250 was associated with increased relative discard risk. Although pumping initially reduced discard rates, its protective effect has diminished, warranting further research into pump utilization and organ acceptance practices.

Figure 1. Trends of procurement, pump utilization, and discard across two kidney allocation system eras

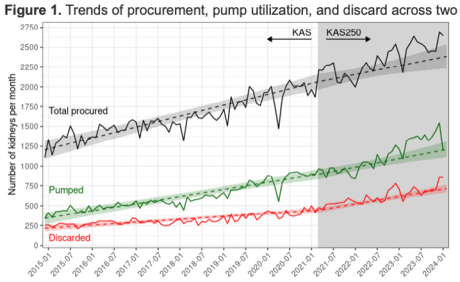

Figure 2. Rates of discard by pump utilization across two kidney allocation system eras

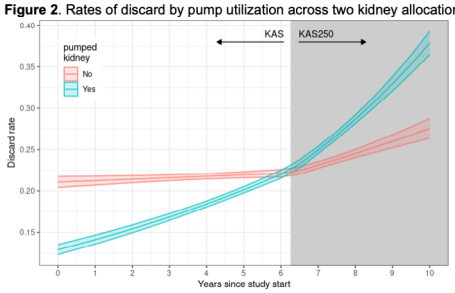

Table 1. Multivariable GEE model estimates of relative risk of discard

	Risk of discard		
Predictors	*Risk Ratios*	*CI*	*p*
Years since study start	1.01	1.00 – 1.01	0.099
Pumped kidneys[1]	0.60	0.57 – 0.64	**<0.001**
Change after KAS250	1.06	1.03 – 1.08	**<0.001**
Years x Pumped	1.09	1.08 – 1.10	**<0.001**
Change after KAS250 x Pumped	0.99	0.96 – 1.02	0.390

[1]Reference group: cold storage; KAS kidney allocation system, KAS 250: distance-based kidney allocation system

BOS_13_7 DECEASED DONOR KIDNEYS EXHIBIT HIGHER LEVELS OF NEUTROPHIL EXTRACELLULAR TRAPS

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Background: Deceased donor kidneys have variable transplant outcomes due to inflammation in the donor. During systemic inflammation, increased neutrophils are recruited to kidneys, potentially contributing to tissue injury and microthrombus formation through the release of neutrophil extracellular traps (NETs). NETs have previously been linked to acute kidney injury and acute antibody-mediated rejection, but NET formation has not yet been characterized in human kidney donors.

Methods: Kidney biopsies and serum of kidney donors [living (LD), n=26; deceased brain dead (DBD), n=26 and deceased circulatory dead (DCD), n=19] were obtained from the TransplantLines Biobank (Netherlands). Biopsies were analyzed for kidney-associated NET formation [immunofluorescence of myeloperoxidase (MPO), DNA and citrullinated histone 3 (CitH3)], platelet microthrombus formation (immunohistochemistry of CD41), and histopathological injury (pre-implantation BANFF criteria). Serum NETs were analyzed using ELISAs for MPO/CitH3-DNA complexes and cell free DNA (cfDNA). Perfusate samples of discarded kidneys (n=36) that underwent hypothermic machine perfusion (HMP) followed by normothermic machine perfusion (NMP) and kidney donor profile indexes (KDPI), were obtained from 34Lives (US). NETs were measured in the perfusate at the end of HMP and NMP.

Results: Increased levels of NETs were detected in biopsies of DCD- (p<0.05) and DBD- (p<0.01) compared to LD kidneys. Serum NETs were increased in deceased donors compared to LD (MPO-DNA, p<0.001; CitH3-DNA, p<0.0001; cfDNA, p<0.01). Deceased donor kidneys also had increased platelet deposition and injury compared to LD kidneys, which positively correlated with NET formation (r=0.4, p<0.05). Discarded kidneys released increased NETs during NMP compared to HMP. The release of MPO-DNA complexes during NMP was significantly associated with KDPI (r^2=0.1, p<0.05).

Conclusions: The results suggest a link between NETs and kidney injury in deceased donor kidneys. In machine perfused kidneys, an association between NETs and KDPI implies that kidneys from donors with a high-risk profile, contain increased NETs. NETs might therefore be a promising therapeutic target in the donor/during preservation and should be explored as a biomarker for injury and inflammation.

Table 1: NETs in kidney biopsies and serum

Measurement	*Living (n=26)*	*Brain-dead (n=26)*	*Circulatory dead (n=19)*	*p-value**
Biopsies				
NETs/mm² (CitH3/MPO/DNA)	11.39	42.72	36.64	0.002
Serum				
CitH3-DNA complexes (AU)	0.83 ± 0.13	2.49 ± 0.21	1.61 ± 0.13	0.0001
MPO-DNA complexes (AU)	1.01 ± 0.1	0.92 ± 0.13	1.60 ± 0.12	0.0005
cfDNA (AFU)	41150 ± 5354	75320 ± 12311	62885 ± 7241	0.0027

*Kruskal-Wallis test. Data expressed as mean ± SEM.
Abbreviations: AFU, arbitrary fluorescent units; AU, arbitrary units; cfDNA, cell-free DNA; CitH3, citrullinated histone 3; MPO, myeloperoxidase; NET, neutrophil extracellular trap.

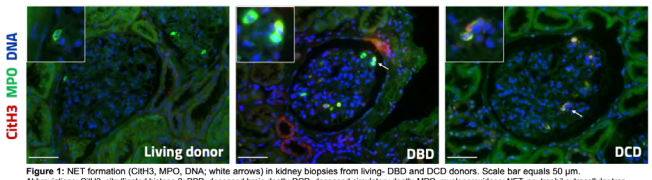

Figure 1: NET formation (CitH3, MPO, DNA; white arrows) in kidney biopsies from living- DBD and DCD donors. Scale bar equals 50 µm.
Abbreviations: CitH3, citrullinated histone 3; DBD, deceased brain death; DCD, deceased circulatory death; MPO, myeloperoxidase; NET, neutrophil extracellular trap.

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BOS_13_8 USING US NATIONAL REGISTRY DATA TO ESTIMATE LIVING KIDNEY DONOR OUTCOMES IN A EUROPEAN COHORT

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Background: Most national studies of living kidney donor (LKD) outcomes come from the United States. Due to different demographics and donor selection criteria, US results may not generalize well to other settings. Here we apply a novel technique to construct a weighted US cohort with characteristics matching a European cohort, and report LKD outcomes in the weighted cohort.

Methods: Using SRTR data on 81,748 US LKDs 2010-2023, we Monte-Carlo selected 5,000 LKDs with characteristics comparable to published data reported from the French CRISTAL-donneur registry 2012-2017, and external race/ethnicity estimates for France. We used weighting-by-the-odds to weight the entire cohort of 81,748 LKDs to approximate the French cohort. We reported 6/12/24-month eGFR in the weighted cohort, perioperative mortality risk, and 6/12/24-month risk of proteinuria, hypertension, and diabetes.

Results: The unweighted US cohort was younger than the French reference cohort, and less likely to be related to the recipient; the weighted US cohort more closely matched the French cohort (Table). Perioperative mortality in the weighted US cohort was 0.007%. Risk of proteinuria at 6/12/24m postdonation was 5.1%/4.8%/4.7%; of hypertension, 1.2%/1.8%/2.4%; of diabetes, 0.03%/0.04%/0.08%. Mean 6/12/24m postdonation eGFR was 63.5, 64.4, and 65.4 mg/mL/mm^2, lower than the unweighted cohort (66.5/67.5/68.6).

Conclusions: Our methodology can be used to estimate outcomes from the US national registry cohort, accounting for demographic differences. The same technique could be applied to comparative studies of outcomes between countries, without the need to share individual-level data.

Characteristic	Unweighted US cohort	Weighted US cohort	French reference cohort
Median (IQR) age	43 (34-53)	50 (40-58)	51 (43-59.8)
Median (IQR) height (cm)	167.6 (162.4-175.3)	167.6 (160.0-174.0)	167 (160-174)
Median (IQR) weight (kg)	76.0 (65.8-86.6)	70.0 (61.0-80.5)	70 (60-80)
Median (IQR) BMI	26.7 (23.9-29.7)	25.1 (22.6-27.8)	24.8 (22.3-27.7)
Median (IQR) predonation eGFR	101.0 (88.6-112.1)	97.3 (85.7-107.1)	96.8 (87.0-105.9)
% male	36.7%	35.3%	36.9%
% white	71.5%	91.8%	NA
% Black	9.4%	5.1%	NA
% Asian	4.2%	2.1%	NA
% other race/ethnicity	14.9%	1.0%	NA
% bio related to recipient	44.3%	56.5%	59.4%

BOS_13_9 THE CELL-FREE DNA METHYLATION PROFILE OF MACHINE-PERFUSED KIDNEYS IS ASSOCIATED WITH POST-TRANSPLANT FUNCTION

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Background: There is a need for a quantitative marker to predict the function of marginal donor kidneys upon transplantation, but there is not such a tool yet. Biomarkers such as cell-free DNA (cfDNA) have been investigated for their predictive value during machine perfusion of various transplant organs. Nevertheless, while little is known about the epigenome of cfDNA, variations in DNA methylation are associated with chronic injury after kidney transplantation. Our aim was to investigate the methylome of cfDNA released during hypothermic machine perfusion (HMP) and identify differentially methylated regions (DMR) between immediate- and primary non-function (IF, PNF) kidneys to predict early post-transplant function.

Methods: Perfusate was collected from 16 deceased donor kidneys (8 IF vs 8 PNF) after HMP and cfDNA was isolated using the QIAamp Circulating Nucleic Acid kit. Methylated-DNA sequencing (MeD-Seq) was performed by digesting cfDNA with methylation-dependent restriction enzyme LpnPI. Digested cfDNA was sequenced and individual read count scores were obtained for transcription start sites (TSS), gene bodies (GB) and CpG islands. A genomic interval technique was used to detect DMRs, with significance set at $p < 0.05$ and a Benjamini-Hochberg correction for multiple testing.

Results: In total, we tested 12,611 individual regions for differential methylation between IF and PNF kidneys based on read counts. The majority of these regions were mapped to TSSs (62%), while the remainder mapped to CpG islands (22%) and GBs (16%). These individual regions did not show a significant difference between IF and PNF after correction for multiple testing. Nevertheless, using a genomic interval we found a group of 5 significant DMRs which successfully distinguished the IF kidneys from the PNFs through unsupervised hierarchical clustering (Figure 1).

Conclusions: We identified a group of 5 DMRs in perfusate cfDNA that distinguished IF from PNF kidneys. These findings suggest that cfDNA methylation profiling could serve as a biomarker during perfusion to predict post-transplant kidney function.

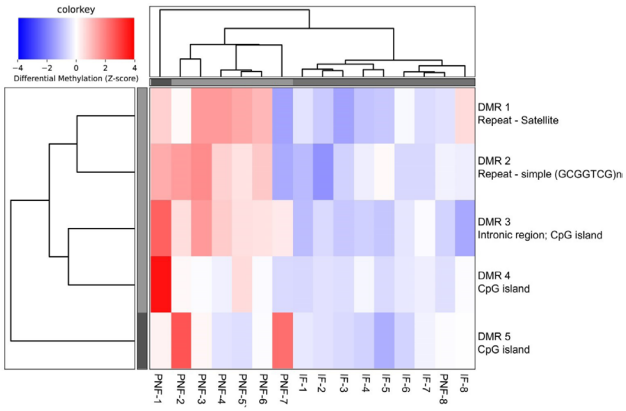

Figure 1. Heatmap showing an unsupervised hierarchical clustering using a group of 5 DMRs in cfDNA between IF and PNF kidneys. Red represents hypermethylation, blue represents hypomethylation.

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BOS_13_10 MITOCHONDRIAL FUNCTION DURING HYPOTHERMIC MACHINE PERFUSION OF THE KIDNEY PREDICTS POST-TRANSPLANT GRAFT FUNCTION

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Background: Hypothermic machine perfusion (HMP) has become a standard graft preservation method for kidney transplantation, but biomarkers with robust predictive capacity towards clinical outcome are required. ATP production by oxidative phosphorylation plays a central role in renal physiology and it can be assessed by mitochondrial respiration measurement in tissue samples. Flavin mononucleotide (FMN), a cofactor of the mitochondrial respiratory system, has been identified as perfusate biomarker in machine perfusion of the liver and in preclinical renal HMP. Herein, we investigated the above parameters during clinical kidney HMP and their link to the postoperative outcome.

Methods: In a single center, prospective clinical trial biopsies of the renal cortex were taken before and after hypothermic machine perfusion (LifePort Kidney Transporter, Organ Recovery Systems) in 64 human kidney grafts, of which 47 were transplanted. Mitochondrial respiration was assessed by high-resolution respirometry. Perfusate samples were analyzed for FMN concentration. OXPHOS capacity, maximal mitochondrial respiration, ATP production efficiency and FMN concentrations were correlated with parameters of short- and long-term outcome, as delayed graft function (DGF), serum-creatinine levels and glomerular filtration rate as clinical endpoints.

Results: Mitochondrial respiration remained stable throughout HMP, whereas a steady increase of FMN concentrations in the perfusate was observed. Pre-transplant mitochondrial respiration and ATP production efficiency were significantly higher in kidneys with good initial function compared to those which developed DGF. FMN concentration after 15 min of perfusion was significantly higher in the DGF group. Mitochondrial respiration correlated with glomerular filtration rate and serum creatinine levels 7 days after transplantation and with serum creatinine levels 3 months and one year after transplantation.

Conclusions: Pre-transplant mitochondrial respiration and FMN concentrations are predictive towards early kidney function during the first postoperative week and mitochondrial respiration correlates with serum creatinine levels even one year after transplantation. The above biomarkers hold a robust predictive capacity towards clinical outcome.

BOS_13_11 RISK FACTORS OF DELAYED KIDNEY GRAFT FUNCTION FOLLOWING DONATION AFTER CIRCULATORY DEATH

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Background: Since September 1st 2011 donation after circulatory death (DCD) organ donation has resumed in Switzerland after the DCD program had been halted for a four-year period due to jurisdictional and medico-ethical discrepancies. This form of organ donation has gained relevance due to the worldwide scarcity of donor organs and now accounts for nearly half of all donations in the Swiss transplant setting. This study collected the data of Swiss DCD kidney transplants (KTs) from 1.09.2011 to 31.08.2024 with the aim to identify risk and protective factors for the occurrence of delayed graft function (DGF), which is a common early complication following kidney transplantation, especially in DCD transplants.

Methods: Of 499 controlled DCD (cDCD) donors within the time frame of the study, 351 kidney donors were identified, of which 711 KTs were procured and transplanted, including 7 double KTs. Donor characteristics and recipient data were exported from the Swiss Organ Allocation System (SOAS). A complete data, multivariable analysis using a logistic regression model for the event of DGF was conducted for the following variables: Donor age and donor comorbidity, cause of death, year of transplantation, functional warm and cold ischemia time (fWIT, CIT), use of abdominal normothermic regional perfusion (aNRP) and hypothermic machine perfusion (HMP). Results are reported in odds ratio (OR) and 95%-confidence interval (CI).

Results: Of 711 (100.0%) KT recipients, 61 (8.6%) were excluded for missing data. 650 (91.4%) recipients qualified for analysis, of which 315 (48.5%) experienced DGF, while 335 (51.5%) did not. We found strong evidence that aNRP (OR 0.19, 95%-CI 0.10–0.35) and HMP (OR 0.54, 95%-CI 0.36–0.81) reduced the odds for DGF. For anoxia (OR 0.59, 95%-CI 0.38–0.92), a weak effect on DGF risk was observed. There was no evidence for effect of fWIT (OR 0.98, 95%-CI 0.72–1.34) and CIT (OR 1.32, 95%-CI 1.01–1.71) on the odds for DGF.

Conclusions: A significant reduction in DGF risk was observed for the use of aNRP and HMP. Anoxia as the cause of death appears to slightly decrease the risk of DGF. FWIT and CIT did not affect DGF occurrence. The results of this study underline the effectiveness of modern procurement and preservation methods used in kidney transplantation, aligning with current research findings.

	Interquartile Difference (IQR)	Odds Ratio (95%-CI)	Chi-Square	d.f.	p-value
Donor Characteristics					
Age (years)	17.0 (48.0–65.0)	1.12 (0.86–1.47)	2.49	2	0.290
Hypertension		1.28 (0.84–1.97)	1.30	1	0.250
Cardiovascular disease		0.78 (0.49–1.23)	1.15	1	0.280
Diabetes		1.29 (0.47–3.56)	0.24		
Cause of Death			5.81	2	0.055
-Anoxia		0.59 (0.38–0.92)			
-other		0.83 (0.48–1.43)			
fWIT (minutes)	11.0 (20.0–31.0)	0.98 (0.72–1.34)	2.05	2	0.360
aNRP		0.19 (0.10–0.35)	27.20	1	<0.001
Transplantation Year	5.0 (2018–2023)	0.98 (0.64–1.51)	0.01	2	1.000
Recipient/Transplant Characteristics					
CIT (hours)	4.0 (7.3–11.3)	1.32 (1.01–1.71)	4.31	2	0.120
Machine Perfusion		0.54 (0.36–0.81)	8.78	1	0.003

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BOS_13_12 A NEW MARKER OF DELAYED GRAFT FUNCTION (D250) PREDICTOR OF GRAFT FUNCTION AND GRAFT SURVIVAL

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Background: The suggested link between delayed graft function (DGF) and long-term renal graft survival is poorly documented using a binary marker of DGF (the need for dialysis). We used a linear marker (number of days to reach creatinine <250umol/l: D250) in a large multicenter cohort (Astre: 11 renal transplant centers).

Methods: Inclusion criteria were: adult patients, transplanted between 2008 and 2020, brain-dead donor, non-preemptive transplant. Donor and recipient clinical and biological data were used to build Cox predictive models; graft lost risk was evaluated by Kaplan Meier analysis. We stratified D250 in 5 subgroups.

Results: The mean D250 for the 8311 patients included was 7.44 days (0 to 59). In multivariate analysis, conventional donor and recipient DGF risk factors (age, hypertension, causes of death, last creatinine, duration of cold ischemia, immunization, etc.) were significantly related to D250, confirming its relevance as a marker of DGF. We exhibited a strong correlation between D250 and renal function at one year (p< 0.001). To lesser extent we identified an interaction of D250 with the risk of rejection (p=0.004). Finally, there was a proportional increase in the risk of graft loss (HR, 1.016) and patient death (HR, 1.024) for each additional day of D250. In Kaplan Meier analysis, renal survival was significantly different in the five D250 subgroups: 11.9 years for D250 < 2 days (group 1), 6.4 years if D250 > 20 days (group 5) (log rank test p<0.001).

Conclusions: Overall, D250 is a good marker of DGF strongly linked to renal function at one year and graft survival. It could be used as a primary endpoint in clinical trials to prevent DGF.

	Groups	N	Mean	P
Serum creatinine M12 *	1	1190	117	<0,001
	2	1448	135	<0,001
	3	1230	143	<0,001
	4	808	152	<0,001
	5	361	175	<0,001

Table 1: Graft function depending of D250 subgroups (Anova test).
* µmol

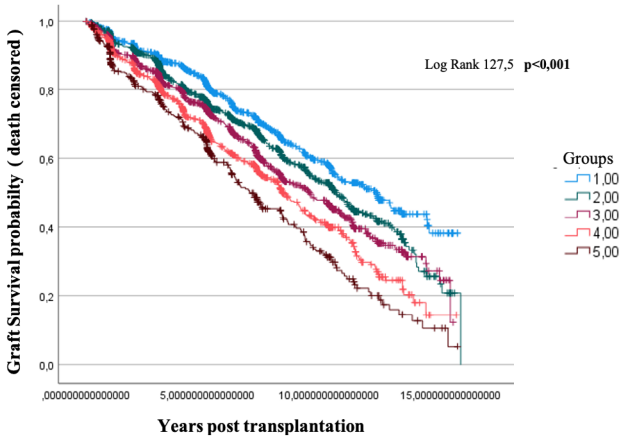

Figure 1: Graft survival depending of D250 subgroups (Kaplan Meier analysis).

BOS_13_13 CONTRAST-ENHANCED ULTRASOUND TO ASSESS KIDNEY QUALITY DURING EX SITU NORMOTHERMIC MACHINE PERFUSION

Samuel James Tingle[1], Chloe Connelly[2], Emily Glover[3], Benjamin Stenberg[4], Andy McNeill[4], Georgios Kourounis[4], Beth Gibson[5], Balaji Mahendran[6], Lucy Bates[7], Madison Cooper[5], Rhys Pook[8], Samantha Lee[5], Marnie Brown[9], Rodrigo Figueiredo[4], Kevin Marchbank[5], Simi Ali[10], Neil Sheerin[11], Colin Wilson[12], Emily Thompson[13]

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Background: Normothermic machine perfusion (NMP) provides opportunity for viability assessment of donated kidneys. Diminished microvascular perfusion, despite adequate total blood flow, is a key pathophysiology in ischaemia-mediated acute kidney injury. Contrast-enhanced ultrasound (CEUS) could allow objective assessment of microvascular perfusion during renal NMP.

Methods: Blood-based NMP was performed on porcine kidneys, and human kidneys declined for transplant (REC15/SC/0161). Porcine kidneys were retrieved with a circulatory death model (25-minute warm ischaemia). CEUS was performed with Philips EPIQ7 Ultrasound machine and sulphur hexafluoride contrast agent, delivered as a bolus into the NMP circuit arterial limb. Microvascular perfusion quality was assessed for cortex and medulla (Figure 1A), and quantified with peak and time-to-peak values. Z-score normalisation allowed combination of cortex/medulla scores into an overall “CEUS-score”.

Results: In porcine kidneys (n=8), decreased quality of perfusion in renal cortex and medulla was correlated with urinary NGAL (Pearson r=0.900; P=0.002 and r=0.745; P=0.034, respectively) and tissue apoptosis (r=0.647; P=0.083 and r=0.805; P=0.016). These findings were confirmed in human kidneys (n=5). In human kidneys, “CEUS-score” at 2 hours was correlated with tissue apoptosis (r=-0.937; P=0.019) and predicted urinary NGAL at 24 hours of NMP (r=-0.925; P=0.024; Figure 1B). Total renal flow was not correlated with these outcomes. A web app (stingle.shinyapps.io/Time_intensity_analysis) and R package (“tican”) were developed for quantitative time-intensity curve CEUS analysis.

Conclusions: CEUS allows point-of-care assessment of microvascular perfusion during renal NMP, which correlates with tissue apoptosis on histology. 2-hour CEUS-score predicts the key biomarker urinary NGAL at 24 hours of NMP in human kidneys. CEUS may therefore be a valuable tool to assess kidney quality in assessment and reconditioning centres. Techniques for CEUS-quantification were developed and disseminated via open-source software.

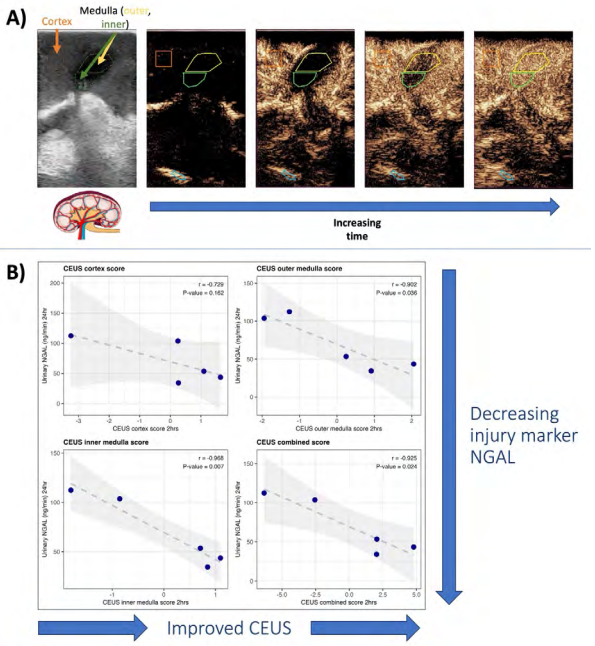

Figure 1 – Contrast enhanced ultrasound during ex situ machine perfusion. A) representative images with regions of interest selected demonstrating sequential perfusion of cortex and medulla. B) Correlation of CEUS scores at 2 hours with injury marker urinary NGAL at 24 hours of NMP. Pearson correlation coefficient and associated p-value are displayed.

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BOS_13_14 CYSTATIN-C AS A BIOMARKER FOR DONOR KIDNEY QUALITY: PREDICTING PRIMARY NON-FUNCTION AND POST-TRANSPLANT OUTCOMES

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Background: Current donor assessment tools include creatinine and inadequately predict transplant outcomes, as they overlook underlying tissue damage. Here, we have hypothesized that donor Cystatin-C may better reflect injury in the kidney, rather than being solely a reflection of filtration function.

Methods: Donors were selected based on the transplant outcomes of their grafts [grafts with primary non-function (PNF), delayed (DGF) and immediate function (IGF)]. Plasma samples collected from QUOD biobank pretransplant from 429 deceased donors [after brain (DBD) and circulatory death (DCD)] were analyzed using Luminex assay. Cystatin-C, creatinine and selected markers of biological stress and injury (CRP, TNFα, TIMP-1, NGAL and KIM-1) were measured and integrated in regression models to study the association with short-term and 12-month transplant outcomes. Both kidney grafts were examined from each donor, when available. In total, 113 grafts (14.7%) had PNF, 179 (23.3%) DGF and 476 (62%) had IGF.

Results: Recipients with PNF received grafts from donors with significantly higher Cystatin-C (8.4 vs. 6.6 vs 6.1 x10-1 mg/L, p<0.001), compared to those with DGF and IGF. Following multivariate analysis, high donor Cystatin-C was independently associated with PNF (COR: 1.06 x 10-1 mg/L, p=0.04) and eGFR 12 months posttransplant (β=-1.10 per 10-1 mg/L, p=0.031). Older donor age, DCD, hypertension and high body mass index significantly associated with higher Cystatin-C during donor management (p<0.05). Creatinine at retrieval was strongly associated with Cystatin-C (β=3.25, p<0.0001), but had no predictive value on the transplant outcomes. Cystatin-C correlated stronger with systemic and tubular stress, defined by TNFα (ρ=0.40, p<0.001), CRP (ρ=0.20, p<0.001), NGAL (ρ=0.39, p<0.001), and TIMP-1 (ρ=0.21, p<0.001), compared to creatinine.

Conclusions: Cystatin-C identified kidneys at higher risk of PNF and worse 12-month transplant function. It correlated stronger with stress and inflammatory markers compared to creatinine and provided a comprehensive reflection of donor quality and systemic injury. Its integration into assessment protocols could improve the current screening process, enable more accurate risk stratification, organ allocation, and tailored pre- and post-transplant care.

BOS_13_15 PROLONGED FUNCTIONAL WARM ISCHAEMIA ASSOCIATES WITH METABOLIC AND PROTEASE DYSREGULATION IN DCD KIDNEYS

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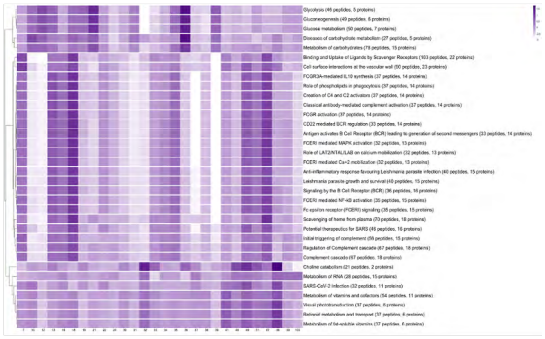
Background: Donation after circulatory death (DCD) includes an inherent period of warm ischemia, which is often prolonged and correlates with increased incidence of delayed graft function following kidney transplant. Functional warm ischemia (fWIT; time donor blood pressure drops <50mmHg after withdrawal of life support until organ cold perfusion) leads to organ hypoperfusion and cellular energy depletion, triggering a cascade of ischemic injury. Ischemia disrupts cellular homeostasis inducing morphological changes and protease dysregulation that contributes to kidney injury. However, the impact of fWIT on kidney injury remains poorly understood. To elucidate fWIT-associated injury, this study used mass spectrometry to profile the protein degradome generated by endogenous protease dysregulation.

Methods: DCD kidney biopsies (n=42) with short (<25 minutes) and long fWIT (30-107 minutes) were prepared according to the High-efficiency Undecanal-based N-Termini EnRichment (HUNTER) protocol and analyzed using mass spectrometry and bioinformatic tools. Protein degradation profiles and changes in protease abundance were further quantified in kidney and hypoxic podocytes and proximal tubule epithelial cells (PTECs) using Western blotting.

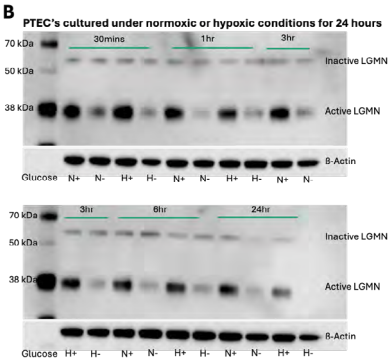
Results: Mass spectrometry identified 2,563 endogenous peptides matched to 1,022 proteins. Degraded proteins associated with proximal tubule injury, metabolic pathways and the cytoskeleton. Pathway analysis of the mapped peptides revealed significant dysregulation in metabolic processes, particularly affecting glucose, lipid and vitamin metabolism (Figure 1A). Prolonged fWIT was also associated with altered protease activity. LGMN activity increased (p<0.001) with fWIT, yet CATB activity (a substrate of LGMN) decreased (p=0.004). LGMN abundance did not change with fWIT yet was significantly reduced in glucose-starved PTECs (but not podocytes) (Figure 1B), indicating a cell-type-specific relationship between LGMN and glucose.

Conclusions: Prolonged fWIT induces metabolic and protease changes in DCD kidneys that may compromise posttransplant function. As a high specificity protease, LGMN and associated regulatory components present promising therapeutic targets to mitigate injury in DCD kidneys and improve transplant outcomes.

1A



1B



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BOS_14_1 A CFCHIP- SEQ LIQUID BIOPSY FOR THE DIAGNOSIS OF CELLULAR REJECTION FOLLOWING LIVER TRANSPLANTATION

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Background: Liver transplantation (LTx) is a vital treatment option for patients with endstage liver diseases. Acute cellular rejection (ACR) is a significant clinical diagnostic and therapeutic challenge at the post-transplant period. The clinical challenge lies in distinguishing ACR from other acute events, such as infections, vascular events, drug toxicity and biliary damage, which necessitates very different therapeutic modalities. Current diagnostic standards require liver biopsy for ACR diagnosis. This leads to a delay in diagnosis, is invasive, and with potentially complications. There is an urgent need for a simple, reliable, and reproducible non-invasive diagnostic test, which could be performed on daily basis, for monitoring post-LTx patients and diagnosing ACR.

Methods: We utilized cell-free chromatin immunoprecipitation followed by sequencing (cfChIP-seq), a novel epigenetic-based liquid biopsy assay we recently introduced (Sadeh et al, Nat. Biotech 2001), to profile circulating cfDNA originating from active genes in plasma samples. The assay allows for interrogation of gene activity in the cell of origin. It provides insights into the extent of liver damage and the molecular states of dying liver cells and immune cells.

Results: We enrolled a cohort of >150 LTx patients and prospectively collected >4000 blood samples through their post-transplant hospitalization. We collected blood samples during 15 biopsy-verified ACR events and 14 non-ACT acute events for 20 patients. We developed a cfChIP-seq signature of genes that distinguish ACR samples from other acute liver damage events. We show that this signature allows the classification of ACR events with AUC of 0.94. This signature provides superior diagnostic performance compared to blood assay of liver enzymes (AUC of 0.75 for ALT and 0.48 for AST). We validated this signature in a follow-up LTx cohort.

Conclusions: We developed an ACR blood test using a cfDNA signature with high accuracy in patients post-LTx. The assay is highly reproducible and robust, suggesting a path toward non-invasive detection, monitoring, and diagnosis of post-LTx ACR.

BOS_14_2 ASSOCIATION OF DONOR-DERIVED CELL-FREE DNA WITH MICROVASCULAR INFLAMMATION PHENOTYPES IN KIDNEY ALLOGRAFTS

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Background: Donor-derived cell-free DNA (dd-cfDNA) has shown to improve the detection of kidney allograft rejection. However, its ability to identify the recently defined microvascular inflammation (MVI) phenotypes in the Banff 2022 Classification remains unclear.

Methods: We included 3,175 pediatric and adult kidney transplant recipients from 20 transplant centers, who underwent allograft biopsy with concurrent assessment of dd-cfDNA, anti-HLA DSA, and functional parameters between September 2011 and October 2024. Clinical and pathological data were integrated to classify biopsies according to the Banff 2022 Classification. We performed uni- and multivariable logistic regressions to determine the independent association between dd-cfDNA and microvascular inflammation phenotypes.

Results: Among the 4,181 allograft biopsies, mild to moderate MVI was diagnosed in 695 (16,6%) cases, including 115 MVI, DSA-negative C4d-negative (MVI, DSA-C4d-), 72 probable AMR (mild MVI with DSA-positivity), 398 AMR and 110 mixed cases. We observed an incremental increase of dd-cfDNA levels from probable AMR (0.67 ? 0.11%) to MVI, DSA-C4d- cases (1.22 ? 0.12%), with highest levels seen in AMR (1.73 ? 0.11%) and mixed rejection (3.69 0.37%) (Figure). Dd-cfDNA (OR 2.12, 95% CI 1.83-2.45, p <0.001), proteinuria (OR 1.32, 95% CI 1.14-1.52, p<0.001), and history of rejection (OR 5.18, 95% CI 3.52-7.53, p<0.001) were associated with MVI, DSA-C4d- in univariate analysis. In multivariable analysis, dd-cfDNA remained independently associated with MVI, DSA- C4d- (adjusted OR 1.68, 95% CI 1.40-2.02, p<0.001). Dd-cfDNA was significantly associated with probable AMR in univariate analysis (OR 1.34, 95% CI 1.08-1.66, p=0.007), and remained independently associated with probable AMR after adjusting for functional parameters and history of rejection (p=0.041).

Conclusions: In this large multicenter prospective kidney transplant cohort, we demonstrated that dd-cfDNA was independently associated with MVI, DSA-negative, C4d-negative, as well as probable AMR (mild MVI with DSA-positivity), highlighting its promising role in diagnosing and guiding treatment for these phenotypes.

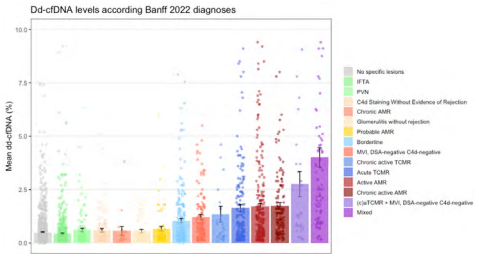

Figure. Mean level of dd-cfDNA according to the Banff 2022 Classification. Each bar corresponds to one histological diagnosis with its mean dd-cfDNA value. Each dot corresponds to an individual dd-cfDNA value. Data are presented as mean± SEM. IFTA, Interstitial Fibrosis and Tubular Atrophy; PVN, polyomavirusassociated nephropathy.

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BOS_14_3 DD-CFDNA PREDICTS OUTCOMES OF KIDNEY GRAFT REJECTION

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Background: The role of donor-derived cell-free DNA (dd-cfDNA) in post-rejection monitoring has not been specifically studied.

Methods: In prospective observational study (NCT06476717) dd-cfDNA was measured at biopsy with rejection and for 3 consecutive weeks (W1, W2, W3) by the Prospera™ test. All biopsies were assessed by histology and by tissue-based transcriptomics (MMDx) in the local lab, all patients received anti-rejection treatment. dd-cfDNA positivity cut-off was set at 1% and graft survival was followed for 6 months after biopsy.

Results: 41 kidney transplant recipients with biopsy-proven rejection by histology or by MMDx were included, 155 dd-cfDNA measurements were available. Biopsies were performed at median 92 days from transplantation, and DSA were present in 17 patients (41%). There were 10 TCMR, 23 ABMR, and 8 non-rejection (NR) assessed by MMDx while all biopsies were classified as borderline, TCMR, ABMR or mixed rejection by histology. Rejection defined by MMDx exhibited distinct dd-cfDNA patterns in the follow up (Figure 1): in TCMR dd-cfDNA decreased in the first week and remained negative while in ABMR it remained above the cut-off in the follow up. There was a striking difference between histology and MMDx readouts, as all of the NR by MMDx were diagnosed as rejection by histology. Dd-cfDNA in these cases was negative upon biopsy and remained negative following anti-rejection treatment thus corroborating the MMDx findings. Higher dd-cfDNA at biopsy was associated with higher risk of graft loss (HR 1.83, 95% CI 1.16, 2.87) at 6 months.

Conclusions: Elevated dd-cfDNA upon biopsy is associated with inferior graft survival. Well-defined therapy of TCMR is associated with dd-cfDNA decrease below the cut-off contrary to the treatment of ABMR. MMDx better classified rejection injury diagnosed by dd-cfDNA than histology.

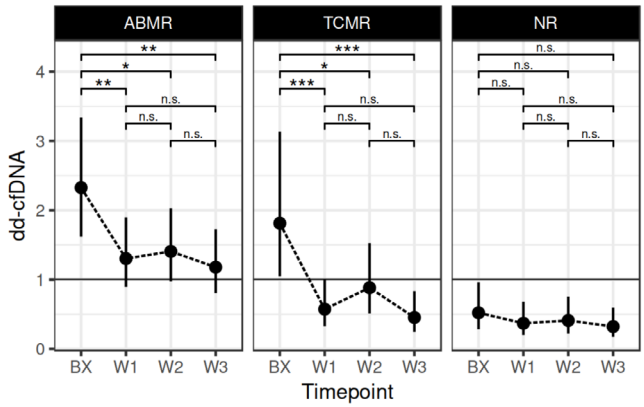

Figure 1 | Donor-derived cell-free DNA evolution in MMDx diagnoses.

BOS_14_4 EPIGENETIC SIGNATURES OF PLASMA CELL-FREE DNA AS NON-INVASIVE BIOMARKERS OF KIDNEY GRAFT LESIONS

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Background: In the standard monitoring of kidney transplant recipients (KTR), only a histological examination of kidney biopsy enables the evaluation of allograft lesions, with several limitations about safety and welfare. Donor-derived cell-free DNA (dd-cfDNA) has shown clinical relevance in multiple fields, but current dd-cfDNA genotyping does not enable assessment of specific KT compartment. The study aimed to highlight the relevance of dd-cfDNA targeted epigenetic analysis (TEA) for non-invasive diagnosis of kidney transplant injuries.

Methods: We performed retrospective multicentric analysis of N=171 plasma dd-cfDNA from adult KTRs, paired with indication biopsy interpreted according to the Banff 2022 classification. Nine epigenetic biomarkers of distinct kidney cells (glomerular/tubular; epithelial/endothelial) were simultaneously quantified on dd-cfDNA using multiplex digital Polymerase Chain Reaction. Epigenetic biomarkers values were used together to build a generalized linear model for the diagnosis of pathological lesions. Model performance was evaluated with Area Under Curve (AUC) of the Receiver Operating Characteristic (ROC) curve.

Results: Model including the 9 biomarkers accurately discriminates biopsies with any histological lesions (sum of all Banff score>=1) versus pristine biopsies (AUC=0.807). Endothelial biomarkers were associated with vascular lesions (sum of g, v, ptc, Cg, Cv, Ah>=1 ; AUC=0.745), especially acute lesions (sum of g, v, ptc>=1 ; AUC=0.787). Tubulo-interstitial lesions were also detected to a lesser extend (sum of i, t, Ci, Ct>=1 ; AUC=0.704).

Conclusions: Endothelial kidney lesions can be quantified through TEA of plasma dd-cfDNA allowing evaluation of kidney graft lesions, especially endothelial lesions. Epigenetic biomarkers emerge as a potential non-invasive tool to evaluate kidney condition in routine KTRs follow-up, combining sensitivity and speed.

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BOS_14_5 INVESTIGATION OF DD-CFDNA WITHIN THE FIRST YEAR FOLLOWING SINGLE LUNG TRANSPLANTATION: A REGISTRY ANALYSIS

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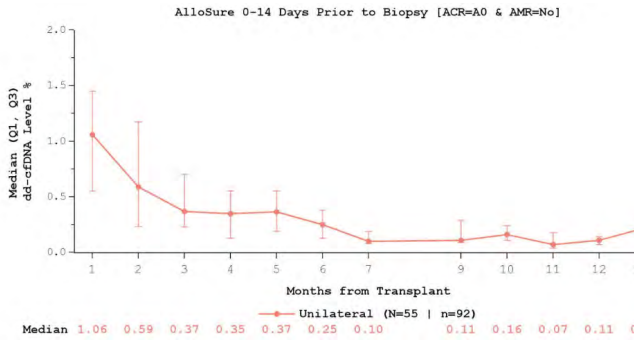
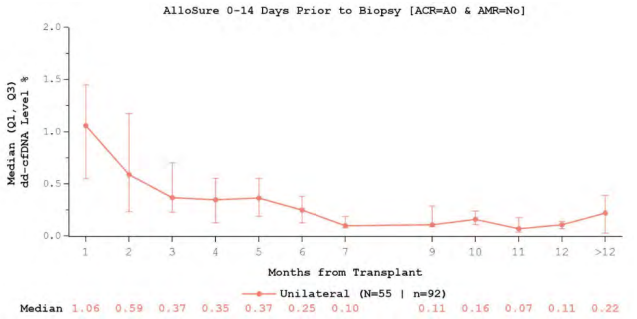
Background: To present the one-year data from the AlloSure Lung Assessment and Metagenomics Outcomes (ALAMO) registry and describe the donor-derived cell-free DNA (dd-cfDNA) in single lung transplant (SLT) recipients (SLTR) with rejection.

Methods: The ALAMO registry was designed as a large, multicenter, prospective registry of lung transplant recipients measuring dd-cfDNA monthly post-transplant for the first year and quarterly thereafter in years 2 and 3. AlloSure (CareDx, Brisbane, CA) dd-cfDNA assay was used. The clinical validity dataset was generated by pairing biopsy with dd-cfDNA that was within 0-14 days prior to biopsy. In the case of multiple dd-cfDNA paired with one biopsy, the closest one was selected for analysis.

Results: Of the 88 SLTR in the ALAMO registry, 60 patients (109 samples) had a paired biopsy with dd-cfDNA. As shown in figure 1, Median dd-cfDNA in SLTRs with A0 and A1 rejection was low at 0.27% and 0.22%, respectively. Patients with A2 rejection on biopsy trended toward higher median dd-cfDNA of 0.87%, although there were few cases of A2 rejection in this cohort. Biopsies characterized as ungradable (Ax) had a median dd-cfDNA of 0.21%. There were no recorded A3 or A4 rejections at the time of capture. As shown in figure 2, dd-cfDNA decayed in months 1 and 2 with baseline levels reached at 3 months in SLTR without AMR or ACR.

Conclusions: This single lung cohort contains a low rate of mild rejection at the time of data capture; however, analyses are ongoing. At present, dd-cfDNA in SLTR without or with minimal biopsy-proven ACR reveal exceptionally low paired dd-cfDNA quantities. In contrast, SLTR with increasing ACR grade demonstrate numerically greater dd-cfDNA quantities. These data demonstrate that SLTR are a unique subset of LTR and require further assessment to delineate interpretation standards for dd-cfDNA.





BOS_14_6 ENHANCING UTILITY OF ANTIBODY TESTING WITH DONOR-DERIVED CELL-FREE DNA POST-HEART TRANSPLANTATION

Indra Bole[1], Mason Mocarski[1], Ayesha Hasan[1], Garrie Haas[1], Rami Kahwash[1], Ajay Vallakati[1], Veronica Franco[1], Vaiibhav Patel[1], Beth Foreman[1], Michael Olymbios[2], Sandra Carey[2], Kathryn Crabtree[2], Madeleine Armer-Cabral[2], Zhiji Zhang[2], Brent Lampert[1]
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Background: Donor-specific antibodies (DSA) are routinely assessed after heart transplant (HT) with sensitive immunoassays. However, not all detected DSAs are associated with adverse events (AE), and conversely, not all episodes of antibody-mediated rejection (AMR) are associated with the presence of DSAs. Donor-derived cell-free DNA (dd-cfDNA) is a noninvasive biomarker of allograft injury. We hypothesize that dd-cfDNA can be used to delineate clinically meaningful DSAs and detect patients at risk for AE in the absence of DSA.

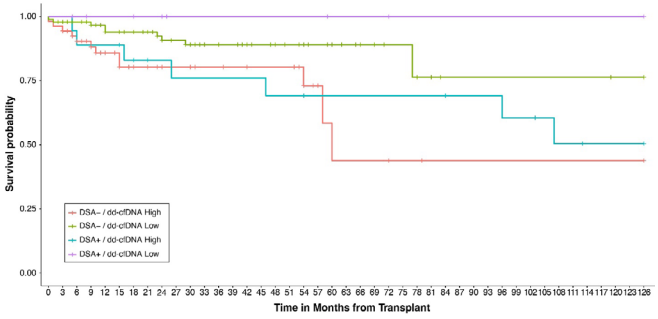
Methods: We conducted a retrospective study of adult HT patients (pts) at Ohio State University, where routine post-transplant monitoring includes both DSA and dd-cfDNA (the Prospera™ test, Natera Inc., Austin, TX). Pts were categorized into four groups based on dd-cfDNA% (positive if ≥0.15%) and DSA status (positive if any DSA ≥2,000 MFI). Kaplan-Meier curves were plotted, for each group, for freedom from all of the following AE: treated rejection, biopsy-proven rejection (ACR ≥2R and/or AMR≥1), graft dysfunction (LVEF ≤ 40), cardiac allograft vasculopathy (ISHLT grade >0), re-transplantation, and death.

Results: 898 paired dd-cfDNA and DSA tests from 170 pts, transplanted from 2006 to 2023, were included in this analysis. Pts were followed for a median of 32 and a maximum of 126 months from transplant. Results are shown in Figure 1. dd-cfDNA%-neg and DSA-neg pts exhibited the greatest freedom from AE, while dd-cfDNA%-pos and DSA-neg pts had the least freedom from AE, followed by pts who were both dd-cfDNA%-pos and DSA-pos.

Conclusions: These data suggest that the presence of DSA alone may not necessarily lead to AE, and dd-cfDNA aids in risk stratification for patients beyond DSA. We also find that dd-cfDNA% rises during AMR episodes without DSA. These preliminary results indicate the potential value of integrating dd-cfDNA into the interpretation of DSA results in clinical care. Further exploration in larger cohorts is warranted.

Outcomes for DSA Positive and DSA Negative Heart Transplant Patients Stratified by High and Low dd-cfDNA Levels

Survival Outcomes	Total (N=28)	DSA− dd-cfDNA Low (N=9)	DSA+ dd-cfDNA High (N=7)	DSA− dd-cfDNA High (N=12)	DSA+ dd-cfDNA Low (N=0)
Adverse Event					
CAV	8 (29%)	4 (44%)	2 (29%)	2 (17%)	***
Biopsy-proven Rejection	7 (25%)	2 (22%)	1 (14%)	4 (33%)	---
LVEF <=40	4 (14%)	2 (22%)	1 (14%)	1 (8.3%)	---
Rejection (requiring treatment)	9 (32%)	1 (11%)	3 (43%)	5 (42%)	---
Total Events (per cohort)	28/170 (16%)	9/90 (10%)	7/18 (39%)	12/53 (23%)	0/0 (0%)



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BOS_14_7 CONCOMITANT ASSESSMENT OF URINARY CHEMOKINES AND DONOR-DERIVED CELL-FREE DNA FOR THE DIAGNOSIS OF KIDNEY REJECTION

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Background: Urinary chemokines and donor-derived cell-free DNA (dd-cfDNA) are non-invasive biomarkers of ongoing kidney allograft rejection. However, back-to-back comparisons of both biomarkers to discern their relative or combined added value remains unexplored.

Methods: From August 2022 to July 2024, urine and blood samples were collected in all consecutive for-cause and surveillance kidney allograft biopsies performed at our center. Biopsies were evaluated following Banff 2022 criteria. Urinary CXCL9, CXCL10, CCL2 and VEGF-A levels were quantified using the ProteinSimple™ platform and normalized to urinary creatinine as log2-transformed values. Dd-cfDNA was measured using the AlloSeq™ cfDNA kit and expressed as a percentage values.

Results: Of 216 patients recruited, 195 provided adequate samples for both biomarkers and biopsy evaluation. For-cause biopsies (n=102) included active ABMR (n=19), borderline changes (n=11), TCMR (n=8), chronic aABMR (n=11), microvascular inflammation (n=3), recurrent primary disease (n=10), and PVAN (n=3). Surveillance biopsies (n=93) included aABMR (n=11), borderline changes (n=3), TCMR (n=2), chronic aABMR (n=3), recurrence (n=1), and PVAN (n=1). Overall, the combination of serum creatinine (SCr), DSA and dd-cfDNA showed the highest diagnostic accuracy for any type of rejection (AUC 0.87). Adding CXCL9 or CXCL10 to SCr and DSA did also show high performance (AUCs 0.80 for both). These differences were fundamentally driven by the higher diagnostic accuracy of dd-cfDNA for subclinical rejection (AUC 0.89). Conversely, in for-cause biopsies, combining SCr, DSA and either dd-cfDNA or CXCL10 showed similarly high performance predicting on-going rejection (Table).

Conclusions: In for-cause biopsies, both urinary CXCL10 chemokine and dd-cfDNA similarly enhance diagnostic prediction when added to clinical scores. However, for subclinical rejection in surveillance biopsies, dd-cfDNA showed superior predictive value than urinary chemokines.

Predictive variable	Overall cohort (n=195) AUC (95% CI)	Biopsies for cause (n=102) AUC (95% CI)	Protocol biopsies (n=93) AUC (95% CI)
SCr	0.64 (0.56-0.72)	0.61 (0.50-0.72)	0.55 (0.41-0.69)
DSA	0.69 (0.64-0.75)	0.72 (0.65-0.80)	0.63 (0.53-0.72)
ddcf-DNA	0.83 (0.78-0.90)	0.80 (0.72-0.89)	0.87 (0.79-0.96)
$[CXCL9/Cr]_U$	0.67 (0.59-0.75)	0.74 (0.64-0.83)	0.53 (0.40-0.66)
$[CXCL10/Cr]_U$	0.67 (0.59-0.75)	0.75 (0.65-0.85)	0.53 (0.40-0.67)
$[CCL2/Cr]_U$	0.60 (0.52-0.68)	0.62 (0.51-0.73)	0.51 (0.38-0.65)
SCr + DSA	0.78 (0.71-0.85)*	0.80 (0.71-0.89)*	0.67 (0.53-0.81)
SCr + DSA + ddcf-DNA	0.87 (0.82-0.92)**	0.85 (0.77-0.93)**	0.89 (0.82-0.95)***
SCr + DSA+ $[CXCL9/Cr]_U$	0.80 (0.74-0.87)	0.85 (0.78-0.83)**	0.67 (0.54-0.79)
SCr + DSA + $[CXCL10/Cr]_U$	0.80 (0.73-0.87)	0.86 (0.79-0.93)**	0.67 (0.53-0.79)

*p<0.05 vs. DSA; **p<0.001 vs. SCr + DSA; ***p=0.05 vs. SCr + DSA

BOS_14_8 VALIDATION OF A PREDICTIVE MODEL FOR ALLOGRAFT REJECTION INTEGRATING DD-CFDNA IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Background: Allograft biopsy remains the gold standard to diagnose rejection. New non-invasive biomarkers are needed to avoid unnecessary biopsies and to diagnose early rejection. This study aimed at validating the performance of a predictive model for allograft rejection including dd-cfDNA in an unselected cohort of pediatric kidney transplant recipients (pKTRs) and to test whether dd-cfDNA improved prediction beyond standard-of-care monitoring in children.

Methods: We included 196 pKTRs, who underwent 367 biopsies with concomitant dd-cfDNA assessment. The primary outcome was acute rejection including borderline cases. We assessed the discrimination of dd-cfDNA alone and compared the discrimination (AUC) of two models previously developed in adult KTx using either standard-of-care (clinical data, eGFR, UPCR, DSA) alone or combined with dd-cfDNA.

Results: dd-cfDNA was strongly and independently associated with the presence of allograft rejection (OR 1.89, 95% CI [1.40; 2.60]) and had a fair discrimination of 0.76, 95% CI [0.69; 0.81] to detect rejection. The prediction model using standard-of-care parameters had a good discrimination for allograft rejection with a ROC AUC of 0.80, 95% CI [0.71; 0.85]. The addition of dd-cfDNA significantly improved the discrimination to 0.84, CI 95% [0.79; 0.90], p=0.01 (Figure 1).

Conclusions: Our model, recently developed in adults, showed good discrimination to predict rejection in children. Although, the model based on standard-of-care had a better discrimination in children than in adults, dd-cfDNA still significantly improved prediction above standard-of-care. A prospective randomized controlled trial is underway to demonstrate the benefit and safety of using this model to avoid unnecessary biopsies in children.

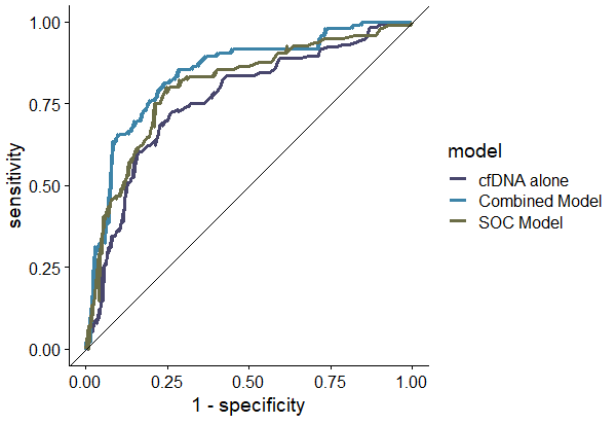

Figure 1: Discrimination of dd-cfDNA, standard-of-care (SOC) and combined model of SOC and dd-cfDNA for the diagnosis of biopsy-proven allograft rejection.

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BOS_14_9 DONOR-DERIVED CELL-FREE MITOCHONDRIAL DNA IN LUNG TRANSPLANATION, ITS RELATIONSHIP WITH PRIMARY GRAFT DYSFUNCTIONS

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Background: Donor-derived cell-free DNA (dd-cfDNA) is a key biomarker for allograft rejection or infection, in lung transplantation. Cell-free DNA consists of nuclear DNA (cfnDNA) and mitochondrial DNA (cf-mtDNA), with mtDNA being highly efficient at inducing damage-associated molecular patterns (DAMPs). However, the detectability and role of dd-cf-mtDNA in lung transplant recipients remain unclear. This study introduces a novel technique for dd-cf-mtDNA detection, analyzes its post-transplant evolution, and correlates it with donor type and primary graft dysfunction (PGD) incidence.

Methods: This prospective, multicenter study included recipients from 40 brain-dead (DBD) and 39 cardiac-dead (cDCD) donors across four Spanish transplant centers. Blood samples were collected from donors pre- (E0) and post-retrieval (E1), and from recipients pre-implantation (R-1), post-reperfusion (R0), and 72 hours post-transplant (R72). Serum cf-mtDNA levels were quantified using real-time qPCR, while donor and recipient mtDNA percentages were determined by deep sequencing of mtDNA hypervariable regions. %dd-cf-mtDNA was calculated at R0 and R72, and its association with PGD was analyzed.

Results: Median cf-mtDNA levels remained stable (R0: 11593.75 [IQR 33958.84], R72: 11218.75 [IQR 41617.19]). Conversely, %dd-cf-mtDNA levels declined from R0 (5 [IQR 1.2]) to R72 (0.8 [IQR 1.2]). The recipients with PGD showed and increased %dd-cfmtDNA showing a towards tendence to statistically significance (5.8 vs 3.8, p=0.10). (Table 1)

Conclusions: %dd-cf-mtDNA can be reliably detected post-lung transplantation and behaves differently from cf-mtDNA. While cf-mtDNA remains stable, %dd-cf-mtDNA decreases within three days. Elevated dd-cf-mtDNA levels may serve as a specific biomarker for graft damage and PGD, highlighting its potential for monitoring transplant outcomes.

		%dd-cf-mtDNA R0	% dd-cf-mtDNA DNA R72
Donor			
	DBD	5.2(2.8, 14.1)	0.7(0.3, 1.5)
	cDCD	5.0(1.7, 10.4)	1.0(0.5, 1.0)
p		0.484	0.709
PGD			
	DBD	3.8(1.9, 8.9)	1.0(0.5, 2.0)
	cDCD	5.8(2.6, 13.3)	0.8(0.3, 1.4)
p		0.184	0.431
PGDIII			
	DBD	5.0(2.0, 11.3)	0.8(0.3, 1.9)
	cDCD	5.1(2.8, 10.5)	0.9(0.6, 1.1)
p		0.982	0.988

*Median (Q1, Q3)

Table 1.: %dd-cf-mtDNA

BOS_14_10 ISLET BETA CELL CELL-FREE DNA AND TRYPSINOGEN FOR DIAGNOSIS OF REJECTION IN PANCREAS TRANSPLANTATION; THE EMPAR STUDY

Nikos Tteralli[1], Georgina Mortimer[2], Laszlo Szabo[3], Kathleen Gillespie[2], Chantal Colmont[4], Ioannis Karniadakis[5], Aida Martinez Sanchez[6], Colin Dayan[7], Argiris Asderakis[5]

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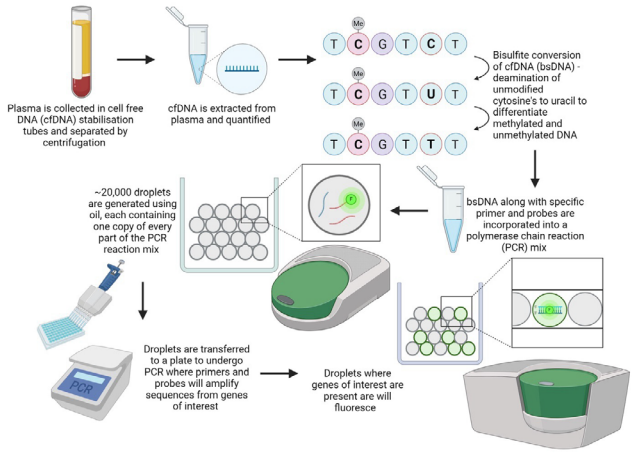
Background: Pancreas transplant rejection diagnosis remains difficult. In SPK often relies on the diagnosis of kidney rejection or the rise of amylase/lipase to prompt a biopsy. 20-30% of cases show discordance between the kidney and pancreas rejection whilst amylase exhibits a transient rise that is not sensitive enough.

Methods: EMPAR is the first prospective study examining the role of a combination of novel biomarkers for pancreas rejection including islet beta cell specific cell free DNA (b-cfDNA), trypsinogen, and micro RNAs. 10 patients with new SPK transplant and 9 admitted with pancreas dysfunction or any infection have been recruited so far. New transplants were sampled pretransplant, post perfusion, at discharge, and monthly thereafter whereas admitted patients on admission, treatment (if they had a biopsy confirmed rejection) and monthly after discharge. Results in admitted patients were associated with the presence of biopsy proven rejection or an alternative diagnosis. Unmethylated b-cfDNA is identified in copies per ml (cp/ml) by droplet digital PCR.

Results: We present the preliminary results for b-cfDNA and trypsinogen in these patients. The baseline pre-perfusion median trypsinogen level was 109 ng/ml (66-223) and raised to 450 post-perfusion; at 3 months post-transplant was 41 (18-88). In the 7 patients with rejection trypsinogen was 122 (11-320) which was increased compared to 3 months post-transplant in stable patients but with some overlapping values. The baseline median pre-perfusion b-cfDNA was 79 cp/ml, and 223 cp/ml post-perfusion; at 2 months post-transplant was 115 cp/ml. In 7 patients with rejection b-cfDNA raised to median of 318 (172-1044) cp/ml on the admission pre-biopsy day and was 126 cp/ml following rejection treatment. This compared to 55 cp/ml in admitted patients without rejection and 115 cp/ml seen in patients 2 months post-transplant. Given the small number of admitted non rejectors no formal statistical testing is presented.

Conclusions: EMPAR is the first human study investigating the role of beta cell specific cfDNA as a marker of acute pancreas rejection. Preliminary results show that it is a promising marker of rejection (both sensitive and specific). The role of trypsinogen requires further analysis.



Trypsinogen was measured with an adapted Delfia Neonatal IRT kit

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BOS_14_11 MAPPING CELL-FREE DNA TISSUE OF ORIGIN IN TRANSPLANT RECIPIENTS THROUGH METHYLATION SIGNATURES

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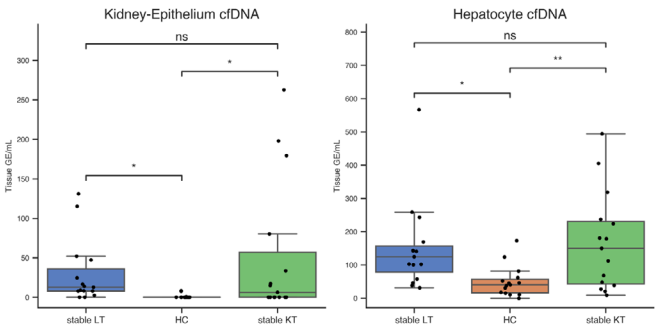
Background: Donor-derived cell-free DNA (dd-cfDNA) is a valuable biomarker for solid organ transplant monitoring but has some limitations. Tissue-specific DNA methylation offers an alternative approach to identify cfDNA tissue of origin without relying on donor-recipient genotype differences. Here, we present a targeted sequencing assay to determine cfDNA tissue of origin and dd-cfDNA proportion, addressing limitations in transplant monitoring and advancing patient care.

Methods: Utilizing a comprehensive methylation atlas of 40 human cell types, we developed a targeted hybridization capture panel for deep methylation sequencing of cfDNA. cfDNA was extracted from plasma of kidney (KT) and liver recipients (LT), as well as healthy controls (HC), and subjected to targeted deep methylation sequencing to determine the tissue of origin in genome equivalents/mL (GE/mL).

Results: Genomic DNA analysis showed >93% accuracy for kidney epithelium, hepatocytes, and blood cells with detection sensitivity as low as 0.3%. Mean cfDNA from kidney epithelium was higher in stable liver (n=15: 30 GE/mL) and kidney (n=15: 53 GE/mL) recipients compared to healthy controls (n=15: 1.2 GE/mL, Figure). Hepatocyte cfDNA was similarly elevated (LT: 151; KT: 167; HC: 50 GE/mL). There was no significant difference between transplant groups for both tissues. KT exhibited increased megakaryocyte cfDNA (1280 GE/mL) compared to LT (518 GE/mL) or HC (583 GE/mL). Within 24 hours post-transplantation, only a minority (median: 5%, interquartile range (IQR): 0-12%) of dd-cfDNA in KT (n=13) originated from the kidney epithelium, while a median of 82% (IQR: 60-96%) originated from hepatocytes in LT (n=6). The remaining dd-cfDNA in KT was predominantly of hematological and endothelial in origin.

Conclusions: We developed a targeted deep methylation sequencing workflow that allows accurate tissue of origin deconvolution of cfDNA from a single standard blood collection tube. This enables precise monitoring of organ-specific injury in transplantation, potentially improving the management of transplant recipients, as indicated by distinct tissue damage profiles associated with each transplant type shortly after transplantation and differences between stable recipients and healthy individuals.



BOS_14_12 LONGITUDINAL DD-CFDNA TRENDS AND CLINICAL OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

Suphamai Bunnapradist[1], Jonathan Bromberg[2], Anthony Langone[3], Tarek Alhamad[4], Yen-An Chen[5], Navchetan Kaur[6], D. Giovanni Biagini[5], Sangeeta Bhorade[7], Adam Prewett[6], Zachary Demko[8], Hossein Tabriziani[9], Philippe Gauthier[10], Matthew Cooper[11]

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Background: Donor-derived cell free DNA (dd-cfDNA) is a biomarker of allograft injury and rejection used to monitor transplant (Tx) patients. It is hypothesized that persistently low dd-cfDNA predicts future clinical stability, while elevated dd-cfDNA in the absence of rejection indicates immunological insult or impending rejection. Here, we assessed associations between longitudinal dd-cfDNA trends, pre-Tx risk, and outcomes in kidney-Tx patients with no rejection in the monitoring period.

Methods: Kidney Tx patients from an early analysis of the ProActive study (NCT04091984) that had no rejection within 18 months of Tx and ≥3 dd-cfDNA tests (the Prospera™ test, Natera, Inc) performed 3-18 months post-Tx, were included. Patients were categorized based on pre-Tx risk-status, and based on longitudinal dd-cfDNA trends. Patient outcomes were assessed through 24 months post-Tx. Associations between pre-Tx risk, dd-cfDNA trends, and outcomes were analyzed.

Results: 370 patients with 2040 total dd-cfDNA tests were analyzed. Associations between pre-Tx risk, dd-cfDNA trends, and outcomes are shown below (**figure**). The majority of patients (61.6%; 228/370) had dd-cfDNA levels consistently below 0.3%. dd-cfDNA levels consistently below 0.3% was associated with unremarkable pre-Tx risk status (p=0.025) and a low incidence of adverse events, while elevated dd-cfDNA (highest dd-cfDNA result >0.5%) was associated with a high incidence of adverse outcomes, (p <0.0001). 35.9% of patients with a highest dd-cfDNA result >0.5% and ≤0.99% had an adverse outcome, compared to 77.8% and 93.3% of patients with 1 and 2+ dd-cfDNA results ≥1%, respectively (**table**).

Conclusions: These findings suggest that dd-cfDNA trends may allow stratification of patients by risk. Notably, dd-cfDNA levels consistently below 0.3% may be an indication of future clinical stability. Furthermore, the likelihood of adverse events increased with additional elevations in dd-cfDNA.

Figure1: Sankey diagram depicting the flow of patients (N=370) from different pre-Transplant risk categorizations (left nodes) to groups of dd-cfDNA trends over the course of the observation period (middle nodes) and groups of clinical outcomes (right nodes). High KDPI and High CPRA are defined as >75. dd-cfDNA ≥1% indicates high risk of ongoing rejection. Adverse outcomes are considered the occurrence of any of the following: recurrent disease, future rejection, death censored graft loss, kidney related hospitalization, and/or *de novo* DSA. Moderate concerns include non-rejection histology, allograft dysfunction, post-Tx dialysis, CNI toxicity, and infection complications.

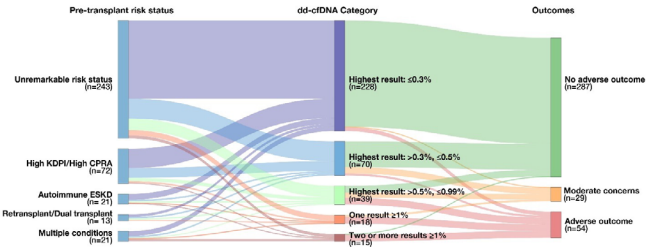

TABLE:
Table shows counts of patients in different dd-cfDNA categories and outcomes. Adverse outcomes are defined as the occurrence of any of the following: recurrent disease, future rejection, death-censored graft loss, de novo DSA, and kidney-related hospitalization. Moderate concerns include non-rejection histology, borderline changes, acute allograft dysfunction, post-Tx dialysis, calcineurin toxicity, HSV/CoViD infection complications.

dd-cfDNA status	No adverse outcomes	Moderate concerns	Adverse outcomes
Highest result ≤0.3%	96.1% (219/228)	0.4% (1/228)	3.5% (8/228)
Highest result >0.3% and ≤0.5%	75.7% (53/70)	18.6% (13/70)	5.7% (4/70)
Highest result >0.5% and ≤0.99%	35.9% (14/39)	28.2% (11/39)	35.9% (14/39)
One result ≥1.0%	0% (0/18)	22.2% (4/18)	77.8% (14/18)
Two or more results ≥1.0%	6.7% (1/15)	0% (0/15)	93.3% (14/15)

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BOS_14_13 CORRELATIONS OF DD-CFDNA WITH HISTOLOGY AND MOLECULAR ABMR ACTIVITY AFTER IMLIFIDASE DESENSITIZATION

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Background: Imlifidase desensitization enables HLA incompatible (HLAi) kidney transplantation in highly sensitized patients. However, frequent for cause and follow-up biopsies are a substantial burden both for patients and health-care providers. Biopsy-based transcriptomics and non-invasive rejection monitoring using dd-cfDNA improve diagnostics and reduce biopsy burden.

Methods: This is a retrospective, observational study aiming at evaluating correlation between dd-cfDNA levels, histology and molecular diagnostics using the validated MMDx platform in a local laboratory in 7 patients who had undergone HLAi kidney transplantation using imlifidase. Dd-cfDNA levels were determined using Prospera test around the time of biopsies performed late in the follow-up. Ten samples were analyzed in total. Correlations were evaluated by Spearman's correlation coefficient (r). Banff-based activity index was defined as sum of t+i+g+ptc+v+2xC4d, while chronicity index was 2xcg+ci+ct+cv.

Results: The median time from transplantation to dd-cfDNA measurement was 202 days (IQR 85, 370), and 1 day (IQR –40, 44) between measurement and biopsy. There were good correlations between dd-cfDNA levels and molecular rejection (r = 0,77), ABMR (r = 0,51), g (r = 0,56) and PTC scores (r = 0,47) determined by MMDx. Similarly, there was correlation for Banff-based activity index (r = 0,45), MVI (r = 0,46), and glomerulitis (r = 0,43) determined by histology. No correlations were found for Banff-based chronicity index (r = 0,18), IF/TA (r = 0), or molecular fibrosis scores (r = -0,07).

Conclusions: Dd-cfDNA levels correlate well with markers of ABMR activity, but not chronicity, both in histology and biopsy-based transcriptomics in HLAi transplantation after imlifidase desensitization. Therefore, dd-cfDNA monitoring may replace late follow-up biopsies even in this specific, high-risk population.

BOS_14_14 MONITORING OF DD-CFDNA AND MIRNA FOR EARLY DETECTION OF GRAFT DYSFUNCTION IN ADULT LIVER TRANSPLANT RECIPIENTS

Judit Julián[1], Olga Millán[2], Pablo Ruiz[3], Esther Titos[4], Alba Díaz[5], Yiliam Fundora Suárez[6], Jordi Colmenero[7], Constantino Fondevila[4], Joan Anton Puig[4], Mercè Brunet[8]

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Background: The diagnosis of graft dysfunction (GD) remains a challenge in liver transplantation (LT), necessitating the identification of reliable non-invasive biomarkers. Donor-derived cell-free DNA (dd-cfDNA) has emerged as a promising biomarker for this purpose. Additionally, microRNAs (miRNA), particularly miR-155, miR-181, and miR-122, have been identified as potential biomarkers for GD by our group. This study aims to evaluate the combination of both biomarkers

Methods: Prospective, observational study conducted in a cohort of 70 patients followed during the 1st year after LT. Liver function tests, pharmacokinetic monitoring, miRNA and dd-cfDNA analysis were performed on predetermined time points. dd-cfDNA was quantified by multiplex PCR and miRNAs by qPCR

Results: A total of 437 patient samples were analyzed for miRNA signature and dd-cfDNA levels. During follow-up, 46 episodes of GD were identified, with biopsies confirming 14 acute rejection (8 moderate, 6 mild). Other diagnoses included 15 cases of cholestasis, 9 active CMV infections (>1000 cp), 5 ischemia-reperfusion injuries (IRI), and 3 non-specific inflammatory responses. Clinical characteristics did not differ significantly across groups. dd-cfDNA levels exhibited a decreasing trend after IRI, with significant differences observed between stable patients and those at risk for rejection after the 2nd week, demonstrating higher dd-cfDNA levels ($p<0.01$) in the second group. The optimal dd-cfDNA cut-off for diagnosing rejection was 9.88%, with a sensitivity of 1, specificity of 0.67, positive predictive value of 17.5%, negative predictive value of 100%, and an area under the receiver operating characteristic curve (AUROC) of 0.812 (95% CI 0.757-0.868). Notably, cholestasis patients also exhibited a significant increase dd-cfDNA levels, suggesting its potential role in diagnosing this condition. In this cohort, we confirmed the predictive and diagnostic capacity of the miRNA signature previously studied by our group.

Conclusions: The combination of dd-cfDNA and miRNA offers a promising approach for diagnosing GD in LT. miRNAs are effective in detecting rejection early, particularly within the first weeks post-transplant, while dd-cfDNA becomes more useful for ongoing monitoring and late rejection or cholestasis detection

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Updates on cell-free DNA, cross-organ

BOS_14_15 PREDICTIVE VALUE OF ABSOLUTE LEVELS OF DONOR-DERIVED CELL-FREE DNA IN EARLY DETECTION OF LUNG ALLOGRAFT DYSFUNCTION

Majd Alkhouri[1], Jan Havlin[2], Andrea Zajacova[3], Alzbeta Dutkova[4], Jan Balko[4], Dmitry Rakita[4], Libor Fila[5], Robert Lischke[6], Tereza Kotowski[4], Kristyna Vyskocilova[4]

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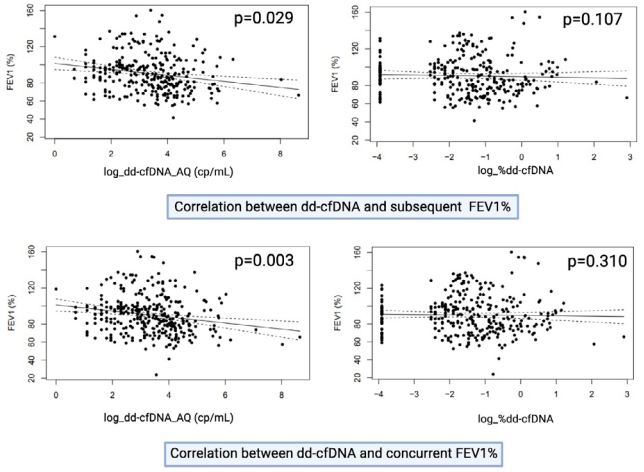
Background: Monitoring donor-derived cell-free DNA (dd-cfDNA) in peripheral blood is a promising non-invasive method for assessing lung allograft health after transplantation. However, fluctuations in the total amount of circulating cell-free DNA may affect the measured plasma dd-cfDNA fraction. This study aimed to investigate the association between both the fractional (%dd-cfDNA) and absolute quantities of dd-cfDNA (dd-cfDNA_AQ) and lung allograft function

Methods: Patients who underwent bilateral lung transplantation (LuTx) between May 2022 and September 2023 with follow-up at our center were considered for inclusion. Samples for dd-cfDNA analyses were prospectively collected between the 3rd and 24th month post-transplant. Associations between estimated %dd-cfDNA, dd-cfDNA_AQ, and pulmonary function tests (FEV1% and FVC% predicted) were assessed (1) at the same time point and (2) between prior dd-cfDNA levels and subsequent lung function to evaluate the predictive value of dd-cfDNA. Linear mixed-effects models were used for statistical analysis.

Results: A total of 414 samples from 41 lung transplant (LuTx) recipients were included (mean 9.7 samples per patient). A significant negative association was observed between concurrently measured dd-cfDNA_AQ and FEV1% (p = 0.003), while %dd-cfDNA showed non-significant association (p = 0.310). Prior dd-cfDNA_AQ levels were significantly associated with a subsequent FEV1% decline (p = 0.029), suggesting predictive potential, whereas %dd-cfDNA remained non-significant (p = 0.107). No significant association was found between dd-cfDNA levels and FVC% at either concurrent or prior measurements. The mean interval between measurements was 1.8 months (SD ± 1.1 months).

Conclusions: An increase in absolute dd-cfDNA levels, in contrast to the dd-cfDNA fraction, was significantly associated with a decline in pulmonary function, suggesting that the absolute quantity of dd-cfDNA may be more reliable biomarker for early detection of lung allograft dysfunction and timely clinical intervention. Further investigation is required.

Figure: Association of donor-derived cell-free DNA(dd-cfDNA) and FEV1% from concurrent and preceding measurements



FEV1%: forced expiratory volume in one second (percent predicted),% dd-cfDNA: fraction of donor-derived cell-free DNA, dd-cfDNA_AQ: absolute quantity of donor-derived cell-free DNA

Challenges and innovations in transplant survival

BOS_15_1 HLA EPLET MATCHING AS A PROGNOSTIC BIOMARKER OF KIDNEY TRANSPLANT OUTCOMES

Marc Raynaud[1], Zeynep Demir[2], Kevin Louis[3], Agathe Truchot[4], Solaf Alawadhi[5], Renata Ponsirenas[6], Roslyn Mannon[7], Anat Tambur[8], Carmen Lefaucheur[9], Alexandre Loupy[10]

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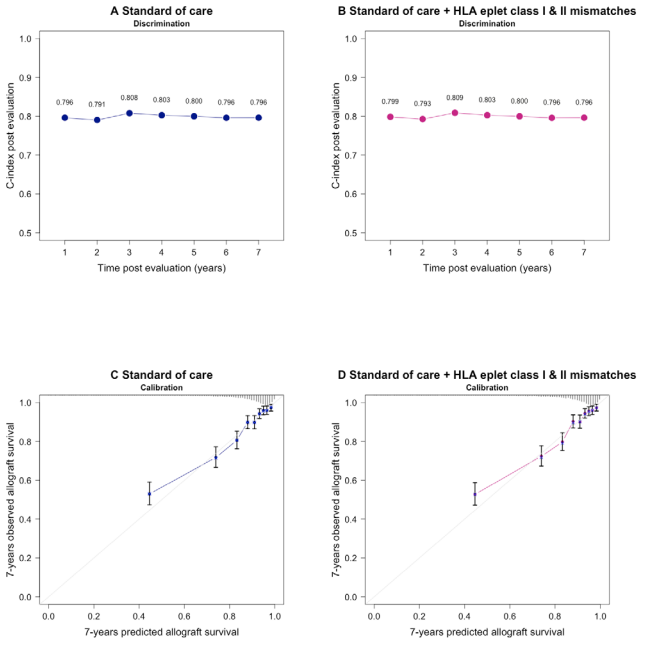
Background: HLA eplet matching has emerged as a potential biomarker for optimising organ allocation and improving patient management. However, its clinical relevance in terms of prognostic value is not demonstrated. We aimed to investigate the association between HLA eplet mismatches and long-term allograft failure, and its additional value beyond standard of care parameters.

Methods: The Paris Transplant Group qualified cohort (NCT03474003) consisted of 3,612 deeply phenotyped adult patients, prospectively enrolled at the time of transplantation in four french centers. The HLA eplet class I and II mismatch scores were calculated through high-resolution HLA typing, which encompasses the identification of specific configurations of epitopes (eplets) on both donor and recipient HLA molecules (HLAMatchmaker). Clinical, functional, histological and immunological parameters were collected for each patient. The iBox prediction system was used to evaluate the ability of HLA eplet mismatches to predict the long-term allograft survival beyond standard of care parameters.

Results: The median follow-up post transplantation was 8.8 years (IQR 6.0-11.9), with 510 (14.1%) allograft failures occuring during the follow-up. The median number of HLA eplet class I and II mismatches were respectively 16 (IQR 10-21) and 11 (IQR 5-17). When stratifying the population according to the quartiles of the HLA eplet class I and II mismatches, no differences were observed in terms of long-term allograft failure (log-rank test for class I and II mismatches: p=0.365 and 0.920 respectively). The HLA eplet class I and II mismatches were not independently associated with long term allograft failure, with HR=1.00 (CI 0.99-1.01, p=0.856) and HR=1.00 (CI 0.99-1.01, p=0.863), respectively. Last, addition of HLA eplet class I and II mismatches to a standard of care (iBox) model did not increase its performance (c=statistics 0.796 vs 0.796 for the standard of care iBox model respectively. Similarly, the addition of HLA eplet mismatches to the standard of care iBox model did not improve the model's calibration.

Conclusions: Our study shows in a large, deeply phenotyped population of kidney recipients, that HLA eplet matching does not add value to standard of care parameter for prognostication of long-term allograft outcome.



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Challenges and innovations in transplant survival

BOS_15_2 IMPACT OF ISLETS TRANSPLANTATION ON DIABETIC COMPLICATIONS / MORTALITY IN TYPE 1 DIABETES RECIPIENTS

Quentin Perrier[1], Clément Jambon-Barbara[2], Laurence Kessler[3], Orianne Villard[4], Fanny Burron[5], Bruno Guerci[6], Sophie Borot[7], Matthieu Roustit[8], Ekaterine Berishvilli[9], Luc Rakotoarisoa[3], Marie-Christine Vantyghem[10], Emmanuel Morelon[5], Eric Renard[4], Camille Besch[3], Thierry Berney[5], Pierre-Yves Benhamou[11], Sandrine Lablanche[11]

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Background: Islet transplantation (IT) emerges as a promising intervention for the treatment of patients with unstable type 1 diabetes (T1D). If IT metabolic outcomes are well described, evidence is lacking regarding its impact on long-term diabetic complications and long-term safety. The objective was to evaluate the impact of IT on diabetic complications and cancer incidence.

Methods: This was a retrospective, multicentre, cohort study including patients from GRAGIL/TRIMECO trials (intervention group) and from the French Healthcare database (SNDS) (synthetic control group). Two distinct cohorts of IT recipients were analysed: IT after kidney transplantation (IAK) and IT alone (ITA). They were matched with T1D patients from the SNDS using a propensity score as 1:1 for IAK and 1:10 for ITA. The primary outcome was a composite criterion including death, dialysis, amputation, non-fatal stroke, non-fatal myocardial infarction and transient ischemic attack. Secondary outcome was cancer. Hazard Ratio (HR) and p-values were obtained with Cox proportional hazards analysis and log-rank test respectively.

Results: The study included 61 ITA matched to 610 T1D controls and 45 IAK matched to 45 T1D controls, over a median follow-up period of more than 10 years. Compared with T1D control subjects, ITA and IAK recipients had a significantly lower composite outcome risk (HR, 0.39 [95% CI, 0.21-0.71]; p=0.002 and HR, 0.52 [0.30-0.88]; p=0.014 respectively), seem driven by reduced mortality (HR, 0.22 [0.09-0.54], p<0.001) for ITA and reduced dialysis (HR, 0.19 [0.07-0.50], p<0.001) for IAK. Both groups showed no significant changes in cancer risk.

Conclusions: This study suggests long-term benefits of IT on diabetes-related outcomes. Furthermore, despite the use of immunosuppressive drugs following IT, we observed no significant increase in the risk of cancer. Altogether, these findings highlight a favourable risk-benefit ratio of IT in managing patients with unstable T1D.

BOS_15_3 A NOVEL MEASUREMENT FOR PARENCHYMAL STIFFNESS OF RENAL ALLOGRAFT IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background: The evaluation of allograft fibrosis status is very important for kidney transplant management with the increase in the number of long-term post-transplant and/or elderly donor kidney cases. Transplant kidney biopsy has been cited as a method for evaluating interstitial fibrosis and tubular atrophy (IF/TA) of renal allograft, but it is very invasive and has shortcomings in terms of sequency and quantitation. Transient elastography (TE) is a device that mainly measures cirrhosis by transmitting shear waves of a certain frequency from the body surface under ultrasound. Originally, it was thought that it cannot be measured in organs deep from the body surface such as auto-kidneys, but it is thought that it can be measured in transplanted kidney located at iliac fossa.

Methods: A total of 495 recipients underwent living-donor kidney transplantation at our institution between 2001 and 2023, were included in this study. All of them were performed TE (FibroScan®expert630, Echosense Paris, France), TE measured parenchymal stiffness in a volume that approximated a cylinder of 10mm in width and 25-55mm in length by spleen stiffness measurement mode (Figure). The allograft kidney function, IT/TA by biopsy result, were compared and analyzed.

Results: The measurement of parenchymal stiffness was successful in 478 of 495 patients (96.6%). For TE result, median stiffness of renal allograft parenchyma was 49.4 kPa. For the correlation with fibro scan median values, recipients' serum creatinine level, eGFR, and IFTA showed statistically significant difference (p <0.01, in each). Further, when divided to 2groups (eGFR >40 and ≤40), allograft kidney age, renal allograft parenchyma, and recipients' hemoglobin level showed significant difference (p <0.01).

Conclusions: Renal function deterioration and IF/TA progression showed strong correlation with renal allograft parenchyma. For assessment of parenchymal stiffness of allograft, TE will be a very useful measurement.

	Spearman's rank correlation coefficient(ρ)	P value
eGFR	0.22	<.01
serum creatinine (mg/dL)	-0.26	<.01
hemoglobin (g/dL)	0.16	.07
age at kidney transplantation (years)	0.08	.45
years elapsed after transplantation (years)	-0.26	.03
IF/TA (%)	-0.38	<.01

Table 1. Correlation with renal allograft parenchyma

	eGFR>40 (N=252)	eGFR≦40 (N=226)	p
allograft kidney age (years)	62.4 ± 8.7	68.3 ± 11.5	<.01
recipient age (years)	55.2 ± 12.7	56.3 ± 9.4	.78
renal allograft parenchyma (kPa)	55.8 (32.7, 92.2)	44.7 (22.9, 56.8)	<.01
hemoglobin (g/dL)	13.4 (12.6, 14.1)	12.6 (11.9, 13.4)	<.01

Table 2. Confounding factors in assessment

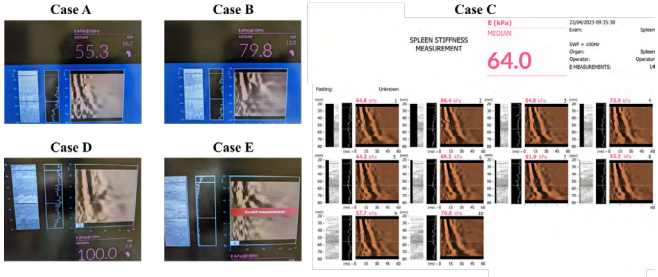

Figure. Measurement Examples.

Case A-C: Parenchymal stiffness of renal allograft was quantified. Case D: hard parenchyma case (> 100kPa), and Case E: Invalid measurement case (insufficient distance).

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Challenges and innovations in transplant survival

BOS_15_4 IMMUNOSUPPRESSION AFTER ALLOGRAFT FAILURE: IMPACT ON RETRANSPLANTATION, SENSITIZATION AND SURVIVAL

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Background: Managing immunosuppression (IS) after kidney transplant (KT) failure is a challenging situation. Their continuation may be protective against sensitization for patients awaiting a subsequent transplant but should be balanced with risks of infections and neoplasia.

Methods: We retrospectively enrolled all first KT recipients who presented allograft failure between 2010 and 2020 and were listed for a second kidney transplantation in our French center. Immunosuppressive drugs exposition data were collected. Anti HLA immunization was assessed at graft lost and during follow-up by Luminex Solid-Phase Assay. Main outcomes were re-transplantation and patient death, assessed until end of 2022.

Results: 660 KT recipients presented allograft loss, of which 223 patients were included in the final analysis. They were followed for a median time of 5.90 years (interquartile range [IQR], 3.52-9.01) after graft loss. They were mainly men (61.88%), with a mean age of 54.71 years. The main causes of graft loss were rejection/allograft glomerulopathy (28.25%), chronic fibrotic lesions (23.32%), or unknown (23.56%), and median time to graft loss was 8.40 (IQR, 3.61-15.03) years. At the time of graft loss, mean calculated Panel Reactive Antibody (cPRA) was 24.44 ± 32.69. IS, except for steroids as the sole agent, was maintained for a mean time of 8.04 ± 8.19 months. IS was maintained at 6 (M6) and 12 months for 43.94% and 16.57% of them, being at M6 mainly calcineurin inhibitors (74.71%), used alone (58.43%). Being exposed to IS at M6 was associated with a higher probability of retransplantation (log-rank p = 0.04, Fig 1A) compared to patients in whom IS was stopped before M6. At M6, mean cPRA was higher in patients who stopped IS versus those who maintained (61.73 ± 41.03 vs 39.28 ± 41.71, p < 0.01) and versus baseline (22.65 ± 33.70, p < 0.01) (Fig 1B). However, we observed a higher risk of death (censored at re-transplantation) during follow-up in patients who were maintained on IS at M6 (log-rank p = 0.025, Fig 1C). Analysis of IS exposition as a time-dependent variable are ongoing.

Conclusions: Maintenance of IS therapy during 6 months after graft failure appears to prevent sensitization and favor re-transplantation. Stratification of patient individual risk-benefit should be further studied.

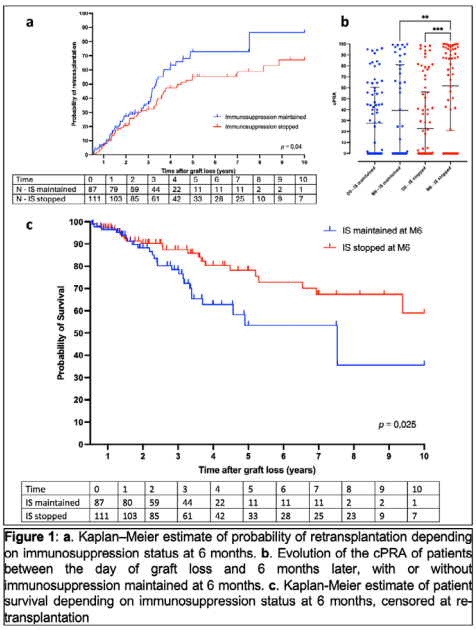

Figure 1: **a.** Kaplan–Meier estimate of probability of retransplantation depending on immunosuppression status at 6 months. **b.** Evolution of the cPRA of patients between the day of graft loss and 6 months later, with or without immunosuppression maintained at 6 months. **c.** Kaplan-Meier estimate of patient survival depending on immunosuppression status at 6 months, censored at re-transplantation

BOS_15_5 OUTCOMES FOLLOWING LIVER TRANSPLANTATION IN OBESE RECIPIENTS IN THE UK - A STUDY OVER FOUR DECADES

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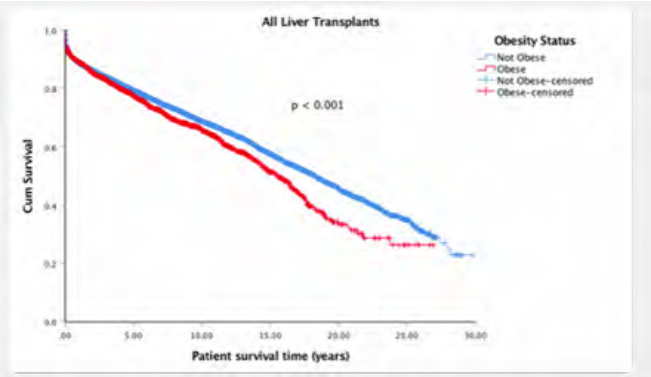
Background: Obesity affects more than 60% of adults in the UK, with MASLD cirrhosis an increasing indication for liver transplantation. We postulate that obesity affects recipient outcomes with worsening co-morbidity profile post transplantation.

Methods: A retrospective UK-wide study was performed of all patients who underwent liver transplantation between 1980 to 2019. 18,325 patients were included and outcomes of liver transplantation in the obese (n=3,424) and non-obese recipients (n=14,901) compared. Obesity was defined using the WHO criteria. Anonymized data were extracted from NHSBT Registry.

Results: Patient demographics (obese vs non-obese) included mean age of 53.17±10.77 vs 42.37±19.94 years, male 63.9% vs 56.3%, BMI 33.98±5.01 vs 23.06±4.10 and UKELD 55.06±5.94 vs 54.95±6.21. Obese patients required a longer period of ventilator support (3.44±0.15 vs 3.85±0.10 days; p=0.025), despite similar ITU stays (6.01±0.22 vs 6.09±0.11 days; p=0.763). There were no differences in postoperative complications, including biliary leak (p=0.343), biliary strictures (p=0.196); or infections including fungal (p=0.721), respiratory (p=0.489), blood (p=0.234), urine (p=0.230) or wound (p=0.567). Patient survival was reduced in the obese cohort (p<0.001). However, no difference was noted in graft survival (p=0.977). Obese recipient survival was significantly reduced following transplantation with a liver from donors after brain death (DBD) (p=0.002), but not from donors after circulatory death, living donor or domino transplants (p=0.142, 0.339 and 0.939 respectively). Obese patients had an increased incidence of renal dysfunction at 12 and 60 months post transplantation (p<0.001 and p=0.002, respectively). A trend of more obese recipients with diabetes was noted (21.7±3.1%, 20.0±1.2%; p=0.602).

Conclusions: Post transplant patient survival is lower in the obese population with significantly lower survival with DBD grafts. Obese patients have worsening co-morbidity profile post liver transplant with deteriorating renal function and diabetes, highlighting the importance of improved management of obesity in the peri-transplant period.



Patient survival was reduced in the obese cohort (p<0.001) (Figure 1)

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BOS_15_6 DONOR TYPE AND PRE-EMPTIVE TRANSPLANTS PLAY A BIGGER ROLE THAN HLA MATCHING IN PEDIATRIC TRANSPLANTS

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Background: Donor kidney allografts are matched to recipients considering various factors including similarities in Human Leucocyte Antigens (HLA) expressed by the donor and prospective recipients. Poorly HLA matched transplants have poorer long-term outcomes, however it is unclear whether living donation or pre-emptive transplantation can counteract the effects of HLA mismatches. We reviewed the outcomes for all paediatric kidney transplants in the USA over a 33-year period by different HLA matches, and aimed to identify other factors which may contribute more significantly to long-term outcomes.

Methods: Data were retrieved on all kidney transplants performed in paediatric recipients in 1987-2020 in the USA, from the United Network for Organ Sharing. These were analysed by number of HLA mismatches and compared between pre-emptive and non-pre-emptive transplants and by donor type. Data were compared using chi-square test, ANOVA and Kaplan-Meier survival analysis.

Results: 21,500 patients were included for analysis. Patients with unfavourable HLA matches had higher rates of delayed graft function (10.0% vs 6.6%, p<0.01) and lower graft survival (53% vs 62% at 10 years, p<0.01). Patients with unfavourable HLA matched transplants from living donors had better allograft survival than patients with favourable HLA matched transplants from deceased donors (56% at 10 years vs 51%, p<0.01). Patients with pre-emptive unfavourable HLA matched transplants had better allograft and patient survival than patients with non-pre-emptive favourable HLA matched transplants (61% at 10 years vs 59%, p=0.02 and 96% vs 91%, p<0.01 respectively).

Conclusions: Living donation and pre-emptive transplantation have a more significant impact on clinical outcomes for paediatric kidney transplant recipients and lead to better graft and patient survival regardless of HLA matching. Patients with eligible living donors may consider proceeding with living donation despite an unfavourable HLA match.

BOS_15_7 TRENDS AND OUTCOMES IN KIDNEY RE-TRANSPLANTATION IN THE UNITED STATES: A LONGITUDINAL ANALYSIS

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Background: Kidney re-transplantation offers a substantial mortality benefit compared to long-term dialysis for patients with graft failure; however subsequent graft failure remains a challenge. Evaluating outcomes for kidney re-transplantation is crucial to enhance patient care and potentially prevent the need for subsequent transplants.

Methods: A retrospective longitudinal analysis of the SRTR database was done for kidney re-transplants performed in the United States from January 2000 to May 2023. Patients were then divided into subgroups based on the transplant date and the number of previous transplants.

Results: Based on the inclusion and exclusion criteria, a total of 34,230 patients were evaluated (12,224 in 2001-2011 and 22,006 in 2012-2023). Notably, DCD donors were significantly higher in the 2012-2023 cohort (21.3% vs 8.8%, p-value<0.001). Both patient and graft survival were increased in the more recent timeframe (5-year survival 84.8% vs 83.7% for patient survival and 75.9% vs 69.3% for graft survival, p-value<0.001). There were higher graft failure rates in patients with a higher number of previous transplants (5-year survival 73.4% vs 71.8% vs 62.3% in patients with one, two, and three or more previous transplants, respectively, p-value<0.001). Delayed graft function (HR: 1.69 [1.60-1.79] in 2000-2011 HR: 1.79 [1.63-1.97] in 2012-2023) and higher KDPI (HR: 1.96 [1.70-2.26] in 2000-2011 HR: 2.34 [1.82-3.01] in 2012-2023) have increased the chance of graft failure in both time groups. Graft thrombosis contribution as an etiology for graft failure has increased in the more recent timeframe (OR=2.94 [2.20, 3.92] in patients with one and OR=3.13 [1.58, 6.79] in patients with two or more previous transplants).

Conclusions: Kidney re-transplant outcomes have improved considerably in recent years; however, each consequent transplant has a poorer prognosis compared to previous ones. It is therefore imperative to have a careful approach to re-transplants with certain risk factors including higher KDPI and delayed graft function. Moreover, further evaluation is necessary to determine why graft thrombosis contribution increased as an etiology for graft failure.

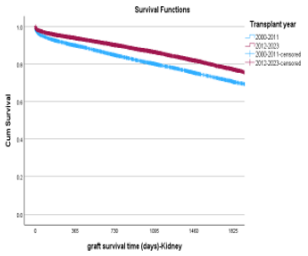

Figure 1. Graft survival rate for all kidney re-transplant patients comparison between the 2000-2010 and 2011-2023 groups (p<0.001)

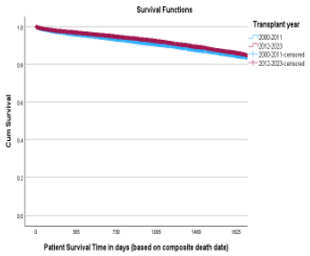

Figure 2. Patient survival rate for all kidney re-transplant patients comparison between the 2000-2010 and 2011-2023 groups (p<0.001)

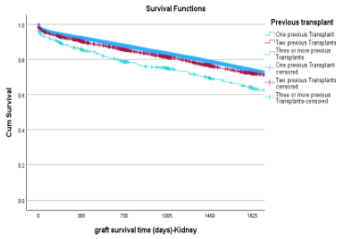

Figure 3. Graft survival rate comparison between the patients with one previous kidney transplant, two previous kidney transplants, and three or more previous transplants (p<0.001)

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BOS_15_8 FACTORS ASSOCIATED WITH EARLY MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS ≥70 YEARS OLD

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[1]Hospital del Mar; Hospital del Mar - Hospital del Mar Research Institute; Nephrology, [2]Hospital del Mar; Nephrology Department, [3]Hospital del Mar; Hospital del Mar; Nephrology, [4]Hospital del Mar, [5]Hospital del Mar; Nephrology, [6]Marta Crespo Barrio; Nephrology

Background: Older adult kidney transplant recipients (KTRs) face an increased risk of mortality during the first year post-transplant, with a 12-month post-transplant survival rate below 90%. Little is known about early mortality after returning to dialysis. This study aimed to identify factors associated with early mortality to improve outcomes in this vulnerable population.

Methods: We conducted a retrospective single-center study of 210 KTRs aged ≥70 years who received deceased donor grafts between 2012 and 2020. Median follow-up until death or April 2024 was 29.24 [8.34–46.88] months, regardless of graft functionality. Early mortality was defined as death occurring within 18 months post-transplant.

Results: The mean recipient age was 74.3±4 years, and 32.8% were women. During follow-up, 31 (14.8%) KTRs died early after transplantation. Patients in the early mortality group were older (75.5 vs. 74, p=0.012) and had a higher prevalence of cerebrovascular disease (CVD, 29% vs. 13.4%, p=0.027). No differences were observed in donor characteristics between groups. Recipients in the early mortality group had a higher incidence of non-functioning grafts (PNF, 25.81% vs. 11.17%), delayed graft function (DGF, 54.17% vs. 33.33%), and longer initial hospital stays (25 vs. 14 days). Additionally, they achieved poorer renal function: nadir creatinine (2.09 vs. 1.53 mg/dL) and eGFR at 3 months post-transplant (24 mL/min vs. 36.66 mL/min). Multivariate analysis confirmed pre-transplant CVD (HR 4.8 [1.8–13.1], p=0.002), PNF (HR 15.4 [1.7–141.1], p=0.016), and eGFR at 3 months post-transplantation (HR 0.93 [0.87–0.99], p=0.029) as independent predictors of early mortality. No differences in mortality causes were observed between groups.

Conclusions: Early mortality occurred in 14.8% of KTRs aged ≥70. PNF, poor renal function, and pre-transplant CVD were identified as significant risk factors for early mortality in this age group. Targeted interventions to optimize renal function in these patients could also enhance their survival.

Allograft failure causes (% total available data)	One previous transplant (n=4114)		p-value[a]	OR[a,b] [95%CI]	Two or More Previous Transplants (n=754)		p-value[c]	OR[c,b] [95%CI]
	2000-2011 (n=3150)	2012-2023 (n=964)			2000-2011 (n=592)	2012-2023 (n=162)		
graft thrombosis	109 (3.5%)	92 (9.5%)	<0.001	2.94 [2.20, 3.92]	20 (3.4%)	16 (9.9%)	0.001	3.13 [1.58, 6.19]
Infection	87 (2.8%)	26 (2.7%)	0.91	0.97 [0.62. 1.52]	14 (2.4%)	6 (3.7%)	0.35	1.58 [0.60, 4.19]
Primary non-function (graft never functioned post-transplant)	184 (5.8%)	17 (1.8%)	<0.001	0.28 [0.17, 0.47]	40 (6.8%)	2 (1.2%)	0.01	0.17 [0.04, 0.72]
Recurrent disease	230 (7.3%)	67 (7%)	0.71	0.94 [0.71, 1.25]	43 (7.3%)	14 (8.6%)	0.55	1.20 [0.64, 2.26]
Acute rejection	429 (13.6%)	148 (15.4%)	0.17	1.15 [0.93, 1.40]	92 (15.5%)	25 (15.4%)	0.97	0.99 [0.61. 1.60]
Chronic rejection	1226 (38.9%)	275 (28.5%)	<0.001	0.62 [0.53, 0.73]	223 (37.7%)	41 (25.3%)	0.003	0.56 [0.37. 0.82]
Other causes	885 (28.1%)	339 (35.2%)	<0.001	1.38 [1.19, 1.61]	160 (27%)	58 (35.8%)	0.02	1.50 [1.04, 2.17]

[a] The calculated values are for the comparison between 2000-2011 and 2012-2023 patients in the group with one previous transplant
[b] OR was calculated based on comparing a particular cause to all other reasons for graft failure between 2000-2011 and 2012-2023 patients
[c] The calculated values are for the comparison between 2000-2011 and 2012-2023 patients in the group with two or more previous transplants
[d] Each cause contributed to less than one percent of total graft failures in both groups

BOS_15_9 SELF-REPORTED NON-ADHERENCE DETECTED BY THE BAASIS PREDICTS ALLOGRAFT REJECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: After kidney transplantation adherence towards immunosuppressive medication is crucial for graft survival and its assessment is challenging in routine post-transplant care. The Basel-Assessment-of-Adherence-to-Immunosuppressive-Medications-Scale (BAASIS) is a validated self-report tool to assess non-adherence, however its ability to predict clinically relevant outcomes remains to be evaluated.

Methods: The prospective AdTorque study includes a cohort of 226 consecutive kidney graft recipients transplanted at the Medical University of Vienna between 01/2018 and 12/2019. In a real-world setting medication adherence was monitored for the first 2 years applying the BAASIS at the first outpatient visit and at months 3, 6, 9, 12 and 24 post-transplant. Assessing the implementation and persistence phase of adherence the BAASIS contains five items rating the daily dose-intake, drug-holidays, dose-timing, dose-changes and discontinuation. Non-adherence was defined by any positive response to one of these items. The primary endpoint was biopsy-proven allograft rejection defined by the BANFF meeting report during a maximum follow-up of 4 years after transplantation.

Results: Of all 226 recipients (median age 56 years [IQR 46-63], 75 [33%] female), 125 recipients (55%) reported non-adherence at least once. Self-reported non-adherence increased from the first outpatient visit to month 3 (from 11% to 31%) and remained stable between month 6 to 24 post-transplant (between 27% and 32%). During a median follow-up of 3.7 years (IQR 1.0-4.0) non-adherent recipients experienced more allograft rejections than adherent patients (24%, n=30 vs. 7%, n=7; P<.001). In a time-dependent Cox regression, the adjusted (recipient sex, age at transplantation and history of previous transplantation) hazard ratio for the association between allograft rejection and previously reported non-adherence was 2.90 (95% CI 1.51-5.58; P=.001).

Conclusions: Self-reported non-adherence occurred already in early phases post-transplant and was associated with an increased risk for allograft rejection. Our findings support the clinical value of the BAASIS and its implementation into routine post-transplant care may facilitate the detection of clinically relevant medication non-adherence.

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BOS_15_10 EARLY ACUTE T CELL-MEDIATED REJECTION AND KIDNEY ALLOGRAFT OUTCOMES

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Background: Kidney transplant rejection can either be T cell-mediated (TCMR) or antibody-mediated. With routine use of T-cell targeted therapies for both prevention and treatment, TCMR is broadly considered clinically benign. We hypothesized that irrespective of its severity, TCMR diagnosed in the first-year post-transplantation still poses a major clinical challenge with suboptimal therapeutic response that portends premature allograft loss.

Methods: We conducted an observational cohort study of all adult patients who underwent kidney transplantation between January 2013 and December 2019 at six centers in the US and Europe. We examined the prevalence of TCMR in the first-year post-transplantation, assessed clinical and histological response to treatment, and whether treatment-response influenced allograft survival. Patients routinely underwent at least 2 surveillance biopsies plus for-cause biopsy, unless there was a medical contraindication.

Results: We analyzed 5828 patients with 9780 biopsies in the first-year post-transplantation, of whom 824 (14.3%) had TCMR (clinical TCMR, 55%; subclinical TCVMR, 45%). Despite treatment, 37% of patients still demonstrated clinical deterioration (failed to return to within 80% of baseline) and 33% had persistent TCMR (≥1A) on follow-up biopsies. This lack of therapeutic response was noted across all TCMR-grades and seen in both subclinical and clinical TCMR. While only 51% of patients with clinical improvement had complete histological resolution of rejection, 44% with clinical deterioration had persistent rejection, indicating a clinical-histological mismatch in treatment-response. TCMR was associated with increased seven-year graft loss (HR, 2.3; 95% CI, 1.95-2.7; p<0.001). Importantly, histological persistence was associated with increased seven-year graft loss (HR, 2.6; 95% CI, 1.8-3.8; p<0.001) compared to resolution, irrespective of TCMR-severity and independent of potential confounders.

Conclusions: TCMR in the first-year post-kidney transplantation persists despite treatment and negatively impacts long-term allograft survival, prompting the need for closer monitoring and newer therapeutics.

BOS_15_11 OUTCOMES OF KIDNEYS RECIPIENTS RECEIVING KIDNEYS FROM DONORS WITH THIN BASEMENT MEMBRANE NEPHROPATHY

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Background: Kidney transplantation is the best treatment for end-stage renal disease. The outcomes of recipients who received kidneys from the donors with thin basement membrane nephropathy (TBMN) are uncertain. This study compares outcomes of the recipients of kidneys from TBMN donors versus those from donors with normal biopsies.

Methods: All recipients who received kidneys from donors who underwent kidney biopsies due to hematuria between January 2016 and May 2024 were included. Recipients were divided into the "Normal" group, comprising those who received kidneys from donors with normal biopsies, and the "TBMN" group, comprising those who received kidneys from donors with TBMN. Clinical outcomes were collected for all recipients at the last follow up.

Results: A total of 271 potential kidney donors underwent kidney biopsies due to microscopic hematuria. Ultimately, 93 donors proceeded with kidney donation. Among the recipients, 54 received kidneys from donors with normal kidney biopsies, while 39 received kidneys from donors diagnosed with TBMN. Post-transplant systolic blood pressure was lower in the TBMN group compared to the normal group (p = 0.061), though this difference was not statistically significant (Table 1). Creatinine levels and urine albumin creatinine ratios were similar between the two groups (p > 0.1). Hematuria was more prevalent in the TBMN group (87% vs. 73%). Both graft survival and patient survival rates were approximately 98%, with no significant differences observed between the two groups (Table).

Conclusions: Recipients of kidneys from donors with TBMD demonstrate comparable graft survival and clinical outcomes to recipients of kidneys from donors with normal biopsies.

Characteristic	Overall N = 93[1]	Normal N = 54[1]	TBMN N = 39[1]	p-value[2]
Follow up days	1 062 ± 790	1 139 ± 829	956 ± 730	0·26
Last systolic BP	127 ± 19	130 ± 17	122 ± 21	0·061
Last diastolic BP	79 ± 8	79 ± 8	80 ± 9	0·71
Last creatinine (µmol/l)	110 ± 98	115 ± 114	103 ± 69	0·52
Albumin creatinine ratio	8 ± 28	4 ± 7	15 ± 41	0·14
Hematuria	72 (79%)	38 (73%)	34 (87%)	0·10
Patient Survival	90 (97%)	51 (94%)	39 (100%)	0·26
Graft Survival	90 (98%)	52 (98%)	38 (97%)	>0·99

[1] n (%); Mean ± SD
[2] Fisher's exact test; Welch Two Sample t-test; Pearson's Chi-squared test

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BOS_15_12 SINGLE CENTRE OUTCOMES FOR ISOLATED SMALL BOWEL TRANSPLANTATION

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Background: Intestinal transplant (ITx) is treatment option for some patients with complicated and irreversible intestinal failure (IF). ITx covers a range of procedures including both liver and non-liver containing grafts. Despite this, ITx outcomes are reported collectively. In this study we assessed outcomes over a 10-year period at a single UK transplant centre for isolated small bowel transplants (ISBTx) for intestinal failure non-malignant aetiology.

Methods: A retrospective review of patient charts who underwent ISBTx between January 2015 and December 2024 at a single UK transplant centre was conducted. Data collected included patient demographics, patient and graft survival, incidence of rejection, Graft Vs Host Disease (GVHD) and Post-Transplant Lymphoproliferative Disorders (PTLD). Patients receiving ISBTx for malignant aetiologies (pseudomyxoma peritonei, neuroendocrine and desmoid tumours) were excluded. Statistical analysis was performed using Kaplan-Meier survival curves.

Results: Twenty patients (13 male, 7 female) underwent ISBTx during the study period, with an average age at transplant of 47 years (23-63 years). Patient survival at 1 year was 96%, and at 5 years was 77% (Figure 1). Graft explant occurred in 3 cases (15%) - 2 due to graft ischaemia, 1 for chronic rejection. 1 was re-transplanted. Patients not retransplanted were re-started on parenteral nutrition. There was 1 case of PTLD and no cases of GVHD. Acute rejection occurred in 45% of patients; 11% indeterminate histology, 11% grade 1, 33% grade 2 and 45% grade 3 rejection. Chronic rejection was observed in 5%. 75% of acute rejection occurred in the first year, 63% was successfully treated with pulsed methylprednisolone monotherapy. The median length of stay post-transplant was 41 days (21-76 days), with a median ITU stay of 3.5 days (2-6 days). Following ISBTx, 85% of patients required no ongoing parenteral support.

Conclusions: ISBTx for benign IF indications delivers excellent outcomes in terms of patient and graft survival in a cohort of patients that would otherwise have limited options. Rejection remains a significant challenge, although this is treatable if detected early. The ongoing focus should be on improving referral pathways and earlier identification of at-risk patients with IF leading to timely transplantation.

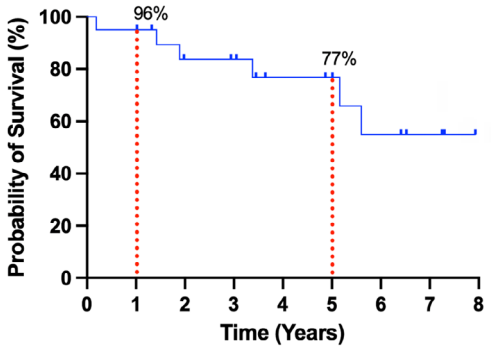

Figure 1: A Kaplan Meier Curve demonstrating survival post Isolated Small Bowel Transplant

BOS_15_13 LOW BASELINE FEV3/FEV6 IS ASSOCIATED WITH CHRONIC LUNG ALLOGRAFT DYSFUNCTION AND DEATH AFTER LUNG TRANSPLANT

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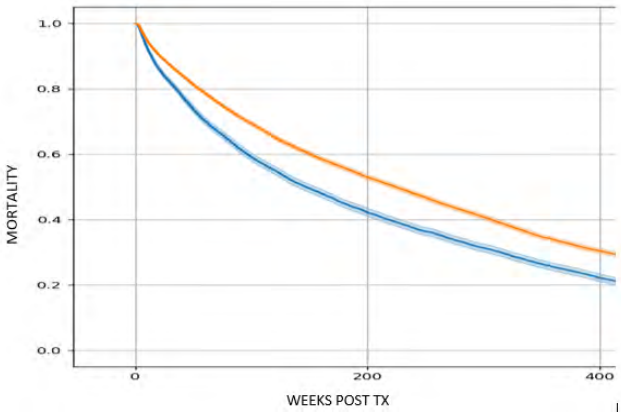
Background: Chronic lung allograft dysfunction (CLAD) is defined by a persistent decline in the forced expiratory volume in 1 second (FEV1). The FEV1 is insensitive to detect distal small airway dysfunction, the site known to be affected early in CLAD. The FEV3/FEV6 % (FEV3/6) is proposed as an index of peripheral airway disease. We hypothesise that FEV3/6 is a sensitive measure of injurious allograft processes. The goals of this study were to determine the prognostic significance of FEV3/6 on chronic lung allograft dysfunction (CLAD) and death.

Methods: A retrospective cohort analysis was conducted of all bilateral lung transplant recipients at a single centre, between Jan-2003 and Dec-2023, with ≥3 FEV3/6 measurements. Baseline FEV3/6 % was defined as the highest single value after LTx. Low baseline FEV3/FEV6 was defined as < 25th centile of the best FEV3/6 value. Time-dependent multivariate Cox regression was used to measure the association between baseline FEV3/6 and risk of CLAD and death.

Results: A total of 28840 values were analysed from 734 included patients. The median (IQR) number of FEV3/6 measurements per patient was 34.5 (IQR 40). The median (IQR) time to baseline FEV3/6 was 20.7 weeks (IQR 26.67) with a mean best FEV3/6% 98.7 (SD 2.5). 196 (26.7%) patients had an abnormal baseline FEV3/6. Low baseline FEV3/6 values by 12 months after LTx were independently associated with both CLAD HR 1.15 (95%CI 1.11-1.1.19, p-value <0.05) and death HR 1.28 (95%CI 1.09-1.48, p<0.05.

Conclusions: Low baseline FEV3/FEV6 was significantly associated with CLAD and survival. There may be benefits in routine monitoring of FEV3/FEV6 after lung transplantation to identify patients at risk of poor outcomes.



Graph: Kaplan-Meier curves comparing time-to-death probabilities for patients with low baseline FEV3/FEV6 (Blue), compared to patients with normal baseline FEV3/FEV6 (Orange) (log rank, p-value < 0.05)

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BOS_15_14 THE PROGNOSTIC VALUE OF RED CELL DISTRIBUTION WIDTH TO ALBUMIN RATIO IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The red blood cell distribution width to albumin ratio (RAR) has recently emerged as a reliable prognostic marker for adverse outcomes in various patient populations. This study aimed to evaluate the association between RAR and the long-term outcomes in kidney transplant recipients.

Methods: This retrospective study included 2096 adult kidney transplant recipients who underwent transplantation at Severance Hospital between 2006 and 2020. Recipients were categorized into tertiles based on their RAR values at 1 year post-transplant. The associations between RAR and the risk of death with a functioning graft were analyzed using multivariable Cox regression models.

Results: Post-transplant RAR values showed a decline within the first 6 months and stabilized thereafter, with a mean RAR of 3 at 1 year post-transplant. In multivariate Cox proportional hazard analyses, the highest tertile of RAR was identified as an independent predictor of mortality in kidney transplant recipients, even after adjusting for donor characteristics and graft function. Additionally, when RAR was analyzed as a continuous variable, increased RAR remained an independent risk factor for death with a functioning graft (Hazard ratio, 2.047; 95% confidence interval, 1.432–2.926; $P < 0.001$). In contrast, pre-transplant RAR values were not associated with death with a functioning graft.

Conclusions: This study demonstrates that elevated RAR values after kidney transplantation are associated with an increased risk of death with a functioning graft. RAR may serve as a simple, reliable, and cost-effective marker to identify high-risk individuals in clinical practice, enhancing long-term risk stratification and patient management.

BOS_15_15 IMPACT OF MAINTAINING IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANT FAILURE

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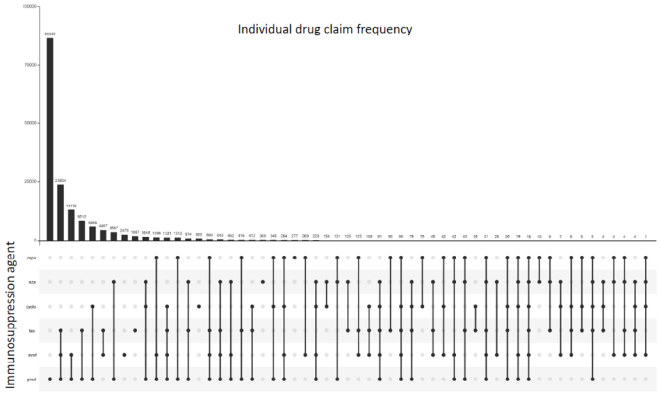
Background: The management of immunosuppression after kidney transplant failure is highly variable. Some clinicians maintain immunosuppression to reduce allosensitization and facilitate repeat transplantation; others taper immunosuppression due to concerns of potential infection or malignancy. The impact of maintaining versus withdrawing immunosuppression on cause-specific dialysis mortality and rate of retransplantation is understudied.

Methods: We utilized data from the United States Renal Data Systems with associated Medicare prescription drug claims. Descriptive statistics were generated to compare those maintained on immunosuppression versus those in whom it was withdrawn. We constructed multivariable cox models for mortality by immunosuppression use; cause-specific mortality was also explored. We also performed analyses where we considered death as a competing risk for retransplantation

Results: We assembled a cohort of 56,702 failed kidney transplant recipients incident to dialysis from 1/1/06-12/31/20 and with medication claims; of these, 44,532 had at least one immunosuppression drug claim. Prednisone was most common (96%), followed by mycophenolate (30%) and tacrolimus (21%) (figure1). Those maintained on immunosuppression were older, female, African-American and relisted for another transplant. Continuing immunosuppression was associated with a reduced risk of death overall (aHR 0.89, 95% CI 0.83-0.96) and death due to cardiovascular disease (aHR 0.82, 95% CI 0.70-0.96). No significant difference was noted in death due to infection (aHR 0.84, 95% CI 0.61-1.14). When considering the competing risk of death, continuing immunosuppression was associated with an increased likelihood of both living donor (aHR 1.25 95% CI 1.12-1.39) and deceased donor retransplantation (aHR 1.35, 95% CI 1.22-1.50). Among patients who were not relisted for transplantation, immunosuppression was not associated with an increased risk of death (aHR 1.07, 95% CI 0.98-1.17).

Conclusions: Maintaining immunosuppression after return to dialysis was associated with a reduced risk of death and increased likelihood of retransplantation. Further study is needed to determine the optimal regimen for this patient population.



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BOS_16_1 MEASURING FCRIIIA ENGAGEMENT: A NOVEL ASSESSMENT OF HLA ANTIBODY PATHOGENICITYE

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Background: Single antigen bead (SAB) testing enables monitoring of HLA-specific antibody binding of the F(ab) fragment but does not assess the antibody's effector functions which are mediated by the Fc portion binding to Fc receptors (FcgRs), present on innate immune cells. NK cells express the activating FcγRIIIA and are implicated in antibody mediated rejection (AMR). Using single HLA expressing cells as an antibody capture tool, we measured HLA antibody-dependent activation of FcγRIIIA.

Methods: Post-transplant sera from n = 5 patients was used to coat 14 single HLA expressing cells (Class 1 A*01:01; A*02:01; A*03:01; A*24:02; B*07:02; B*15:01; B*27:05; B*35:01; B*44:02; B*57:01; DQB1*0201 DQA1*0501; DQB1*0301 DQA1*0503; DRB1*0401 DRA*0101; DQB1*0402 DQA*04010), as well as positive and negative controls. Binding data experiments were conducted, before sera-coated single HLA expressing cells were incubated with FcγRIIIA/NFAT-RE/luc2 engineered Jurkat T cells, which generate luciferase following FcγRIIIA engagement. Experiments were repeated 3 times for reproducibility. Relative fold induction, compared to serum-coated HLA negative cells is represented, in addition to SAB Luminex data of relevant DSAs.

Results: Following incubation with sera coated single HLA expressing cells, FcγRIIIA engagement is evident, as measured by luciferase expression, relative to HLA negative controls (p<0.005). Data for Luminex DSA+ve patients without AMR, together with FcγRIIIA engagement assay results (**Fig 1A-F**) demonstrate no FcγRIIIA binding DSA, compared to DSA+ve patients with AMR (**Fig 2 A-D**), whose DSA do engage the FcγRIIIA receptor.

Conclusions: HLA specific ab has demonstrable and variable engagement of FcγRIIIA, and thus NK cells, which corresponds with clinical evidence of AMR. This assay provides a novel and important assessment of HLA specific antibody pathogenicity, which has the potential to correlate with patient outcomes, or precision delisting of HLA ab specifications. Further work using FcγRIIA expressing cells, as well as additional samples from DSA+ve patients with and without AMR is planned.

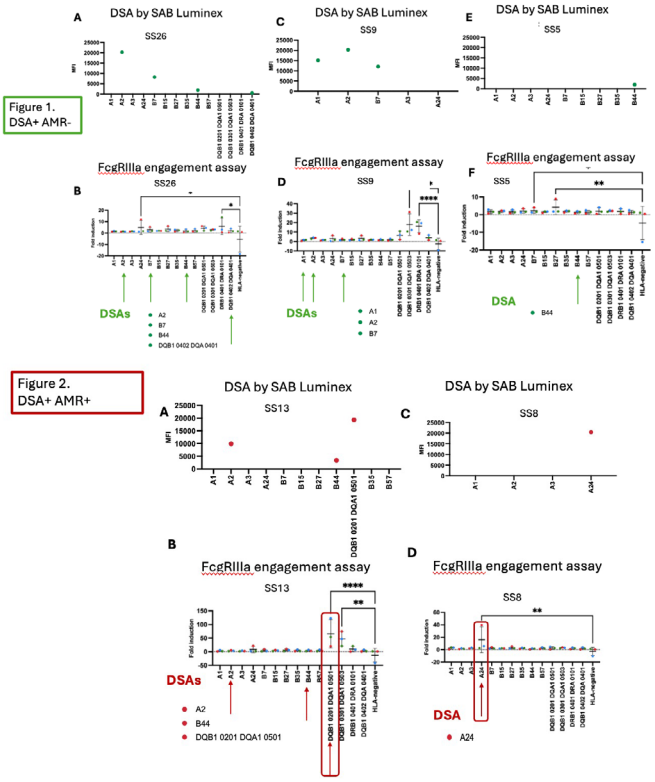

Fig 1

BOS_16_2 FCGR3A F158V REVEALS DISSOCIATION BETWEEN COMPLEMENT ACTIVATION AND ADCC

***Thomas Vanhoutte*[1], Karolien Wellekens[2], Elisabet Van Loon[3], Priyanka Koshy[4], Maarten Coemans[5], Dirk Kuypers[6], Maarten Naesens[7]**

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Background: Evidence for involvement of CD16a (Fc fragment of IgG IIIa receptor, FCGR3A) expressing NK cells and monocytes as prime agents in the process of human kidney transplant rejection is expanding quickly. FCGR3A mediates antibody-dependent cellular cytotoxicity (ADCC) after engagement with donor-specific antibodies (DSA) bound to graft cells. A functional genetic polymorphism in the *FCGR3A* gene results in a high-affinity (V158 allele) or low-affinity receptor (F158 allele). Large cohort studies reporting on the impact of the FCGR3A F158V genotype on graft histology and -outcomes are currently lacking.

Methods: We studied the impact of the FCGR3A F158V genotype on graft histology, -functional decline, and -failure in a large, unselected observational cohort study of 1259 kidney transplantations with 5435 post-transplant biopsies.

Results: In the whole cohort, and particularly in transplantations complicated with rejection, the FCGR3A F158V genetic polymorphism appeared as a significant and independent predictor of accelerated graft functional decline and primary graft failure. The V/V158 genotype significantly associates with a higher rate of occurrence of chronic active antibody-mediated rejection (HR: 9.446, p=0.005). The V158 allele significantly associates with lower C4d without rejection rates in a dose-dependent manner (HR for F/V158: 0.541, p=0.041; HR for V/V158: 0.286, p=0.039). After exclusion of ABO-incompatible transplantation this association remained significant. No associations between FCGR3A F/158V genotype and other Banff rejection phenotypes were found.

Conclusions: Our study findings suggest that the affinity of FCGR3A is a key element in the pathobiology of AMR. Low-affinity of this receptor, predicted by the F158 allele, associates with abrogation of downstream ADCC, even in the presence of complement activation hallmarked by C4d deposition. These results validate FCGR3A F158V as a significant risk genotype for adverse graft outcomes, suggest that it acts mechanistically through coupling of complement activation and ADCC as allo-injury mechanisms and provide an immunobiological explanation for the C4d without rejection phenotype in ABO-compatible grafts.

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BOS_16_3 EXTRACELLULAR VESICLES PRODUCED BY REGULATORY B CELLS: NEW APPROACH IN KIDNEY TRANSPLANTATION

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[1]Cr2ti-Umr1064; Chu Hôtel Dieu Nantes, [2]Cr2ti - U1064, [3]Cr2ti-U1064, [4]Université de Nantes - Inserm Umr 1064 - Crti; Cr2ti-U1064, [5]Inserm U643 Itert; Cr2ti-U1064, [6]Msc-Med, Inserm U7057, Université de Paris, [7]Crti -Inserm Umr1064 -Itun; Cr2ti-U1064; Chu Nantes, Inserm, Universite Nantes, [8]Cr2ti Inserm Umr1064; Cr2ti-U1064; Umr 1064, [9]Cr2ti Inserm Umr1064; Cr2ti-U1064

Background: Kidney transplantation remains the best therapeutic option for patients with end-stage renal disease. However, it requires lifelong immunosuppressive therapy, with side-effects and an overall negative impact on long-term graft survival. Some patients display operational tolerance after discontinuation of these treatments. The search for clinical history and biomarkers has enabled us to identify in these patients an increase of regulatory B cells (Breg) that inhibit the proliferation of effector T cells. However, the mechanism of action of these cells remains poorly understood. Given the ability of various immunomodulatory cells to have activity through the secretion of extracellular vesicles (EVs), we hypothesized that Breg cells might mediate their suppressive effect through this mechanism.

Methods: B cells were cultured for 3 days using different stimulation protocols to generate Breg or non-Breg. Their EVs were then produced spontaneously or through mechanical stimulation and isolated from the supernatant by differential centrifugation. We characterized their type by cryo-electron microscopy and western blot, and their content by mass spectrometry. EVs from Breg or non-Breg were then cultured for 72 h with anti-CD3/CD28 bead activated CD4+T cells to characterize their regulatory potential on CD4+ T cell proliferation and apoptosis.

Results: We demonstrated that Breg release EVs with an exosome phenotype and that can dose-dependently inhibit CD4+T cell proliferation and induce their apoptosis in vitro. Analysis of the content of EVs from Breg revealed a significant enrichment in 11 proteins differentially expressed compared to EVs from non-Breg and involved in the regulation of proliferation and programmed cell death of effector T cells. Finally, we showed that mechanical stimulation increases EV production by a factor of 3, without altering the suppressive properties.

Conclusions: Due to their inhibitory potential and the possibility to increase their secretion, EVs from Breg open new approaches in kidney transplantation, as therapeutic targets and biomarkers.

BOS_16_4 MICRORNAS AND CHEMOKINES AS BIOMARKERS OF REJECTION IN LIVER TRANSPLANTATION: VALIDATION OF A SCORE

Pablo Ruiz[1], Olga Millán[2], Judit Julián[3], Gonzalo Crespo[4], Yiliam Fundora Suárez[5], Jordi Colmenero[4], Mercè Brunet[6]

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Background: Circulating microRNAs (miRNAs) and chemokines may be used to predict T-cell-mediated rejection (TCMR) in liver transplantation (LT). In a previous study, a logistic regression model based on plasma levels of miRNAs 155-5p, 181a-5p, and CXCL-10 showed excellent correlation with the prediction and diagnosis of TCMR.

Methods: A prospective cohort study was conducted with 151 LT recipients, followed for one year post-surgery. Patients with abnormal liver function tests (LFTs) underwent liver biopsy (LB) to rule out TCMR. Plasma samples were collected at predefined time points to analyze miRNA expression (miR-155-5p, 122-5p, 181a-5p, 483-3p, 885-5p, and 194-5p) and chemokine levels (CXCL-9, CXCL-10, and CXCL-11), and their ability to predict and diagnose TCMR. To correlate plasma expression of miR-155-5p, 122-5p, and 181a-5p with tissue expression, 27 liver tissue samples were collected (9 patients with normal LFTs and 18 with TCMR).

Results: Forty patients (26.5%) were diagnosed with TCMR. Circulating miRNAs (155-5p and 122-5p) showed increased expression and reflected tissue-level miRNA changes in patients with TCMR. Plasma miRNAs 483-3p, 885-5p, 194-5p, and chemokines CXCL-9 and CXCL-11 also exhibited significant elevation in TCMR. Circulating miRNAs 155-5p, 181a-5p, and CXCL-10 demonstrated the best performance, confirming the highest logistic regression score for TCMR: AUROC 0.95 (95% CI 0.93-0.96) for prediction and AUROC 0.99 (95% CI 0.98-0.99) for diagnosis. When assessing biomarkers specifically at the time of the LB, miRNAs 155-5p and 181a-5p identified all patients with rejection (AUROC=1).

Conclusions: The correlation between circulating miRNA levels and liver tissue expression confirms their value for the prediction and diagnosis of TCMR. The score based on miRNAs 155-5p, 181a-5p, and CXCL-10 provided the best predictive and diagnostic model for TCMR.

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BOS_16_5 IDENTIFYING LEUKOCYTE POPULATIONS AS BIOMARKERS FOR CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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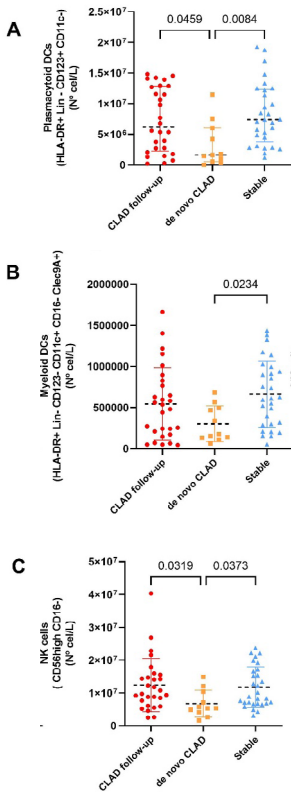
Background: Lung transplantation (LT) is the last option for end-stage respiratory diseases, but long-term survival is limited by chronic lung allograft dysfunction (CLAD). Early CLAD detection is crucial to avoid irreversible damage. Identifying biomarkers to reduce subjectivity in CLAD diagnosis by understanding its biological mechanisms is beneficial for LT patients. This study aims to determine which leukocyte populations in peripheral blood are altered in CLAD after LT.

Methods: This case-control study included 68 clinically well-defined lung transplant patients, divided into three groups: stable control (N=29), CLAD follow-up (N=28), and de novo CLAD (N=11). Leukocyte subpopulations in peripheral blood were analyzed using flow cytometry and five DuraClone panels: IMPhenotyping Basic, IM TCRs, IM Treg, IM Granulocytes, and IM Dendritic Cell (Beckman Coulter, Germany). Flow-Count fluorospheres were used for absolute cell count quantification following the manufacturer's protocol.

Results: Five leukocyte subpopulations showed significant differences in absolute cell counts among the patient groups. Plasmacytoid dendritic cells (HLA-DR+Lin- CD123+ CD11c-) (Fig. 1a) and myeloid dendritic cells (HLA-DR+ Lin- CD123- CD11c+ CD16- Clec9A+) (Fig. 1b) were significantly reduced in the de novo CLAD group compared to both the follow-up CLAD and stable groups. NKreg cells (CD56high CD16-) were also lower in the de novo CLAD group versus the stable group (Fig. 1c). Significant differences were also observed in the low-frequency TCRγδ+ Vδ2+ and Treg Helios+ CD39- populations.

Conclusions: These findings provide valuable insights into the leukocyte populations involved in CLAD onset. Specifically, de novo CLAD patients exhibited reduced levels of plasmacytoid dendritic cells, MDC1, and NKreg cells, all of which are key regulatory cell types.

Project "PI22/01103", funded by ISCIII and co-funded by the EU.



BOS_16_6 PERIPHERAL BLOOD B CELL CYTOKINES PREDICT RENAL ALLOGRAFT OUTCOMES BEFORE TRANSPLANTATION

Aravind Cherukuri[1], **David Rothstein[2]**

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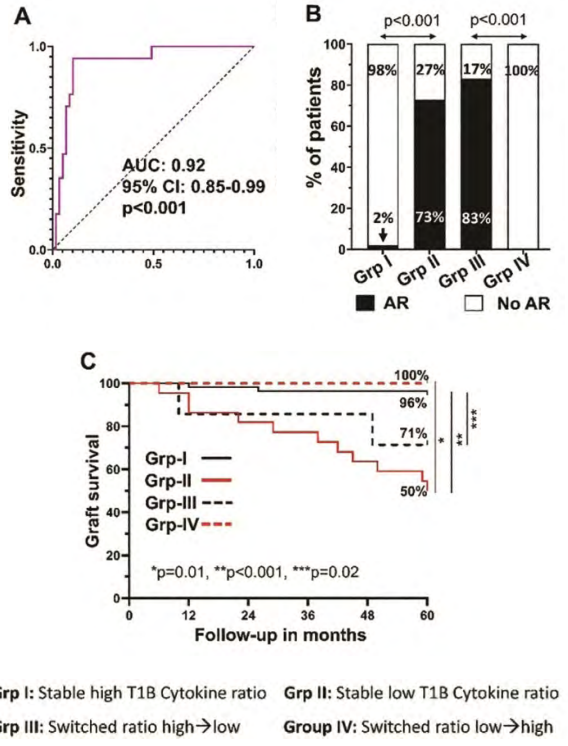
Background: The IL-10:TNFα ratio expressed by transitional-1 B cells (T1B) in peripheral blood 3 mos post-transplant is a measure of Breg:Beff balance and predicts both renal allograft rejection (AR) by 1 yr (ROC AUC 0.92) and an ~30% decrease in 5-yr graft survival (GS). We asked whether this same biomarker could also risk-stratify outcomes pre-transplant, allowing individualized immunosuppression from the outset.

Methods: We examined the IL-10/TNFα cytokine ratio of peripheral blood T1B cells by flow cytometry (after 24h CD40L+CPG stimulation) both before and 3 mos after transplant, in 116 patients who had 3 and 12 mos surveillance allograft biopsies (Bx) or any for-cause Bx in the 1st post-transplant year. We asked whether the pre-transplant T1B cytokine ratio remained stable 3 mos post-transplant and predicted subsequent AR and 5-yr graft survival.

Results: Patients with AR in the 1st year had a significantly lower pre-transplant T1B cytokine ratios (p<0.001). In fact, a low pre-transplant cytokine ratio predicted subsequent AR (ROC AUC 0.79, p<0.001). At a cut-off of 1.3, 61% of patients had high and 32% had low T1B cytokine ratios. In 75% of the patients, the pre-transplant cytokine ratio remained stable 3 mos post-transplant. In these patients, the pre-transplant ratio predicted AR even more strongly (ROC-AUC 0.92, p<0.001, Fig 1A). For example, 2% of patients with a stable high ratio (Grp-I) vs. 73% with a stable low ratio (Grp-II), had subsequent AR (Fig 1B). In 25% of patients, the pre-transplant cytokine ratio changed (from high to low or low to high), and their clinical course then tracked with that predicted by the 3-mos ratio. Thus, 73% of patients whose ratios switched from high to low (Grp-III) had AR; while none of those whose ratios switched from low to high (Grp-IV) had AR (Fig 1B). Finally, Grps I (96%) and IV (100%) had excellent 5-yr GS, while Grps II (50%) and III (71%) had significantly poorer GS (Fig 1C).

Conclusions: The T1B cytokine IL-10/TNFα ratio strongly predicts subsequent transplant course even before exposure to an allograft or immunosuppression - suggesting that it provides a measure of an individual's basal immunological reactivity. Current studies aim to identify patients whose ratios are stable vs. switchable, paving the way for an excellent predictive biomarker before transplantation.



Grp I: Stable high T1B Cytokine ratio **Grp II:** Stable low T1B Cytokine ratio

Grp III: Switched ratio high→low **Group IV:** Switched ratio low→high

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BOS_16_7 LONGITUDINAL ASSESSMENT OF ALLOREACTIVE MEMORY T AND B CELLS IN THE EUTRAIN KIDNEY TRANSPLANT COHORT

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Background: Alloimmune memory challenges allograft outcomes. While in vitro assessment of donor-reactive memory T and B cells in vitro is feasible, their combined assessment and translation into clinical kidney transplant (KT) outcomes remain unexplored.

Methods: We explored the clinical impact of circulating donor-specific memory T (DST) and B cells (mBC) in 728 samples from 557 KT patients in the EUTRAIN project prior and at the time of for-cause and/or 3/12-months surveillance biopsies to predict BPAR. DST and mBC responses were assessed using the IFN-γ ELISPOT and HLA B-cell FluoroSpot assays. DST and mBc were analyzed in 200 and 105 patients preKT and in 267 and 151 at the time of kidney biopsy, respectively.

Results: PreKT, 46/200 (19.8%) and 23/105 (9.9%) of patients were DST+ and mBC+, respectively. 7/73 (9.6%) were DST+/mBC+ and 49/73 (67.1%) DST-/mBC-. PreKT DST and mBC+ showed no significant associations with main clinical factors, but mBC+ associated to DSA and DSA MFI (p=0.015, p=0.013). High frequencies of preKT DST associated with high BPAR rates (p=0.007), especially TCMR (p=0.003), but not ABMR. Induction therapy with T-cell depletion abrogated preKT DST-associated risk. High preKT mBc frequencies associated with both TCMR and ABMR (p=0.037, p=0.029). Patients with both preKT DST+/mBC+ had a significantly higher BPAR risk than DST-/mBC- patients. Multivariate analyses identified preKT DST+/mBC+ as independent predictors of BPAR. PostKT, 46/267 (17.2%) of patients were DST+ and 82/151 (54.3%) mBC+. PreKT data showed 179/244 (73.4%) persistently DST-, 31/244(12.7%) persistently DST+, 35/81 (43.2%) persistently mBC-, and 19/81 (23.5%) persistently mBC+. PostKT high DST frequencies associated with ongoing BPAR (p=0.011), mainly TCMR (p=0.024), and especially those with also preKT DST+ (p<0.001). PostKT DST+ associated with higher serum creatinine levels at 12months (p=0.05). No direct association was found between circulating mBC and BPAR, neither TCMR nor ABMR at the time of biopsy, although patients lacking detectable DST and mBC had the most pristine kidney allografts (p<0.05).

Conclusions: We describe the kinetics of circulating anti-donor T and B-cell alloreactivity influencing the development of allograft rejection in low-immunological risk kidney transplant patients.

BOS_16_8 URINARY AND BLOOD MRNA BIOMARKERS FOR DETECTING KIDNEY ALLOGRAFT REJECTION (THE KTD-INNOV STUDY: NCT03582436)

Evgenia Preka[1], Valentin Goutaudier[2], Olivier Aubert[3], Maud Racape[4], Agathe Truchot[5], Marta Sablik[6], Marc Raynaud[7], Éric Vicaut[8], Michelle Elias[9], Gillian Divard[10], Richard Danger[11], Beatrice Charreau[12], Didier Bouton[13], Christine Randoux-Lebrun[14], Jean-Luc Taupin[15], Pierre-Antoine Gourraud[16], Magali Giral[17], Moglie Le Quintrec[18], Emmanuel Morelon[19], Lionel Couzi[20], Christophe Legendre[21], Nassim Kamar[22], Dany Anglicheau[23], Carmen Lefaucheur[24], Sophie Brouard[25], Alexandre Loupy[26]

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Background: Blood and urinary mRNA biomarkers are non-invasive tools with potential for detecting kidney allograft rejection. However, their ability to provide added diagnostic value beyond current standard-of-care (SOC) patient monitoring remains unclear.

Methods: In this prospective study, adult kidney transplant recipients were enrolled across seven French referral centres between July 2018 and December 2019 (ClinicalTrials.gov, NCT03582436). During the first-year post-transplantation, we quantified 19 blood and 12 urinary mRNA biomarkers during kidney allograft biopsies, including both protocol-specified and clinically indicated procedures. Primary outcome was the occurrence of allograft rejection, including antibody-mediated rejection (AMR), T cell-mediated rejection (TCMR), and mixed rejection, classified according to the Banff 2019 criteria.

Results: Overall, 733 kidney transplant patients (64.1% male, 35.9% female) were included, with 1,549 biopsies paired with the mRNA biomarkers. The cumulative incidence of rejection was 9.7% (95% CI; 7.6%-12.1%). None of the blood biomarkers tested (AKR1C3, CD3E, CD4, CD40, CD8A, CD9, CTLA4, ENTPD1, FOXP3, GZMB, ID3, IL7R, MS4A1, MZB1, POU2AF1, POU2F1, TCL1A, TLR4, and TRIB1) had a significant association with allograft rejection (Fig.1A). However, among the 12 urinary biomarkers (CXCL9, CD25, CD3, Perf, NKG2~4, FN1, PSMB10, PSMB9, αSMA , IP10, GZB, ECadh), eight-out-of-twelve, CXCL9 (p=0.001), CD3 (p=0.001), Perforin (p<0.001), NKG2~4 (p<0.001), PSMB10 (p=<0.001), PSMB9 (p=0.005), aSMA (p=0.043), IP10 (p=0.006) were significantly associated with allograft rejection (Fig.1B). Moreover, PSMB9 was the only urinary biomarker to show a discriminatory ability between TCMR and AMR (p=0.022, higher in TCMR). Despite these findings, integrating urinary biomarkers with SOC monitoring parameters failed to improve predictive accuracy compared to SOC monitoring.

Conclusions: Urinary mRNA—but not blood—biomarkers showed significant associations with kidney allograft rejection during the first year post-transplantation. Nonetheless, these biomarkers did not improve predictive performance when added to existing SOC practices, underscoring the need for further research to optimise non-invasive diagnostic strategies.

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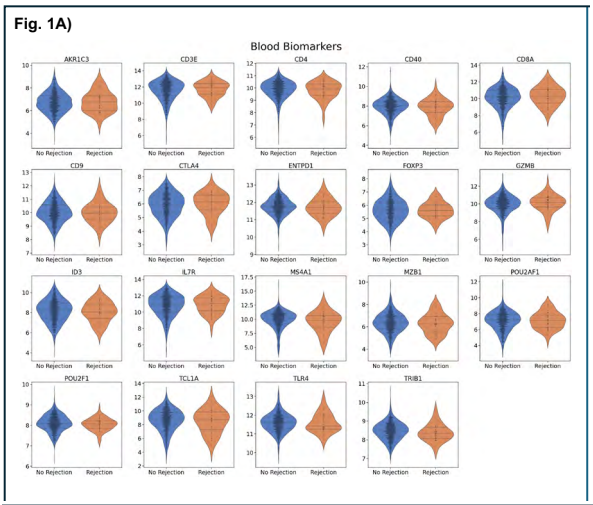

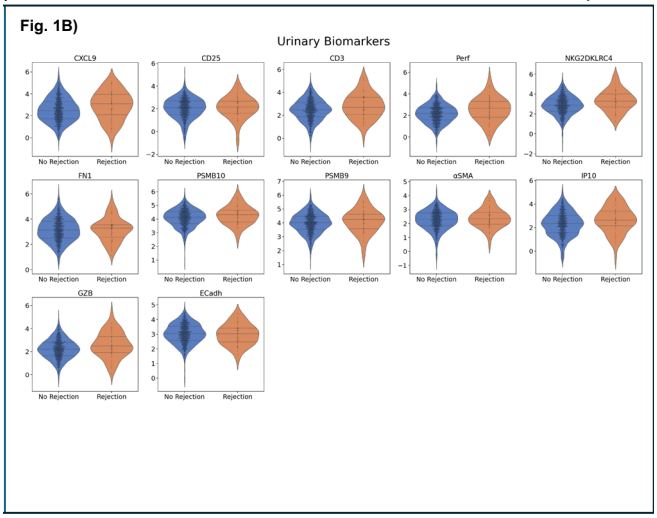

Figure 1. Violin plots showing the univariate association of A) blood and B) urinary biomarkers at the time of biopsy with kidney allograft rejection.

BOS_16_9 DEEP PHENOTYPING OF URINARY CELLS WITH CYTOF REVEALS CD8+CD38+ T CELLS AS BIOMARKER TO DETECT TCMR

Nina Goerlich[1], Christopher Skopnik[2], Diana Metzke[2], Emil Grothgar[3], Leonie Wagner[3], Mira Choi[4], Lennard Ostendorf[3], Pouneh Mirkheshti[3], Fabian Halleck[5], Klemens Budde[6], Paolo Cravedi[7], Miguel Fribourg[8], Kerstin Amann[9], Jan Klocke[3], Sabine Baumgart[10], Philipp Enghard[3]

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Background: Non-invasive monitoring and early detection of rejection are of high priority in kidney transplantation. In our previous work, we established urine flow cytometry (FC) as tool for non-invasive kidney transplant monitoring and rejection detection. We hypothesized that an even deeper phenotyping of urinary cells improves the diagnostic yield of urinary T cells. Therefore, we established Cytometry by time of flight (CyTOF) analysis of urine cells to derive an improved biomarker for the detection of rejection. Our findings were subsequently confirmed in a FC-based validation cohort.

Methods: A total of 157 urine samples from kidney transplant recipients (KTR) were collected from patients undergoing indication transplant biopsy. Of these samples, 57 were analyzed in the discovery CyTOF cohort. CD8+CD38+ T cells were identified as a potential biomarker for T cell-mediated rejection (TCMR), which was confirmed in a validation cohort (n=100) using FC. Additionally, we analyzed a publicly available scSeq dataset of KTR biopsies and urine to investigate our biomarker and its expression in TCMR with an additional method.

Results: By utilizing high-dimensional mass cytometry, we identified CD8+CD38+ T cells as a potential biomarker for TCMR. Reassessment of publicly available scSeq datasets demonstrated that CD38 expression in CD8+ T cells in kidney transplant tissue corresponds to CD38 expression in urinary CD8+ T cells. We translated our finding to FC and validated urinary CD8+CD38+ T cells in a validation cohort. CD8+CD38+ T cells showed an AUC of 0.956 to diagnose TCMR and exceeded prior published biomarkers.

Conclusions: Urinary CD8+ CD38+ T cells are a new biomarker for TCMR, validated by 3 independent methods in 3 patient cohorts.

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BOS_16_10 IGG SUBCLASS PROFILES PREDICT C1Q-BINDING ACTIVITY IN HLA ANTIBODIES AMONG KIDNEY TRANSPLANT RECIPIENTS

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Background: The single antigen bead (SAB) assay is widely used to detect and characterize HLA IgG antibodies in transplant recipients. However, the IgG subclass composition and its relation to C1q-binding activity remain unclear. This study investigated IgG subclass composition and C1q binding activity in kidney transplant recipients.

Methods: We analyzed 4,218 HLA IgG bead reactions from the sera of 37 kidney transplant recipients using SAB and C1q-binding assays. IgG subclasses (IgG1-4) were further assessed using a modified SAB assay with replacing monoclonal secondary antibodies. The cut-off mean fluorescence intensity (MFI) value for HLA IgG and C1q positivity was defined as 1,000.

Results: The distribution of HLA loci among the 4,218 bead reactions included HLA-A (n=589), HLA-B (n=950), HLA-C (n=304), HLA-DR (n=900), HLA-DQ (n=700), and HLA-DP (n=775). IgG positivity was found in 15.1% (639/4,218) of beads, of which 35.5% (227/639) were C1q positive. For 639 IgG-positive beads, the MFIs for IgG1, IgG2, IgG3, and IgG4 subclass are (153 [0-10369], mean [min-max]), (16 [0-2928]), (50 [0-3764]), and (71 [0-4431]), respectively. For 227 C1q-positive beads, the MFIs for IgG1, IgG2, IgG3, and IgG4 subclass ranges are (2265 [0-10369]), (7 [0-269]), (135 [3764]), and (151 [0-4431]), respectively. IgG MFI strongly correlated with IgG1 MFI (r=0.8492, P<0.0001), while correlations with other subclasses were weaker (r=0.1008–0.2943, P<0.0001). Among C1q-positive bead, HLA-DQ C1q MFIs showed a strong correlation with IgG1 MFIs (r=0.6277), whereas HLA-A, HLA-B, HLA-C, and HLA-DR loci demonstrated weak to moderate correlations (r=0.2291–0.3970). No significant correlation was observed for HLA-DP. An IgG1 MFI of ≥ 50 predicted C1q positivity with 75.3% sensitivity and 95.1% specificity, while increasing the threshold to ≥405 improved specificity to 98%.

Conclusions: IgG1 levels were strongly associated with C1q-binding activity. Assessing IgG subclasses can provide valuable insights into complement-activating antibody profiles in kidney transplantation.

BOS_16_11 ASSOCIATION OF DUAL NONINVASIVE BIOMARKERS WITH 10-YEAR ALL CAUSE KIDNEY ALLOGRAFT LOSS

James Fleming[1], **Christabel Rebello**[2], **Blade Robelly**[2], **Lihui Zhao**[2], *John Friedewald*[3]

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Background: KTx is the treatment of choice for ESKD, but long-term outcomes remain suboptimal. The independent impact of noninvasive biomarkers, alone and in combination, on long-term graft survival has not been evaluated.

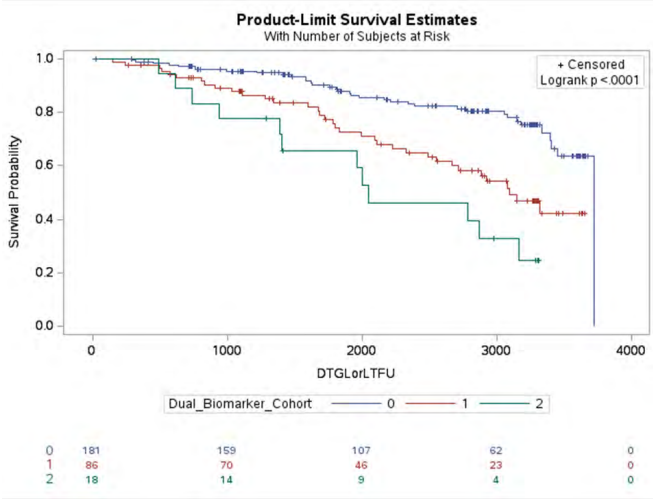
Methods: Subjects from the CTOT-08 multicenter 24-month study were matched with the SRTR database to collect 10-year all cause graft loss (ACGL). A Cox Regression analysis used baseline covariates (Black race, diabetes as cause of ESKD, living donor, recipient age, donor age) as well as clinical acute rejection events and the combination of positive GEP and dd-cfDNA as time-varying covariates. Stepwise selection was used to determine the final model. A Kaplan Meier Curve evaluated 3 cohorts based on the highest quartile of positive biomarkers: Dual Biomarker 0 (≤ 3 positive GEP AND ≤ 3 positive dd-cfDNA tests), Dual Biomarker 1 (> 3 positive GEP OR > 3 positive dd-cfDNA tests), and Dual Biomarker 2 (> 3 positive GEP AND > 3 positive dd-cfDNA tests).

Results: The 285 subjects had an average of 10 visits during the 24 months of CTOT follow-up. Eighty subjects had graft loss. The Kaplan Meier curve demonstrates a significant difference in 10-year ACGL between cohorts (p<0.0001) (Figure 1). The final Cox model included Dual Biomarkers, diabetes, living donor, clinical acute rejection, and donor age, although only Dual Biomarkers (aHR 2.13), living donor (aHR 0.61) and clinical acute rejection (aHR 3.25) were independently associated with ACGL.

Conclusions: In the longest prospectively collected multicenter analysis of outcomes associated with biomarkers, the combination of peripheral blood GEP and dd-cfDNA was independently associated with over a 2-fold greater hazard of All Cause Graft Loss over the 10-year follow-up. This association was found after correcting for well-established risk factors for graft loss, including the impact of clinical acute rejection. In an uncorrected survival analysis, there was a graded increase in risk of ACGL in subjects with multiple positive results for either or both non-invasive tests, demonstrating a more complete risk assessment by having the results of both biomarker modalities. Further research is warranted to better study if and how prospective use of non-invasive biomarkers can impact patient care decisions and potentially mitigate graft loss.

Table 1. Cox Regression Time-to-Event Analysis

Parameter	Adjusted Hazard Ratio	95% Confidence Limits	p-value
Dual Biomarkers	2.13	1.54, 2.94	<0.0001
Living Donor	0.61	039, 0.97	0.03
Diabetes	1.54	0.98, 2.43	0.06
Clinical Acute Rejection	3.25	1.38, 7.65	<0.01
Recipient Age	1.02	1.00, 1.04	0.11



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BOS_16_12 ALLOMAP COST-EFFECTIVENESS FOR HEART TRANSPLANT PATIENTS IN FRANCE. CUPIDON RESULTS AND IMPACT

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[1]Hospices Civils de Lyon; Heart Failure and Transplant, [2]Hospices Civils de Lyon; Pole de Santé Publique, [3]Rennes University Hospital, [4]University Hopsital Strasbourg; Cardiac Surgery Department; Cardiac Surgery Department, [5]Grenoble University Hospital, [6]Hôpital Européen Georges Pompidou, [7]Assistance Publique Hopitaux de Marseillle, [8]Hopitaux Universitaires de Montpellier, [9]Assistance Publique Hôpitaux de Paris, [10]Toulouse University Hospitals, [11]Pitié-Salpêtrière Hospital, Assistance Publique des Hôpitaux de Paris (Ap-Hp), [12]Hospital University Nantes- Laennec; University Hospital Nantes, [13]Rouen University Hospital, [14]Hopitaux Universitaires de Bordeaux, [15]Chru de Nancy; Cic-Cardio-Renal, [16]New Civil Hospital, [17]Hospices Civils de Lyon

Background: Graft rejection is one of the main complications of heart transplantation (HT) and requires scheduled invasive endomyocardial biopsies (EMB). AlloMap® is a non-invasive genomic blood test that identifies patients with a low probability of moderate or severe acute cellular rejection (ACR) and its use could prevent protocolized EMB. A cost-effectiveness analysis of the Allomap test was carried out in 12 specialist centers, to assess the impact of using this test in the french setting.

Methods: CUPIDON is a multicenter, open-label, randomized controlled trial (NCT02602691). Between 2016 and 2020, included patients were randomized from the 6th month post-HT between two strategies for ACR monitoring : an innovative non-invasive strategy based on the first-line use of AlloMap (Group A) ; and the invasive standard of care of each center based on systematic EMB (Group B). Patients were followed-up for 30-month. Quality of life and QALYs were measured using a self-administered EQ5D questionnaire. Cost analysis was performed from the perspective of the healthcare system on the basis of actual hospital stay data.

Results: 190 patients were included. The initial characteristics were comparable between groups. 1069 biopsies and 841 ALLOMAP tests were performed. Median number of biopsies performed per patient was 2 in group A (n=98) vs. 8 in group B (n=92). 14 patients had no biopsies. There was no difference in survival without rejection, death or graft dysfunction between groups (HR=1.286; p=0.32). In the main analysis, the average cost per patient was estimated at €39,069 for the Allomap strategy compared to €23,689 for the Biopsies strategy. The difference in QALYs was not significant between groups. Biopsies strategy became more expensive than the Allomap strategy when the price of the test fell below €799.

Conclusions: The availability of the ALLOMAP test under real-life conditions in France has enabled a clear reduction in the number of biopsies performed during the first 3 years following HT, without exposing patients to an increase in rejection events, death and graft dysfunction compared with those followed by a conventional biopsy strategy. ALLOMAP is expected to be cost effective for a price below 799€ in a french setting. According to these results the usual HT patient follow-up may have to be reconsidered.

BOS_16_13 NON-INVASIVE NK CELLULAR HUMORAL ACTIVATION TEST FOR HUMORAL REJECTIONS IN KIDNEY TRANSPLANTS

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Background: Kidney transplantation (KT) is the optimal treatment for end-stage renal disease, but antibody-mediated rejection (ABMR), driven by donor-specific antibodies (DSAs), remains a major challenge. Natural killer (NK) cells contribute to ABMR through antibody-dependent cell-mediated cytotoxicity (ADCC), making them a potential target for non-invasive diagnostic tools. The NK-Cellular Humoral Activation Test (NK-CHAT), which measures NK cell activation, introduces an innovative approach to evaluating the risk of ABMR.

Methods: This prospective observational cohort study evaluated the efficacy of NK-CHAT in detecting ABMR in KT recipients. Participants were stratified into 3 groups: no major abnormalities (NOMOA), ABMR, low-risk (no preformed DSAs), and high-risk (presence of preformed or *de novo* DSAs). NK-CHAT assessed NK cell degranulation (CD107a) and cytokine production (IFN-γ) in peripheral blood mononuclear cells (PBMCs) stimulated by antibody-coated donor PBMCs. The study included serial evaluations over six months post-transplantation. Statistical analyses were performed to compare NK cell activity across groups and time points.

Results: NK-CHAT activity, measured by CD107a and IFN-γ expression, was significantly elevated in the ABMR group compared to NOMOA, particularly from 1 to 6 months post-transplantation. High-risk patients showed heightened preoperative NK-CHAT activity and gradual reactivation over time, while low-risk patients maintained low NK-CHAT activity throughout. Early NK-CHAT activation was observed in some high-risk patients by postoperative day 7, correlating with ABMR progression. NK cell receptor profiles did not differ significantly across groups, emphasizing functional activation as a key diagnostic marker.

Conclusions: The NK-CHAT assay demonstrates potential as a non-invasive tool for detecting ABMR, particularly in high-risk patients with DSAs. It enables early identification of rejection risk, supporting timely interventions and personalized management.

Figure 1. Flow Cytometric Analysis of NK Cell Activation in Kidney Transplant Recipients

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BOS_16_14 NONINVASIVE DIAGNOSIS OF RENAL ALLOGRAFT ACUTE CELLULAR REJECTION THROUGH ACTIVE GRANZYME B IN URINE USING A NOVEL PROBE

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Background: Acute rejection is a frequent complication of renal transplantation, requiring invasive allograft biopsy for diagnosis. Previous methods to develop a non-invasive test rely on amplification methods or have limited clinical utility beyond highly specialised laboratories. No point of care test for acute cellular rejection currently exists, which could reduce treatment delays and improve transplant outcomes.

Methods: We recruited 94 consecutive patients undergoing investigation for acute allograft dysfunction. All patients had previously demonstrated stable transplant function. Urine specimens were collected from each patient, with active Granzyme B (GzmB) measurements performed using a patented fluorescent probe. Results were available within two hours. Total GzmB activity was correlated with allograft status and histopathological diagnosis. Ethical approval was gained (GN22RE301).

Results: Overall, 22 patients (24%) had biopsy-confirmed acute cellular rejection. No GzmB activity was measured in patients with BK nephropathy, urinary tract infection, or recurrent primary disease. Analysis demonstrated that acute cellular rejection could be predicted with a sensitivity of 69.6% and specificity of 88.7%, with a corresponding PPV of 66.7 and NPV of 90.1%. Accuracy was 84%. In patients with acute cellular rejection, probe GzmB measurements correlated with rejection severity in biopsy samples and fell sequentially with creatinine following intravenous methylprednisolone treatment.

Conclusions: We demonstrate the potential of a future point of care test to non-invasively diagnose acute rejection of renal allografts. We were able to identify acute cellular rejection with high specificity from patient urine samples, which correlated with severity and treatment response. Work is underway to further develop the near patient test and improve its predictive power.

BOS_16_15 FEASIBILITY OF VASCULARISED SKIN ALLOGRAFT FOR REMOTE SITE MONITORING OF ALLOGRAFT REJECTION IN KIDNEY TRANSPLANTATION

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Background: Monitoring for chronic Renal Allograft rejection remains a significant concern in the long - term. Serum creatinine measurement is a late indicator when tissue injury has already taken place. Ultrasound - guided percutaneous kidney biopsy has become a standard procedure for assessing allograft pathology. However, this is an invasive procedure and carries the risk of several complications. The present study evaluated the feasibility of vascularised skin flap to monitor for rejection.

Methods: Kidney and radial forearm free flap from same brain-dead donor were retrieved and implanted in the recipient's right iliac fossa by transplant surgeons and thigh by plastic surgeons respectively. Creatinine, skin examination, skin biopsy and renal allograft biopsy were obtained at post- perfusion, 1 month, 3 month and at last follow up. Biopsies of kidney and skin graft were also planned for graft dysfunction occurred. All patients were induced with Anti- Thymocyte Globulin. In post-transplant period, four patients received tacrolimus, mycophenolate mofetil and steroid while one patient was on cyclosporine instead of tacrolimus.

Results: The mean age of five patients and donors was 38.8 ± 8.5 and 45 ± 10.89 years. All donors were male while three recipients were male. One male patient had radial forearm free flap loss due to hematoma and bleeding post op day 2. The mean follow- up of four patients is 50.25 ± 24.05 months. The mean creatinine at Day 0, discharge, 1 month, 3-month, 1 year and at the last follow up were 5.05 ± 2.33, 0.86 ± 0.35, 0.98 ± 0.53, 1.13 ± 0.51, 1.12 ± 0.28 and 1.16 ± 0.35 mg/dl ($p<0.05$) respectively. None of the patient's skin graft showed erythema, induration, edema, necrosis or changes in texture. Graft and Skin biopsy done post- perfusion, 1 month, 3 month and at last follow up did not reveal rejection.

Conclusions: This study demonstrates the potential feasibility of using a vascularized skin flap as a non-invasive tool for monitoring allograft rejection in kidney transplant recipients

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Controversies and standards in organ donation

BOS_17_1 EXTENDING QUALITY ASSURANCE COMPLIANCE IN THE SWISS ORGAN DONATION NETWORKS

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Background: For reasons of established collaborations between hospitals and due to geographical/linguistic circumstances, five regional organ donation networks have been established in Switzerland (Figure 1). Each network is composed of donation specialists in detection and procurements hospitals and is led by an intensive care physician. Swiss legislation requires quality assurance (QA) in accordance with the relevant chapters of the EDQM Guide to the quality and safety of organs for transplantation (EDQM). Swisstransplant wanted to systematically assess the compliance of the QA system in the five networks and to develop measures for improvement and standardization.

Methods: Swisstransplant has developed a checklist with reference to the QA requirements of the EDQM, covering the following topics: Donation process, organisation and responsibilities, staffing, training and continuing education, process and document management, traceability, audits, deviation management, risk assessment, and change management – about 70 questions in total. Swisstransplant carried out seven inventories in the major hospitals representing the 5 networks in 2024. The data collected was analysed using a GAP analysis.

Results: The comparative analysis identified similar shortcomings in most of the networks (Table 1): The need to implement appropriate software for process and document management, the need to define processes for managing risks, changes, deviations as well as internal audits. Three key improvement actions were agreed: first, each network should have a Swisstransplant-funded QA manager as of 2025. Second, a national working group has been defined to standardise key processes and documents. Third, Swisstransplant will support the implementation of new processes in the networks with professional skills and is preparing good practices on the implementation of the EDQM quality requirements.

Conclusions: The method presented allows to identify gaps and trends related to QA in donation networks and to efficiently define measures to fulfil the EDQM requirements. The developed checklist and the QA good practices being developed provide valuable tools that can be applied with few adaptations by any country that considers the EDQM guide as reference.

Figure 1: Geographic representation of the five Organ Donation Networks in Switzerland.

PLDO: Programme Latin de Don d' Organes (6 retrieval and 10 detection hospitals); **CHM**: Organspendenetzwerk Schweiz Mitte (4 retrieval and 17 detection hospitals); **Luzern** (1 retrieval and 7 detection hospitals); **NOO**: Netzwerk Organspende Ostschweiz (1 retrieval and 4 detection hospitals); **DCA**: Donor Care Association (3 retrieval and 20 detection hospitals)

QA-Requirement (in accordance with corresponding chapter in the EDQM Organ Guide)		Evaluation of networks (number of networks)		
17.5.1 Strategic processes		**Well**	**Satisfactory**	**To be improved**
17.5.1.1 Organizational structure, legal framework, personnel	*Current and managed organizational chart*	2	2	1
	Personalized and signed job descriptions / job specifications		5	
	Person responsible for QM	1	4	
17.5.1.2 Personal Training, further training, research	*Introduction (familiarization) plan*	4	1	
	Periodic competence assessment	4		1
	Documented further training	4	1	
17.5.2 Operational processes				
17.5.2.1 Checklists, protocols	*Existence of complete checklist(s)/protocols for documentation from donor recognition to completion of organ removal*	3	2	
17.5.3 Support processes				
17.5.3.1 Audits / self-evaluations	*Self-evaluation and/or audit process in place*	1	1	3
17.5.3.2 Document management and directories	*Document and process management system, incl. processes*		2	3
	General overview / process map		2	3
	Quality manual available	1	2	2
	Completeness of processes/documents: from donor recognition to completion, training and further education as well as all QM activities themselves		5	
17.5.3.3 Traceability	*Traceability with regard to time, responsible persons and materials/products used (also for withdrawals by external parties)*		5	
17.5.3.4 Deviations	*Handling of deviations and delimitation criteria of the individual systems available is regulated (e.g. hospital CIRS vs. Swisstransplant CIRS)*	1	2	2
17.5.3.5 Risk analyses	*Carrying out documented prospective risk analyses*			5
17.5.3.6 Change management (change control)	*Change control process in place*			5

Table 1: Gap-analysis of the QA-inventory in donation networks. The evaluation of networks shows th number of networks classified as fully compliant (Well), mainly compliant (Satisfactory) or to be improved in relation to the listed requirement.

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Controversies and standards in organ donation

BOS_17_2 IS LIVING KIDNEY DONATION WITH EXPANDED CRITERIA SAFE FOR THE DONOR? LONG-TERM FOLLOW-UP FROM THE CATALAN REGISTRY

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Background: In order to reduce the waiting list for kidney transplantation, Spain has seen a growing number of living donors with expanded criteria in recent years. This implied a great concern for the safety of the donors regarding survival and evolution of renal function.

Methods: Using the Catalan Registry of Kidney Living Donors, we describe the characteristics of 2.510 living donor kidney transplants performed in Catalonia between the years 2000 and 2023 in order to observe long-term donor's survival and the evolution of their renal function.

Results: There is an initial pre-donation difference in the estimated glomerular filtration rate (eGFR) when the donor is >70 years old compared to those under 70 years old (79.5 ml/min vs. 93.4 ml/min, p<0.00). This difference persists throughout the follow-up, with no evidence of progressive long-term eGFR loss in either group. Similarly, the eGFR remains very stable in donors with lower pre-donation CKD-EPI (<70 ml/min) compared to those with higher pre-donation CKD-EPI (>70 ml/min). During the follow-up period, 48 living donors died (1.92%). The main causes were neoplasia (29.2%), infections (8.3%), cardiovascular causes (6.2%) other causes (14.6%) and unknown (41.7%). Just 2 donors required dialysis and were transplanted immediately using deceased donors. The following table shows the results for our main concern, the long term evolution of the living donors' renal function according to different characteristics.

Conclusions: Throughout the follow-up, we found statistically significant differences in post-donation renal function among living donors based on their age and glomerular filtration rate at the time of donation. However, the glomerular filtration rate measured three months after donation remains very stable over 10 years of follow-up, both in living donors with expanded criteria and those without, ensuring that donation in this type of donor is safe in the long term.

Living donors CKD EPI ml/min	Basal	3rd month	1 year	3y	5y	10y	p-value
>70 years n=127	78	51.6	51.9	57.1	55.1	54.8	P=0.0000
<70 years n=1939	93	62.8	64.1	67.1	67.9	68.3	
CKD EPI < 70 ml/min n=163	68	51.3	53.3	56.9	56.4	56.3	P=0.0000
CKD EPI > 70 ml/min n=1903	95,2	63.1	64.3	67.4	68	68.7	
Proteinuria > 150 mg/24 h n=312	91.7	63.6	63.3	64.9	64.6	64.3	p>0'05
Proteinuria < 150 mg/24 h n=2132	93.2	62.5	63.4	66.9	67.5	68	

BOS_17_3 INFLUENCE OF DISTRUST, MISTRUST, AND MISCOMMUNICATION ON COOPERATION TOWARD DECEASED ORGAN DONATION IN INDIA

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Background: In India, a major barrier to deceased organ donation is the widespread lack of trust, which significantly influences public attitudes and behaviors. However, primary research exploring the root causes of this trust deficit, and the spread of misinformation is lacking. This study aims to explore the perceptions and experiences that affect trust in organ donation and how this undermines public cooperation for the public good.

Methods: A qualitative study was carried out with twenty-five focus groups (n = 87), stratified by region, religion, gender, and age. The data were analyzed using framework analysis in NVivo v.20.

Results: While the public acknowledges that organ donation saves lives, a lack of trust in India's healthcare and organ donation system hinders cooperation. Many associate organ donations with no financial cost, but view transplants as accessible only to the wealthy, questioning the altruistic nature of donation and highlighting unequal access for lower socio-economic groups. Low donation rates and negative portrayals in social media and movies further damage trust. The lack of clarity around the affordability of transplants and the underrepresentation of organ recipients from diverse religious, socio-economic backgrounds, and hospitals further erodes trust and hinders cooperation. Additionally, the trust with general healthcare practices in private and public hospitals influenced these issues.

Conclusions: The findings highlight the need for targeted organ donation campaigns to build trust by addressing systemic issues, enhancing transparency, and engaging with community concerns. The limited visibility of public hospitals performing transplants fuels the perception that organ donation benefits only the wealthy, while negative portrayals in social media and films further erode trust. Overcoming these misconceptions is crucial for fostering a positive public attitude towards deceased organ donation.

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Controversies and standards in organ donation

BOS_17_4 UNSEEN RISKS: ELEVATED SUICIDE RATES AMONG KOREAN LIVING LIVER DONORS IN A GLOBAL CONTEXT

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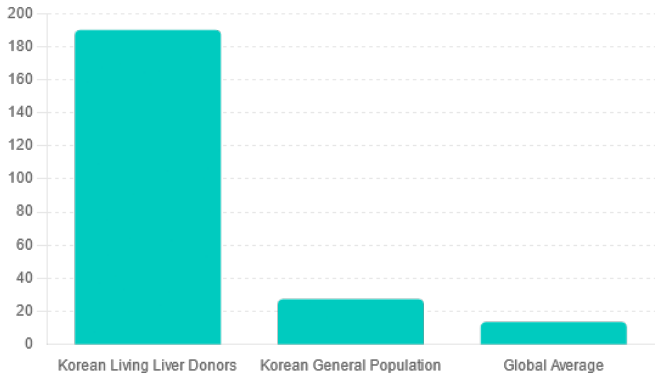
Background: Living donor liver transplantation (LDLT) is a vital solution to organ shortages in Korea, where deceased donor rates are critically low. However, LDLT donors face unique psychosocial risks. Recent studies show their suicide rate is seven times higher than the Korean general population and 14 times higher than the global average. These findings underscore the urgent need for intervention.

Methods: Data from two Korean studies involving 10,000+ LDLT donors were reviewed. Mortality causes, particularly suicide, were analyzed and compared to Korean and global suicide rates, as well as living kidney donor outcomes. Contributing factors, including cultural and healthcare system challenges, were examined.

Results: Korean LDLT donors exhibit a suicide rate of 190 per 100,000, compared to 27.3 per 100,000 in the Korean general population and 13.5 globally. Suicide accounted for 35% of all donor deaths, influenced by inadequate mental health support, familial pressures linked to Confucian values, and unmet expectations post-donation. In contrast, living kidney donors show no significant suicide risk increase.

Conclusions: The findings highlight the critical need for comprehensive mental health strategies for LDLT donors. Recommendations include mandatory psychological evaluations pre- and post-donation, shorter follow-up intervals, and proactive support for high-risk individuals. Korea's donor suicide rate reflects severe systemic gaps, necessitating immediate policy and clinical interventions.



BOS_17_5 ORGAN DONATION AFTER EUTHANASIA IN THE NETHERLANDS, A SUMMARY OF 12 YEARS

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Background: Organ Donation after Euthanasia (ODE) is possible for patients with hopeless suffering (somatic or psychological), for whom the euthanasia request has been granted and subsequently wish to donate their organs. Excluded are patients with contraindications to donation. Euthanasia has been legal in the Netherlands since 2001, provided that the conditions of the Euthanasia Act (1) are met. Since 2001, euthanasia has been performed about 106,000 times (2). The first ODE in the Netherlands took place in 2012 (3) for a patient suffering from a neurodegenerative disorder. Since then, both the number of requests for euthanasia and ODE have been progressively increasing. Since 2012, it has been possible to donate lungs, liver, pancreas, and kidneys. Since 2021, heart donation has been feasible using the 'heart-in-a-box' method, thereby increasing organ potential. The aim of this abstract is to provide an insight into the background of the ODE procedures.

Methods: Data on organ donation after euthanasia and transplantation was retrieved from the NTS database.

Results: From 1-1-2012 until 1-1-2025, 3504 (3) organ donations took place in the Netherlands, 155 (4.4%) were ODE procedures. Although the average proportion of ODE to post-mortem organ donation over these years was 4.7%, we see a proportion of 8.2% in 2023 and 9.7% in 2024. Of these 155 ODEs, 72 (46%) were men and 83 (54%) were women. 76 (49%) cases were based on somatic burden, and 79 (51%) on psychological suffering. An increase in ODE due to psychological suffering has been observed since 2018 (4). Of these 155 ODEs, 32 (20.6%) hearts, 102 (65.8%) lungs, 100(64.5%) livers, 27 (17.4%) pancreases and 282 (91%) kidneys have been transplanted.

Conclusions: Since 2012, there is a gradual increase in the number of ODE patients, with a large increase in 2023 and 2024. In addition, a shift from somatic to psychological underlying diseases have been seen since 2018. The results show that the ODE patient category is a valuable addition to the already existing donor potential.

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Controversies and standards in organ donation

BOS_17_6 EDUCATING THE FUTURE GENERATION ON BLOOD, STEM CELL AND ORGAN DONATION AND TRANSPLANTATION IN THE UK

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Background: In 2021, blood, stem cell and organ donation and transplantation (BSODT) became part of the national curriculum for secondary schools in PSHE (Personal, Social, Health and Economic) Education for KS 3 and 4(1). NHSBT provide links to PSHE Education Association Quality Assured Resources, on their website (2). There is a lack of data about what is being taught, awareness of available resources and if there are inequalities in accessing information on this subject across the UK.

Methods: Two electronic surveys were designed, (one for primary and one for secondary schools) and circulated to all schools in the Northeast of England January 2024. Questions included the following themes: demographic information; awareness of BSODT; current resources available; local provisions and delivery; challenges in teaching BSODT in Schools;

Results: Responses were captured Jan- Aug 2024 and represented a diverse group from across the Northeast region, including academies, faith schools, voluntary schools, local authority and private. Some primary school and secondary school respondents did not feel confident to teach this topic (61% and 20% respectively). Many were not aware of the existing NHSBT resources but would be interested in using them (85% and 20%). The biggest challenges in teaching this topic, were thought to be the sensitivity of the subject (69% and 100%), and confidence to teach this topic (62% and 40%). Among primary schools, Student age (69%), and the reaction of families to the topic were also of significant concern (54%).

Conclusions: This regional pilot has provided valuable insight into how we can best support our teaching colleagues and facilitate the education around blood, stem cell and organ donation and transplantation in our schools. Following this pilot, we hope to be able to roll this survey out across the UK to obtain a national picture that will enable us to identify areas of focus and inform the format of support for education around organ donation and transplantation in the wider community. Schools should be supported to deliver these messages in a positive way and have accessible, appropriate, tools to do this.

BOS_17_7 UNCONTROLLED DONATION AFTER CIRCULATORY DEATH ONLY LUNG IN PERIPHERAL HOSPITAL IN TUSCANY

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Background: Uncontrolled Donation after Circulatory Death (uDCD) only lung was implemented in the Tuscany Region in 2018 and it is still active both in Arezzo and in Grosseto (peripheral hospitals not equipped with ECMO team). In the present manuscript we describe our 6-year experience since uDCD only lung implementation.

Methods: We report, during the study period (2018 – 2024 October) the number of activations of the transplant coordinators, the number of uDCD donors, actual donors and the number of transplants. Data were compared between the time before and after COVID pandemic. In Italy, death certification requires, according to law, a 20 min no touch period.

Results: During the study period, the number of activations was 125, with a significant and gradual increase over time. The number of actual donors significantly increased in the comparison between before and after COVID pandemic (p=0.01, chi square test). Refusal rates did not differ between the two periods (Table 1) . Two donors were suitable for transplantation and two lung transplants were performed (one double transplant and one single transplant). The Regional Lung Transplant Center is about 80 Km far away from procurement centers (both Arezzo and Grosseto). This led to an adaptation of the local protocols, since ex-vivo perfusion started at the procurement center.

Conclusions: According to our 6-year experience, uDCD only lung proved to be feasible, despite the distance between the procurement centers and the Regional Lung Transplant Center. The increased number of actual donors strongly suggest an empowerment of transplant coordinators.

Key words: uncontrolled donation after circulatory death, only lung program, health care organization, transplant and procurement coordination

	2018-2020	2021-2024	p
Donors	12	35	0.01#
Refusal rates	3	11	0.67#
Actual donors	4	9	0.03#
Transplants		4	

chi square test

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BOS_17_8 BRIDGING PERSPECTIVES ON ORGAN DONATION IN ROMANIA: FOCUS ON DONATION AFTER CIRCULATORY DEATH

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Background: The increased use of donors after circulatory death (DCD) has reduced waiting times, addressing the gap between transplant demand and organ availability. However, DCD practices vary globally due to differences in resources, population needs, healthcare capacity, and cultural values.

Methods: A cross-sectional study using a 20-item questionnaire by the Romtransplant Association explored cultural, social, and professional perspectives on DCD. It was distributed to HCPs, family practitioners, medical students, and the general population via email and social media.

Results: 788 individuals viewed the questionnaire, with an 88.3% agreed to complete it. Of the respondents, 70.7% were HCPs; 90.2% resided in urban areas, and 65.7% were female. The age distribution was as follows: <20 years (0.6%), 21-30 (7.3%), 31-40 (29.3%), 41-50 (24.3%), 51-60 (22.9%), 61-70 (13.6%), 71-80 (1.9%), >80 (0.1%). Significant differences were observed between HCPs and the general population. HCP were less like to discuss donation with their family (p=0.001) and placed less value on the importance of family decisions about donation compared with the general population (p<0.0001). However, HCP had more knowledge about DCD (p=0.0004) and were more likely to self-enroll as a donor (p=0.01). The general population perceived the usefulness of discussing donation with family practitioners more than the HCP (p=0.004). No significant differences were found between groups regarding familiarity with the donation act (p=0.31), its perceived importance (p=0.37), the cultural or religious influences on donation (p=0.06 and p=0.14, respectively), the ethical considerations regarding DCD (p=0.10), or the adequacy of information about becoming a DCD donor (p=0.28).

Conclusions: Despite shared recognition of the lifesaving potential of organ donation, significant disparities persist between HCPs and the general population in attitudes, knowledge and actions regarding donation (both brain dead and DCD). Addressing these differences is essential for fostering a culturally sensitive and unified approach to increasing organ donor registrations and successfully introducing DCD in Romania.

BOS_17_9 A QUANTITATIVE AND THEMATIC ANALYSIS OF PUBLIC ATTITUDES TO DECEASED ORGAN DONATION IN DIFFERENT CIRCUMSTANCES

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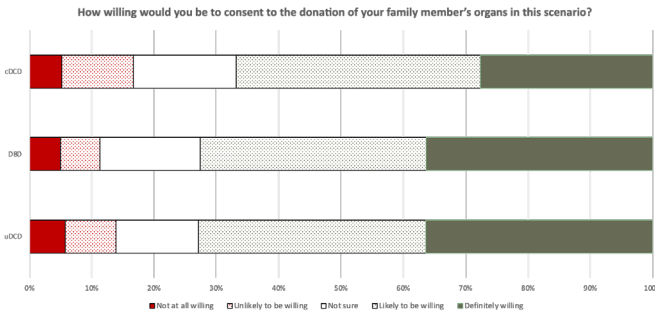
Background: Despite the great shortage of organs for transplantation, retrieval only happens in the UK in controlled settings: donation after brain death (DBD) or following withdrawal of life support (controlled donation after circulatory death, cDCD). No framework exists for death following sudden irreversible cardiac arrest (uncontrolled donation after circulatory death, uDCD). Little is known about the general public's knowledge and attitudes about different donation practices.

Methods: A questionnaire was developed based on a literature review of the ethical issues associated with uDCD; face and construct validity were established. Participants read three scenarios (DBD, cDCD, uDCD) relating to being asked about organ donation (with clear explanations of what was involved, including cannulation and reperfusion of organs for uDCD) in a randomised order. Each vignette was followed by Likert and open-ended questions. Quantitative and thematic analyses were undertaken.

Results: 505 UK participants, representative of ethnicity, gender and age completed the survey. Participants were likely/definitely willing to donate in 366/504 (73%) for DBD; 336/505 (67%) for cDCD; and 368/503 (73%) for uDCD. 96% believed uDCD is already part of donation practice. Qualitative analysis revealed altruism as the most dominant theme. Participants did not want organs wasted, wanted to respect loved-ones' wishes, and thought organ donation would provide comfort for the bereaved. For uDCD 71% agreed/strongly agreed that prioritising the chance to donate, including invasive techniques, was most important, noting the value of time for discussion; 93% thought they would need less than 4 hours to decide. A small proportion of people did not support organ donation in any situation, largely for bodily integrity and religious reasons.

Conclusions: The UK public broadly supports donation in all circumstances, including uDCD, which the majority think already happens. There is unlikely to be public objection to the introduction of organ donation after sudden irreversible cardiac arrest in the UK.



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BOS_17_10 UTILIZATION OF LIVER GRAFTS OBTAINED FROM DONATION AFTER MEDICAL ASSISTANCE IN DYING: THE CANADIAN EXPERIENCE

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Background: Limited information is available regarding outcomes of liver transplantation (LT) with grafts obtained following medical assistance in dying (MAiD) donors. We aimed to assess the post-LT outcomes in MAiD donors.

Methods: LTs from MAiD donation after circulatory death (DCD type V) were compared with DCD type III between 2016 (legalization of MAiD in Canada) and 2023 across all Canadian transplant centers. Primary outcomes included recipient and graft survival rates at years 1, 3, and 5. Secondary outcomes included any postoperative complications and biliary complications. Follow-up was at least one year.

Results: Overall, 313 patients were transplanted with 56 (17.9%) and 257 (82.1%) DCD-V and DCD-III, respectively. DCD-V donors were older (p<0.0001) and had shorter warm ischemic time (p=0.006). Early allograft dysfunction according to Olthoff criteria was higher in the DCD-III cohort (57.5% vs 42.9%, p=0.047), however DCD-V had longer hospital stay (15 vs 21.5 days, p=0.011). For DCD-V, patient survival was 89.3%, 85.7% and 85.7% at 1-,3- and 5-years, whereas graft survival was 82.1%, 78.6% and 78.6% at 1-,3- and 5-years. These survival rates did not differ significantly from those in the DCD-III cohort (mortality: p=0.629, graft survival: p=0.986). Adjusted multivariable analysis demonstrated that DCD-V was not independently associated with graft loss (OR:1.35; 95%CI:0.39-4.68; p=0.639) which was confirmed at multivariable Cox regression analysis (HR:1.58, 95%CI:0.59-4.27, p=0.363). Overall, occurrence of any post-operative complications did not differ between the groups. Notably, there was an increased incidence of overall biliary complications in DCD-V (23.1% vs 32.1%), but not statistically significant (p=0.153).

Conclusions: Liver grafts from MAiD donor may be successfully transplanted with comparable outcomes to DCD-III and contributed to a 21.8% increase of DCD activity across Canada. These results justify additional efforts to consider MAiD as a valuable additional source of liver grafts. Further studies and larger clinical experience are necessary to validate these results.

BOS_17_11 KEY PERFORMANCE INDICATORS ORGAN DONATION SHOW HIGHEST NUMBER OF DONORS IN THE NETHERLANDS AFTER CHANGING DONOR ACT

Nichon Jansen[1], Martin Heemskerk[2], Aline C. Hemke[3], Michael Kuiper[4]

[1]Dutch Transplant Foundation; Na; Policy / Research, [2]Dutch Transplant Foundation; Dutch Transplant Foundationn; Research, [3]Dutch Transplant Foundation; Dutch Transplant Foundation; Researcg, [4]Dutch Transplant Foundation; Medical Center Leeuwarden; Policy

Background: In July 2020, the Netherlands changed its donor act from an opt-in model to an opt-out system. The primary goal was to register the donor preferences of 7 million unregistered residents out of a total population of approximately 14 million Dutch inhabitants aged 18 and older, thereby increasing the number of donors. Implementation was completed in July 2021. This study evaluates the new act by analysing the key performance indicators (KPIs) for organ donation.

Methods: Data from the Donor Register were used to compare differences between 2019 and 2021. National data on deceased patients in intensive care units (ICUs) were used to analyse the KPIs: potential organ donors; consultation of the Donor Register; family approach; consent; referral; organ retrieval. Starting point was the number of deaths in ICUs. The year 2019, before changing of donor act, was compared with the years following implementation (2021 – 2024).

Results: After implementation of the new act, the whole population over 18yo was registered: 34% “Yes”, 31% “No”, 24% “No objection”, and 11% “Decision by next of kin”. In comparison to 2019, when 6.4 million residents were registered: 58% “Yes”, 31% “No”, and 11% “Decision by next of kin”. The KPIs demonstrate the largest increase in the number of potential donors, positively influencing all subsequent KPIs. The strongest effect is seen in the number of given consent following family approaches, compared to 2019 (see Figure 1). The year 2024 resulted in the highest number in donors (see Figure 2). The number of deaths decreased from 7,373 in 2019 to 6,743 in 2024.

Conclusion: The KPIs for organ donation have improved after changing the donor act, culminating in the highest number of donors in 2024. There are more potential donors, despite a decline in the number of deaths. Consent for donation, relative to the number of family approaches, is much higher compared to 2019. The registration of all residents’ donation preferences appears to have had a positive impact. However, other factors also contribute to the increase in donors. These factors include; an increase in donors after euthanasia, use of extended criteria donors, and machine perfusion techniques.

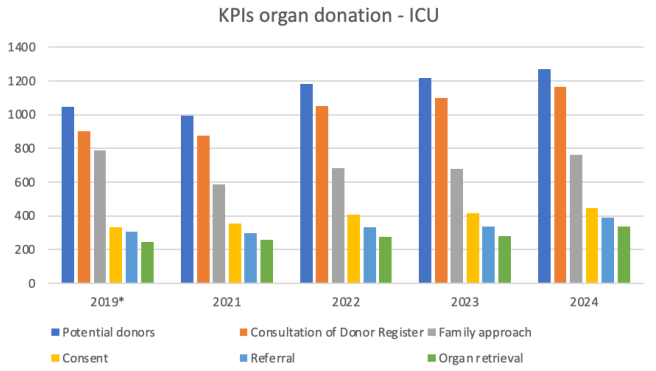

Figure 1. Key performance indicators donation – ICUs 2019*, 2021 - 2024
*2019= reference year

Figure 2. Number of donors in the Netherlands 2001 - 2024

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BOS_17_12 THE WEAKNESS OF EVIDENCE ABOUT OPTING-OUT SYSTEMS EFFICACY: RESULTS OF A SYSTEMATIC ANALYSIS OF PANEL STUDIES

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Background: In the last decade, there has been an important debate about the advantages of implementing presumed consent (opt-out) donation policies. Evidence based on panel studies mostly support the superiority of presumed consent systems for achieving higher donation and transplantation rates. Nevertheless, the analysis of the existing evidence from the point of view of program evaluation frameworks shows serious methodological limitations. The aim of this work was to perform a systematic analysis of the robustness of evidence derived from panel studies comparing opting-out and opting-in systems outcomes.

Methods: An exhaustive literature search was performed to identify the existing panel studies that aimed to compare the efficacy of opting-out and opting-in donation systems. Fifteen works were identified within the period 2003-2023. A conceptual model of factors conditioning deceased organ donation pathway was built (Figure 1), which identifies ten potential factors that should be controlled to allow a reliable evaluation of the effect of donation consent policies (DCP) on organ donation rates. Panel studies were examined to determine the degree in which control factors were adequately considered. A score of 0 (no inclusion), 1 (partial inclusion) or 2 (adequate inclusion) was given to each intervening factor for each study. Quality of samples and methods were also assessed.

Results: Table 1 summarizes the results of quality assessment.

Although a significant proportion of the studies use appropriate samples and methods of analysis, none of them adequately includes those factors that need to be controlled for a reliable analysis of the effects of DCPs on deceased organ donation rates.

Conclusion: Panel studies that have compared donation rates between systems with opting-in and opting-out policies do not adequately control those factors that potentially influence rates of deceased organ donation, lacking therefore the necessary reliability to isolate the effect of DCPs from other factors. It is not possible to reliably attribute the differences found in donation rates between opting-in and opting-out systems in the existing panel to the mere effect of DCPs.

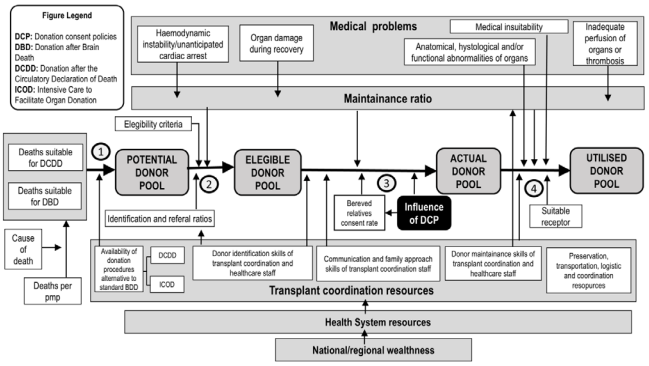

Figure 1. Conceptual model of factors that condition organ donation pathway

Authors (year)	Sample	Control factors' quality score	Quality of sample	Quality of statistical análisis
Abadie & Gay (2006)	22 countries,1993-2002	4/20	++	++
Arshad et al. (2019)	35 countries,, 2016	4/20	-	+
Bilgel (2012)	24 countries. 1993–2006	6/20	++	++
Bilgel (2013)	30 countries, 2008–2009	5/20	+	++
Coppen et al (2005)	10 European countries, 2000–2002	1/20	-	-
Coppen et al (2008)	10 countries. 1995-2005	1/20	+	-
Costa-Font et al. (2021)	28 European countries 2002-2010	6/20	++	++
Gimbel et al.(2003)	28 European countries 1995-1999	0/20	+	+
Healy (2005)	17 countries, 1990–2002	2/20	++	+
Horvat (2010)	44 countries, 1997–2007	3/20	++	-
Johnson & Goldstein (2003, 2004)	17 European countries. 1991-2001	2/20	++	+
Neto et al. (2007)	34 countries 1998-2002	4/20	++	++
Shepherd et al. (2014)	48 countries. 2000-2013	4/20	++	++
Ugur (2015)	27 European countries, 2000–2010	5/20	++	++
Vela et al.(2021)	10 USA states and 12 European countries. 2016	1/20	-	-

Quality of sample: (-) Highly restrictive temporal or/and geographical sample; (+) Limited temporal or/and geographical sample; (++) Adequate temporal and geographical sample
Quality of statistical analysis: (-) Unclearly specified or no statistical analysis; (+) Univariate analysis; (++) Multivariate analysis

Table 1. Quality assessment of panel studies

BOS_17_13 VARIABILITY OF AFTERCARE FOR ORGAN DONOR FAMILIES: INSIGHTS FROM ORGAN PROCUREMENT PERSONNEL

Macey Levan[1], Jasmine Akhtar[2], Tessa Flower[3], Carolyn Sidoti[3], Katya Kaplow[3], Brendan Parent[4], Karen Vanterpool[3], Brittany Koons[5], Allan Massie[6]

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Background: Aftercare support for organ donor families is essential. Aftercare support is facilitated by the recovering organ procurement organization in the immediate post-donation period and helps donor families navigate the emotional challenges following their loss. Despite evidence suggesting donor families have an increased risk of adverse mental health outcomes, including complicated grief, there are no standardized bereavement assessments and a paucity of research examining the availability and quality of aftercare support services. We conducted a qualitative study to better understand practice patterns and attitudes of organ procurement personnel regarding aftercare.

Methods: Semi-structured interviews were conducted with employees from 22 different organ procurement organizations to explore the structure of aftercare programs, support services, data collection practices, donor family feedback, and challenges in providing aftercare services. Two independent coders used thematic analysis to synthesize the data.

Results: Interviews with personnel revealed significant heterogeneity in aftercare program structures, with variation in program duration, communication schedules, data collection, and support services offered. Aftercare support needs differ based on family composition, language, social determinants of health, and relationship to the donor. Personnel expressed conflicting opinions about integrating a bereavement assessment into their intake process, highlighting the individuality of grief experiences. Barriers to providing comprehensive aftercare support included limited access to mental health services, low response rates on feedback surveys, inadequate resources and staffing, and internal disconnect between family support teams and aftercare coordinators. Facilitators to providing comprehensive aftercare support included fostering connection between donor families, standardizing data collection procedures, and addressing families' unique needs through support services (Figure 1).

Conclusions: These findings underscore the variability of aftercare programs across organ procurement organizations and emphasize the need for support that is tailored to individual families' situations, preferences, and social determinants of health.

Figure 1. Themes identified about aftercare support services

Heterogeneity across OPO aftercare program structure	• Program duration and communication schedule • Internal support services • External support referrals • Data collection and service allocation
Heterogeneity across donor family grief support needs	• Bereavement assessments as a means to assess support needs • Family experiences and circumstances
Barriers to providing grief support services	• Challenges around mental healthcare access • Low response rates on feedback surveys • Limited resources • Varied communication between family support coordinators and aftercare coordinators
Facilitators to providing grief support services	• Fostering connection and encouraging participation • Standardized and comprehensive data collection procedures • Meeting families where they are

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Controversies and standards in organ donation

BOS_17_14 ASSESSING HRQOL IN NON DIRECTED VERSUS DIRECTED KIDNEY DONORS: IMPLICATIONS FOR THE PROMOTION OF NON-DIRECTED DONATION

Assaf Vital[1], Eytan Mor[2], *Tammy Hod*[3]

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Background: Living kidney donation has increased significantly, but little is known about the postdonation health-related quality of life (HRQoL) of non-directed donors (NDs) vs. directed donors (DDs).

Methods: We thus examined the outcomes of 112 living kidney donors (82 NDs, 30 DDs).

Results: For the primary outcomes – namely, the mean physical component summary (PCS) and mental component summary (MCS) scores of the 12-item Short Form Survey (SF-12) questionnaire – scores were significantly higher for the NDs vs. the DDs (PCS: +2.69, MCS: +4.43). For secondary outcomes, NDs had shorter hospital stays (3.4 vs. 4.4 days), returned to physical activity earlier (45 vs. 60 days), exercised more before and after donation, and continued physical activity post-donation. Regression analyses revealed that donor type and white blood cell count were predictive of the PCS-12 score, and donor type was predictive of the MCS-12 score. Nondirected donation was predictive of a shorter hospital stay (by 0.78 days, $p < 0.001$) and the odds of having PCS-12 and MCS-12 scores above 50 were almost 10 and 16 times higher for NDs, respectively ($p < 0.05$).

Conclusions: These findings indicate the safety and potential benefits of promoting nondirected donation. However, careful selection processes must be maintained to prevent harm and exploitation.

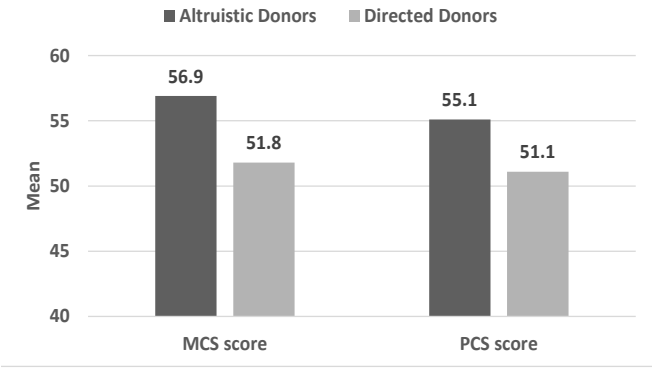

Figure: SF-12 questionnaire results: Mean MCS-12 and PCS-12 scores for nondirected vs. directed donors.

BOS_17_15 THE DECEASED TRANSPLANT RECIPIENTS: AN OVERLOOKED SOURCE OF ORGAN DONORS

***Dai Nghiem*[1]**

[1]University of California Davis Medical Center; Division of Transplantation

Background: Of 105,117 patients waitlisted in the US in 2024, only 46,630 patients got transplanted. To bridge the gap, we suggest using functioning transplanted (TO) or native (NO) organs of the deceased recipients.

Methods: The characteristics of 280,670 recipients dying with normal graft from 13 publications (SRTR, UNOS, ANZDATA, Euro-Transplant and the National French Medical Information) were analyzed.

Results: Death with functioning grafts occurred in 15-25% from CV disease. While GS of LRD kidneys was1475 days vs.1382 days for deceased donor kidneys, the TO livers and hearts lasted 25 and 11 days, respectively. As the TO kidney donor was 47 yo with CR 1.27 mg/dL vs. 1.0 mg/dL in the original donors, selection was based on eGFR. Biopsy was done to rule out damage. As cells from the original donor were not available, a negative virtual cross-match and a negative flow-cytometry crossmatch were required. Non-sensitized patients were preferred. Quadruple IS with depleting antibody and short course of steroid was used. Unlike the rejected organs, the functioning transplants do not have adhesions, thus facilitating their procurement. The donor iliac artery bearing the kidney was used for transplantation. The TO kidneys had lower 5-year GS than the NO with 75% and 78%, respectively. As the 5-year PS is 40% on hemodialysis, 50% on peritoneal dialysis, and 5,000 waitlisted individuals dying annually, patients waiting for TO and NO organs were informed when they were offered the unusual organs. The same findings apply to the NO and TO livers, hearts and lungs with 5-year GS of 74%, 70%, 76% and 50%, respectively. All together, with an annual patient attrition rate of 20-25% due to CV disease, we would expect 9,326 to 11,650 (20 to 25% of 46,630) deceased transplant donors. As one donor provides 2.9 organs, we would have additional 27,045 to 33,785 organs.

Conclusions: 1)TO and NO organs constitute a sizable source of organs. 2) They provide excellent long term function. 3) New allocation is needed to allow rapid organ placement. 4) Efforts should be developed to familiarize the public, the patients, the intensivists, the nursing staff, the OPOs staffs and the transplant community with these overlooked organs.

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BOS_18_1 INVESTIGATING INEQUALITIES IN ACCESS TO PAEDIATRIC KIDNEY TRANSPLANTATION

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[1]University of Bristol; Medical School, [2]University of Bristol; University of Bristol; Bristol Medical School: Population Health Sciences, [3]University of Bristol

Background: Our understanding of whether access to kidney transplantation inequities exist for UK children is lacking. To date, socioeconomic and ethnic inequities in access to pre-emptive kidney transplantation have been described, but no research has investigated associations with access to waitlist activation or transplantation in general.

Methods: We performed an analysis of UK Renal Registry and NHS Blood & Transplant data. The study population comprised incident patients <18 years starting kidney replacement therapies (KRT) in the UK between 1/1/96-31/12/20. Multivariable logistic regression and Cox proportional hazards models were used to determine associations between exposures (ethnicity, socioeconomic deprivation (SED) and sex) and outcomes: 1) waitlist activation for deceased donor kidney transplantation; receipt of 2) any 3) deceased donor 4) living donor kidney transplant.

Results: Adjusted Cox regression results show lower hazard of being waitlisted for females (HR 0.88, 95% CI 0.81, 0.95) compared to males; for those in the most deprived SED group (HR 0.67, 95% CI 0.59, 0.76) compared to the least deprived; and those from a Black ethnic background (HR 0.81, 95% CI 0.65, 0.99) compared to children of White ethnicity. Once waitlisted, associations with sex and SED were attenuated. However, lower hazards remained for children of Black ethnicity (HR 0.74, 95% CI 0.56, 0.97) compared to children of White ethnicity. Adjusted odds of receiving a living donor transplant within two years of starting KRT were lower for those in the most deprived SED group (OR 0.28, 95% CI 0.21, 0.26) compared to least deprived, and children of Black or Asian ethnicity (OR 0.40, 95% CI 0.24, 0.65; OR 0.47, 95% CI 0.37, 0.60) compared to children of White ethnicity.

Conclusions: Higher relative area-level deprivation and Black ethnicity are associated with lower access to waitlisting and living donor transplantation; reassuringly, variations in access to transplant are attenuated once waitlisted, suggesting interventions equitably supporting timely consideration and preparation for waitlisting are needed. Similar SED and ethnicity associations were noted for living kidney donor transplant access.

BOS_18_2 THE POTENTIAL OF NOVEL KIDNEY EXCHANGE ALGORITHMS FOR BOTH INCOMPATIBLE AND COMPATIBLE PAIRS: A SIMULATION STUDY

Mattheüs F. Klaassen[1], Marry de Klerk[2], Marije C. Baas[3], Hanneke Bouwsma[4], Laura B. Bungener[5], Maarten H.L. Christiaans[6], Twan Dollevoet[7], Kristiaan Glorie[8], Sebastiaan Heidt[9], Aline C. Hemke[10], Margriet F.C. de Jong[11], Judith A. Kal-van Gestel[12], Marcia M.L. Kho[13], Jeroen D. Langereis[14], Karlijn A.M.I. van der Pant[15], Claudia M. Ranzijn[16], Dave L. Roelen[17], Eric Spierings[18], Christina E.M. Voorter[19], Jacqueline van de Wetering[20], Arjan D. van Zuilen[21], Joke I. Roodnat[22], Annelies E. de Weerd[23]

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Background: The Dutch kidney exchange program (KEP) is currently implementing a novel algorithm, that allows ABO-incompatible (ABOi) transplantation for long waiting (LW) and selected highly immunized (sHI) patients. Additionally, it prioritizes sHI patients and allows them for "low-level" HLA-incompatible (HLAi) transplantation. We simulated these novel options along with additional KEP scenarios.

Methods: Monte Carlo simulations were performed on a database containing all Dutch KEP participants, non-directed donors (NDDs), and the deceased donor waitlist between 2018-2023, and a sample of 20% of national directed compatible pairs (CPs). We simulated the following scenarios, with 10 simulation runs each: • Current algorithm; • Novel algorithm: - priority for sHI (vPRA≥85%, dialysis ≥2 years and either declined for or ≥2 years in Eurotransplant Acceptable Mismatch program); - ABOi matching for sHI and LW (dialysis ≥2 years); • Four variants of the novel algorithm: - Two participating KEP donors per sHI/LW patient; - Allowing HLAi matching (MFI <10.000) for sHI; - Locally transplanted NDDs participating one run in KEP, while limiting their participation to local matches in their center only; - 20% of CPs with HLA A/B/DR mismatches ≥4 participating one run in KEP, with criterion mismatches ≤4.

Results: The simulated novel algorithm as compared to simulated current KEP increased median transplant rate for incompatible pairs (IPs) in KEP (47% versus 33%, p=0.002) and for difficult-to-match subgroups: 37% versus 19% for sHI (p=0.002) and 73% versus 22% for LW (p=0.002). A median of 67 LW/sHI patients were matched ABOi (Table 1). In additional simulations, HLAi matching (simulated for one center) resulted in the highest transplant rate for sHI pairs (49% versus 37%, p=0.004). Domino chains with 143 extra local NDDs facilitated median 76 transplants for IPs (transplant rate 64% versus 47%, p=0.002). Of directed CPs, 39% (n=148) had mismatches ≥4. CPs were matched in KEP in 71% and increased transplant rate for IPs (51% versus 47%, p=0.02).

Conclusions: Allowing ABOi and HLAi matching can increase transplant rates for difficult-to-match patients. KEPs should urge clinicians to counsel all NDDs and mismatched compatible pairs about KEP participation, as this improves HLA matching and multiplies match rates in KEP.

Table 1: Simulated transplant rates for different KEP scenario's (median of 10 simulations).

	Median number of transplants (% of participants)					ABOi/HLAi transplants (% of total transplants)
	Incompatible pairs			Compatible pairs (n=19)	NDDs (n=25)	
	All (n=472)	sHI (n=53)	LW (n=90)			
Simulated KEP algorithms						
Current algorithm	153 (33%)	10 (19%)	20 (22%)	11 (58%)	25 (100%)	-
Novel algorithm (ABOi & priority)*	223 (47%)	19 (37%)	64 (73%)	12 (61%)	25 (100%)	67 (26%) ABOi
+ two donors for sHI/LW paired patients	225 (48%)	20 (36%)	64 (71%)	12 (60%)	25 (100%)	65 (25%) ABOi
+ HLAi matching for sHI (simulated for one center only)	225 (48%)	27 (49%)	66 (72%)	11 (60%)	25 (100%)	65 (25%) ABOi 5 (2%) HLAi 2 ABOi & HLAi
Simulated novel algorithm (ABOi & priority)* with additional KEP participants						
+ locally participating NDDs (n=143)	301 (64%)	22 (42%)	69 (76%)	13 (70%)	168 (100%)	65 (14%) ABOi
+ 20% of compatible pairs mismatched ≥4 (n=148)	239 (51%)	20 (36%)	65 (72%)	113 (71%)	25 (100%)	62 (17%) ABOi
+ locally participating NDDs (n=143) + 20% of compatible pairs mismatched ≥4 (n=148)	312 (66%)	22 (41%)	69 (77%)	119 (74%)	167 (99%)	63 (11%) ABOi

sHI = selected Highly Immunized; LW = Long Waiting; NDD = Non-Directed Donor; KEP = Kidney Exchange Program; ABOi = ABO-incompatible; HLAi = HLA-incompatible.
*Priority for sHI patients only, ABOi matching allowed for sHI and LW patients.

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BOS_18_3 OUTCOMES FOR LIVER TRANSPLANTATION OUTSIDE STANDARD LISTING CRITERIA IN UK USING A NATIONAL APPEALS PANEL

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Background: In UK, there are minimum-listing criteria within four broad indications (acute liver failure, chronic liver disease, variant syndromes, and primary liver cancer) for the selection of adult and paediatric patients for liver transplant. However, there are certain conditions or indications which do not fall within these criteria and therefore get referred to the National Appeals Panel (NAP). The aim of this study was to analyse the outcomes of appeals made to NAP, and study graft/patient outcomes for those who were transplanted.

Methods: A retrospective analysis of all referrals to the NAP from January 2011 to December 2020 was conducted.

Results: Over 10 years, 149 appeals were made to the panel, with 128 (86%) approved for transplant, 19 (12.7%) declined, and 2 (1.3%) withdrawn. Super-urgent appeals had a higher success rate (93%) compared to elective appeals (81.5%). Of the 107 adult recipients (after excluding paediatric and multi-organ cases), 70 (65.4%) were transplanted, 21 (19.7%) died, and 11 (10.3%) were removed from the list. The median age of recipients was 39 years, 58% were female, and the most common indications for transplant were acute liver failure (16.8%), post-liver transplant complications (15.9%), and cholestatic liver disease (14%). Among the 70 transplanted adults, 46% were super-urgent cases, with 19% ventilated and 23% on renal support at transplant. The majority received DBD grafts (92.8%), followed by DCD (5.7%) and one living donor (1.5%). Immediate complications included hepatic artery thrombosis (5.7%), biliary complications (5.7%), and sepsis (25.7%). Graft survival at 1 and 5 years was 95% and 85%, while patient survival was 98% and 90%, respectively.

Conclusions: Despite nearly 50% of transplants being super-urgent, excellent graft and patient survival rates were observed for those transplanted following appeal to the NAP. A very high proportion of appeals are successful, indicating that whilst they did not fulfill standard listing criteria, there was national consensus as to their clinical appropriateness. The study underscores the importance of a national multidisciplinary approach for urgent or uncommon transplant indications.

BOS_18_4 HLA-ASSESS: ENHANCING KIDNEY ALLOCATION AND ACCESS FOR ETHNIC MININORITIES WITH A PROGNOSTIC ALLOIMMUNITY ALGORITHM

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Background: HLA-ASSESS is a validated algorithm that integrates HLA-DR/DQ amino acid sequence and tertiary structure data to stratify primary alloimmunity risk. This study evaluates the potential of HLA-ASSESS to improve deceased-donor kidney allocation and enhance equitable access to low-risk donors for recipients across ethnicities.

Methods: Data from 22,968 first-adult deceased-donor kidney transplants in the NHSBT registry (2000–2018) were analysed. Multivariable Cox proportional hazards models assessed the association of HLA-ASSESS-based risk stratification with all-cause graft failure (transplant survival). Matchability was evaluated by comparing probabilities of identifying low-risk donors using HLA-ASSESS versus traditional 0DR-0DQ antigen matching for each recipient against the blood group-compatible donor pool (n=16,811) using a one-versus-all approach. Simulations involved 1,000 patients resampled 100 times.

Results: Median graft survival was 13.6 years, with 30.5% experiencing all-cause transplant failure. Adjusted hazard ratios (aHRs) for transplant survival stratified by HLA-ASSESS risk categories were: low risk (aHR: 1.05, 95%CI: 0.96–1.14, p=0.28), medium risk (aHR: 1.08, 0.99–1.17, p=0.08), high risk (aHR: 1.09, 1.00–1.15, p=0.045), and very high risk (aHR: 1.18, 1.08–1.31, p=0.002). HLA-ASSESS was independent of HLA Class-I antigen mismatching and demonstrated robust prediction of transplant survival (AUROC: 65.3, 68.3 and 71.7 at 5-,10- and 15-years post-transplant, respectively). Replacing HLA-DR mismatching with HLA-ASSESS in the NHSBT HLA Levels-based allocation model yielded comparable discrimination and calibration. Across the donor pool, HLA-ASSESS increased access to low-risk donors compared to antigen matching (Figure-1A). Notably, the probability of finding low-risk HLA-DR and -DQ donors was significantly higher using HLA ASSESS compared to HLA-DR/DQ antigen matching for recipients of every ethnic background (Figure-1B).

Conclusions: HLA-ASSESS facilitates precise alloimmunity risk stratification, robust transplant survival prediction, and enhances access to low-risk donors. This approach particularly benefits ethnically diverse populations, promoting equity in kidney transplantation outcomes.

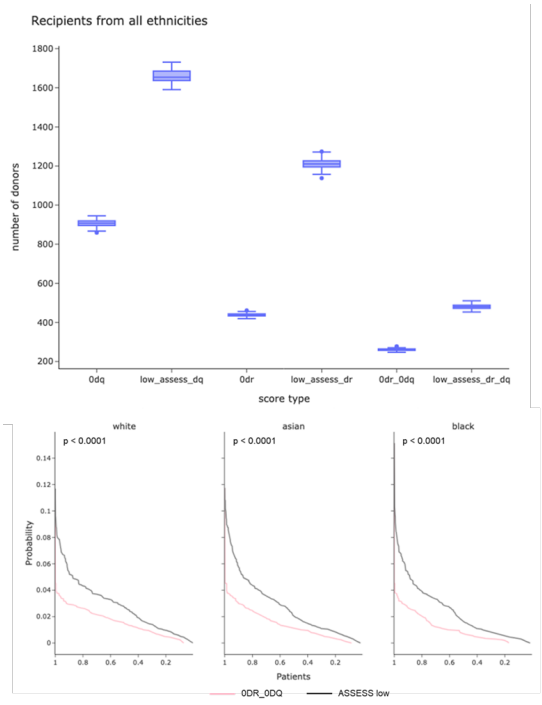

Figure1. A: Access to low immunological risk donors in random samples of 1000 actual kidney transplant recipients using HLA antigen matching versus low-risk HLA ASSESS (results from 100 resampling simulations; the graph depicts average, IQR and range for each group). B: Cumulative probabilities of finding 0DR-0DQ versus low-risk HLA-DR/DQ blood group compatible donors in the NHSBT Transplant Registry (2000-2018) for actual kidney transplant recipients from different ethnic groups.

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BOS_18_5 NRP PLUS SEQUENTIAL END-ISCHEMIC NMP IN DCD LIVER TRANSPLANT EXPANDS DONOR UTILIZATION AND FACILITATES GROWTH

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Background: NRP is a promising technique to improve outcomes in liver transplantation (LTx) from donation after circulatory death (DCD) donors with respect to primary function and biliary complication rates. Recent advancements suggest that NRP with sequential NMP may further enhance graft viability, increase access for patients living remotely, while preserving patient outcomes, particularly for the more marginal DCD graft. The benefit of combining in situ with ex situ perfusion is not known. This study aims to compare the efficacy and outcomes of liver transplants using NRP alone versus NRP followed by sequential NMP.

Methods: A retrospective observational cohort study was conducted, analyzing liver transplant outcomes from DCD donors managed with NRP alone (Group A) and those managed with NRP followed by sequential NMP (Group B). Metrics included the direct clinical endpoints of primary non-function (PNF), ischemic cholangiopathy (IC), biliary complications, and patient and graft survival rates, as well as surrogate markers such as early allograft dysfunction (EAD).

Results: The study included 100 DCD NRP liver transplants, 66 patients in group A and 34 in group B. Patient and graft survival at 1 year were similar in each group (98.5% vs. 97%, p>0.05). There was 1 death in each group. Patient demographics were similar between groups apart from the fact that Group B (NRP + NMP) demonstrated significantly higher number of redo liver transplants, more patients with extensive splanchnic venous thrombosis as well as more recipients from remote locations. Rates of PNF were zero in each group and there was zero incidence of ischemic cholangiopathy in each group. EAD rates were similar (22% Group A vs. 27% Group B, p>0.05). Biliary complications were also not significantly different between the 2 groups.

Conclusion: NRP and sequential end-ischemic NMP allows the safe use of DCD livers in patients previously thought not to be candidates for DCD organs (redo liver transplant, complex hepatectomy and recipients remote from the transplant center). The outcomes of NRP with NMP yields result equivalent to NRP alone in standard recipients. These findings support the adoption of sequential NMP following NRP to enhance graft viability and patient survival in liver transplantation from DCD donors into complicated recipients.

BOS_18_6 PREVALENCE AND CORRELATES OF HEPATIC STEATOSIS AND FIBROSIS IN CKD PRIOR TO KIDNEY TRANSPLANTATION

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Background: Metabolic dysfunction associated steatotic liver disease (MASLD), is closely linked to CKD and increases the risk of hepatic fibrosis and cardiovascular damage. MASLD is common in the general population but data on dialysis patients is limited. We aim to assess the prevalence of MASLD and related factors in kidney transplant patients at the time of list admission.

Methods: We studied 531 kidney transplant patients (age 49±13, 59% male) from 2010-2020. We noted their data at admission. Hepatic steatosis (HS) was gauged by hepatic steatosis index (HSI), with >36 as pathological (HSI+). Advanced fibrosis (>F3) was assessed by Fibrosis-4 index (FIB4), with >1.3 and >2.66 as borderline and pathological (FIB4+), and the NAFLD Fibrosis Score (NFS), with >-1.455 and >0.676 as borderline and pathological (NFS+).

Results: In our study, 67.2% of patients had hemodialysis. At evaluation, 8.8% had diabetes, 15% were obese, and 37.5% had steroid treatment history. Glomerulonephritis and polycystic kidney disease caused nephropathy in 20% and 18% of cases, respectively. HSI, FIB4, and NFS averages were 32.9±6.01, 1.25±1.07, and -1.75±1.5. FIB-4 and NFS correlated strongly (r=0.65, p<0.0001). HS by HSI+ was in 27.5% of patients, while hepatic fibrosis by FIB4+ and NFS+ was in 32.8% and 39.3% of patients. HSI+ patients were older with higher BMI, glucose, and urea levels. FIB4+ and NFS+ patients were older with higher glucose and CRP levels. NFS+ patients had higher BMI. These results confirm the concordance between the two fibrosis markers. In multivariate analysis, BMI and urea were independent risk factors for hepatic steatosis by HSI, while age and CRP were independent risk factors for hepatic fibrosis by both FIB4+ and NFS+.

Conclusions: Our data reveals a high occurrence of MASLD in patients awaiting kidney transplants, particularly in older, overweight individuals. Inflammatory parameters independently predicted hepatic fibrosis, suggesting their potential role. FIB4 and NFS showed a strong correlation, validating their use as fibrosis markers. Future research could shed light on the causes, risk factors, and impacts of HS and fibrosis on kidney transplant outcomes.

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BOS_18_7 THE HAZARD OF REPEATED HLA-DRB1 AND HLA-DQB1 MISMATCHES WITHOUT PREFORMED DSA: A MULTICENTER STUDY

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Background: Repeat kidney transplantations represent up to twenty percent of renal transplants. While retransplantation in the presence of circulating donor-specific HLA antibodies derived from a previous transplantation is generally avoided, the risk of repeated HLA-mismatches in the absence of detectable antibodies is debated. This multicenter analysis evaluated the impact of repeated HLA-mismatches without preformed donor-specific antibodies, separated by HLA-class, on different transplant outcomes.

Methods: We included repeat kidney transplant recipients from January 2009 onwards with data on HLA-A, -B, -C, -DRB1, DRB3/4/5, and -DQB1 of current and previous donors. Repeated mismatches were defined at the split serological antigen level, excluding patients with only HLA-DP or HLA-DRB3,4,5 mismatches. Patients were included if: a] preformed donor-specific HLA-antibodies were never detected before and b] this was confirmed by Luminex assays in the period within six months before transplantation.

Results: A competing risk model accounting for the competing risk of death and adjusting for demographic factors and HLA-mismatch load revealed a significant risk of graft loss within one-year post-transplant for patients with HLA-DRB1 and/or HLA-DQB1 repeated mismatches (HR 3.81 [95% CI 1.43–10.12], P=0.007). Multivariable Cox-proportional hazard modeling revealed a significant risk associated with HLA-DRB1 and/or HLA-DQB1 repeated mismatches for one-year biopsy-proven rejections (HR 1.98 [95% CI 1.04–3.75], P=0.037), and DSA development (HR 9.89 ([95%CI 1.92 – 50.99], P=0.006). No significant risk was found for patients with HLA-class I repeated mismatches.

Conclusions: Based on our results, we suggest to avoid HLA-DRB1 and HLA-DQB1 repeated mismatches when possible

BOS_18_8 ML MODEL TO PREDICT WAITLIST MORTALITY FOR LIVER TRANSPLANT CANDIDATES WITH DECOMPENSATED CIRRHOSIS

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Background: Predicting waitlist mortality for liver transplant (LT) candidates remains a critical challenge due to the complexity of patient profiles and competing risks. Traditional models such as MELD, MELD-Na, and MELD 3.0, while effective in assessing liver dysfunction, lack the precision needed to capture dynamic, patient-specific factors. This study aims to evaluate the performance of an explainable ML model over traditional Model for End-Stage Liver Disease (MELD) scores in predicting 3-month mortality among adult LT candidates.

Methods: We conducted a retrospective cohort analysis using data from the Organ Procurement and Transplantation Network/United Network for Organ Sharing registry, covering patients listed for liver transplantation (LT) from February 27, 2002, to September 30, 2023. Employing LightGBM, we compared its performance against MELD, MELD-Na and MELD 3.0 scores in predicting waitlist mortality. SHAP was used to improve model explainability and to identify critical predictive factors.

Results: Among 94,891 patients, 11,466 died or were delisted within 3 months (mean age 55, raw MELD 31) and 83,425 surviving on the waiting list (mean age 53, raw MELD 16). MELD, MELD-Na and MELD 3.0 achieved AUCs of 0.881 (95% CI: [0.880, 0.882]), 0.888 (95% CI: [0.887, 0.889]) and 0.884 (95% CI: [0.882, 0.885]), respectively. LightGBM demonstrated superior predictive performance over MELD scores, with an AUC of 0.934 (95% CI: [0.933, 0.935]). This corresponded to a sensitivity of 85.51% (95% CI: [85.23, 85.79]) and specificity of 85.77% (95% CI: [85.44, 86.09]). SHAP analysis revealed new key predictors of mortality, beyond traditional MELD components, including patient's functional state, age at registration, degree of ascites, and bilirubin changes over time.

Conclusions: Our explainable machine learning model outperforms traditional MELD-based scores in predicting 3-month waitlist mortality for liver transplant candidates. By integrating dynamic and static factors such as bilirubin changes, functional state, and degree of ascites, this model provides a comprehensive and personalized risk assessment. It represents a promising tool to refine organ allocation strategies and improve patient outcomes, pending prospective validation.

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BOS_18_9 TRENDS IN HEART TRANSPLANTATION IN PORTUGAL: RECENT INCREASES AND THEIR IMPLICATIONS

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Background: Heart transplantation is a vital treatment option for patients with end-stage heart failure. In Portugal, significant efforts have been made to enhance organ donation and transplantation processes, resulting in notable increases in the number of heart transplants. This study aims to analyze recent trends, contributing factors, and their implications for the Portuguese healthcare system.

Methods: A retrospective analysis of national heart transplant data was conducted, focusing on procedures performed over the past two years. Key variables analyzed encompassed annual transplant rates, the number of transplants relative to patients on the waiting list, the distribution of hearts by urgency level, improvements in organ acceptance rates and rate of offers to the Spanish National Transplant Organization - ONT.

Results: Heart transplant in Portugal have increased significantly, with a 43% rise in 2023 and a 56.8% rise in 2024 compared to 2022. This growth is primarily attributed to key reforms, including revised allocation criteria and urgency classifications, which enhanced the distribution of hearts based on urgency levels. Improved organ acceptance rates also played a crucial role, with a significant reduction in non-acceptances due to weight and stature mismatches, organ damage, ABO incompatibility, positive crossmatch, or COVID-positive donors. Some organs that could not be accepted in Portugal were offered to the ONT, representing rates of 8.62% in 2023 and 3.33% in 2024. Furthermore, post-transplant mortality rates showed remarkable improvement, decreasing to 7% in 2023 and reaching 0% in 2024.

Conclusions: The remarkable growth in heart transplant numbers in Portugal over the past two years highlights the transformative impact of strategic reforms in allocation criteria, urgency classifications, and organ acceptance processes. These advancements have not only optimized the equitable distribution of donor hearts but also significantly reduced post-transplant mortality rates. Portugal's success may serve as a compelling model for other healthcare systems, demonstrating how evidence-based policies and innovation can improve outcomes for patients with end-stage heart failure. Continued investment in these areas will be crucial to sustaining and furthering these achievements.

BOS_18_10 DELISTING LOW-LEVEL HLA ANTIBODIES CREATES OPPORTUNITIES FOR HSPS WITH ACCEPTABLE LONGTERM OUTCOMES

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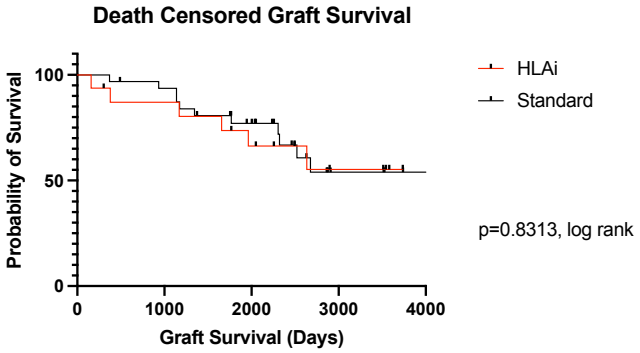
Background: In 2014 we introduced a policy for antibody delisting which permitted low-level HLA incompatible transplants. Antibodies directed against HLA-A, -B, -DR with a median fluorescent intensity (MFI) < 5000, and <8000 MFI for HLA-C and -DQ were removed from the NHSBT profile, aiming for an absolute reduction in calculated reaction frequency (cRF) >=10. Patients were tested using single antigen beads (SAB) every month, and the NHSBT antibody profile was maintained using the most current SAB result. The programme ran until 2020 when it was halted following the onset of COVID.

Methods: HLAi transplants were compared with a control group of standard immunological risk recipients who received contemporaneous transplants that were matched in a 2:1 ratio according to donor type. Clinical outcomes including graft and rejection free survival were assessed.

Results: Sixteen HLAi transplants occurred following a median reduction in cRF of 28 (range 2-62). The median cumulative DSA was 2406 MFI (range 194 – 13118) across up to 3 different HLA class I and II specificities. Cell-dependent cytotoxicity and flow crossmatching was T-cell negative, B-cell negative in 14 cases. Two cases were flow crossmatch B-cell positive. Standard transplants were more likely to have a better matchgrade compared with HLAi transplants (57% level 1 or 2 standard vs 19% level 1 or 2 HLAi, p=0.028). There was no significant difference in the rate of delayed graft function (DGF 4/32, 12% Standard vs 5/16, 31% HLAi, p=0.1377), or cold ischaemia time (mean CIT 13.4h standard vs 14.7h HLAi, p=0.297). Over a median follow up of 2246.5 days (range 159-5435), indication biopsies were performed in 28 patients (16 standard, 12 HLAi). Rejection free survival was significantly reduced in the HLAi group (p=0.01288 log rank), with rejection occurring in 50% of the HLAi group (19% standard). However, HLAi transplants were not associated with reduced death-censored graft survival (p=0.8313, log rank, Figure 1).

Conclusions: Delisting antibody-defined unacceptables using a higher MFI threshold has increased transplanting opportunities in our highly sensitised cohort. Whilst associated with early rejection episodes, long term graft survival is not negatively impacted.



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BOS_18_11 PROTOCOLS FOR LIVER TRANSPLANTATION IN COLORECTAL LIVER METASTAES: CREATING AN INTERACTIVE TOOL FOR PATIENT SELECTION

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Background: Patients with unresectable colorectal liver metastases (CRLM) carry a dismal prognosis- LT showed acceptable results in pioneer studies and now the field is exploding with studies concentrating on refining patient selection. Thus, clinicians may be confused by the abundance and diversity of possible enrolment schemes. We conducted a systematic review with the aim of providing clinicians with a tool to select patients for LT for CRLM protcols.

Methods: A systematic review was conducted for all protocols for LT in CRLM. Both protocol with published data and those with ongoing studies were included. The primary aims were the identification of a) protocol inclusion criteria b) protocol exclusion criteria.

Results: 27 studies were included. Age limits and satisfying performance status were featured in most protocols. Other patient-parameters included weight loss, history of malignancies and current blood tests. Primary rectal or right colonic locations were exclusive in 7% and 4%, respectively. Radical surgery of the primary was required in 52%, while patients could be excluded for inadequate margins (11%), advanced T (22%) or N (19%) staging. BRAF mutation was an exclusion criteria in 44% of protocols, while by microsatellite instability and RAS in 19% and 4%, respectively. The number of hepatic lesions was considered in 18% of protocols and their dimensions in 33%. Extrahepatic disease was not admissible in 63%, while 33% accepted patients with limited resectable lung lesions. Systemic therapy was mandatory in 93% of protocols, with partial response (22%) or stability (63%) required by most. A tool was developed, intended for consultation by clinicians who can input patient data to obtain the names of which protocol(s) (if any), appear suitable for individual patient enrolment.

Conclusions: Selecting candidates for LT for CRLM may be a bewildering task. The newly provided tool may prove useful to encourage widespread consideration of LT as a therapy for CRLM.

BOS_18_12 SAMOTHRACE AI MONITORING OF TELE-HEALTH FOR CIRRHOTIC PATIENTS WITH ACUTE DECOMPENSATION AWAITING LIVER TRANSPLANTATION

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Background: Patients with advanced chronic liver disease (ACLD) are at risk of hepatic decompensation, which often leads to recurrent hospitalizations during the transition from compensated to decompensated cirrhosis. Early detection is essential, especially for those awaiting liver transplantation, to avoid waiting-list dropout. This study aims to assess the feasibility of remote management to prevent acute decompensation (AD) events, combined with a tele-rehabilitation system based on Liver Frailty Index (LFI).

Methods: Individuals with ACLD were monitored using the Samothrace system and compared with contemporaneous matched controls receiving standard follow-up care. Commercially available monitoring devices were linked to the Samothrace app to enable daily recordings of heart rate, blood pressure, weight, body water percentage, and cognitive function (Stroop test and EEG) forming the basis of an AI-driven telemonitoring system.

Results: Since October 2024 Forty-two patients were enrolled, 73% male (n = 31), with a median age of 60 years (SD 7.8) and a median BMI of 28 (SD 5.25). The leading etiology was MASH (40%, n = 17). Most patients were classified as Child-Pugh B (52%, n = 22), and 38% (n = 16) had hepatocellular carcinoma. Comorbidities included diabetes mellitus in 38% (n = 16) and hypertension in 54% (n = 23). A significant proportion had prior hepatic decompensation: 57% (n = 24) with ascites, 26% (n = 11) with bleeding, and 19% (n = 8) with encephalopathy. Based on the Liver Frailty Index (LFI), 59% (n = 25) were pre-frail, 7% (n = 3) were frail, and 40% (n = 17) were robust. Three patients (7 %) underwent liver transplantation during the study.

Conclusions: Although the data are preliminary, the Samothrace system represents a novel and promising approach to managing patients awaiting liver transplantation. By combining continuous remote monitoring with AI-driven insights, this system has the potential to improve clinical outcomes and reduce the risk of drop-out from the transplant waiting list.

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BOS_18_13 ABO-COMPATIBLE KIDNEY ALLOCATION WITH ABO-ADJUSTED CPRA

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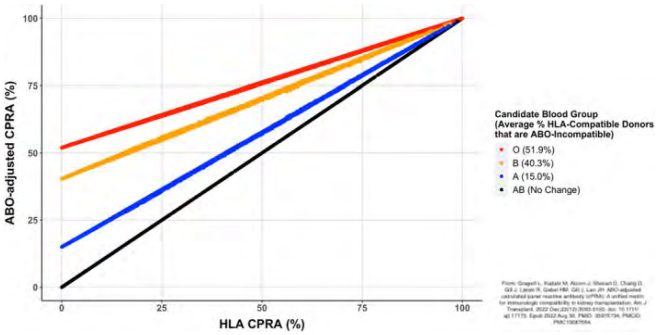
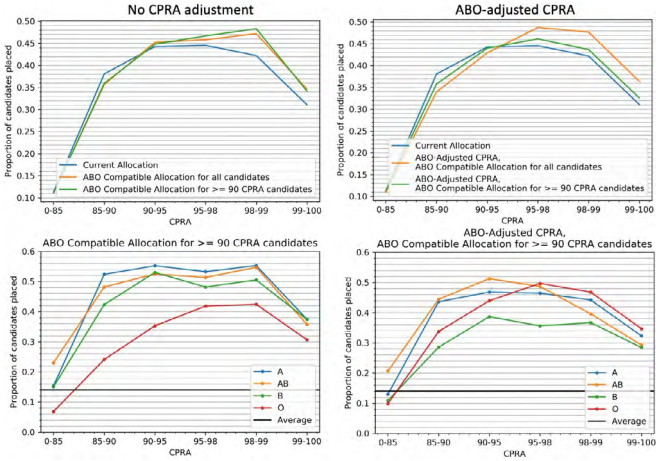
Background: Under the current deceased donor kidney allocation policy, HLA-sensitized and thus severely biologically disadvantaged non-O blood type transplant candidates are systematically excluded from type O donor organ offers, despite the fact that O donors are universally blood type compatible. ABO-restricted allocation policy limits potential transplant opportunities even for very highly sensitized patients who have the smallest HLA-acceptable donor pools. In an era where >25% of kidneys recovered for transplant are discarded, revising allocation policy to enable disadvantaged patients to receive ABO-compatible kidney offers might reduce access disparities and decrease kidney nonuse. To ensure that ABO-compatible transplants are offered to the truly most difficult-to-match candidates, we suggest using a novel ABO-adjusted CPRA metric instead of conventional CPRA.

Methods: Using SRTR data, we modeled the current deceased donor kidney allocation policy in SRTR's new organ allocation simulator (OASim) along with allocation policies where: (1) all candidates or (2) only CPRR >= 90% candidates are eligible for ABO compatible donors. Policies (1) and (2) were evaluated with and without ABO-adjusted CPRA (Fig 1). We looked at the percentage of candidates transplanted in a one-year simulation (3/2021 – 3/2022) stratified by the CPRA and ABO groups.

Results: For O blood type candidates, the ABO-Adjusted CPRA policy for >= 90 CPRA candidates yields a transplantation rate of 0.35 in the 99-100 CPRA category. This is higher than the 0.31 rate under the ABO Compatible Allocation for >= 90 CPRA candidates policy, and higher than the 0.32 rate under the Current Allocation policy. For B blood type candidates, the transplantation rate under the ABO-Adjusted CPRA policy is 0.28 in the 99-100 CPRA category. This is higher than the 0.27 rate under the Current Allocation policy, but lower than for the ABO Compatible Allocation for >= 90 CPRA candidates policy without ABO adjustment.

Conclusions: Incorporating ABO-adjusted CPRA into allocation policy might similarly increase transplants and equity for highly-sensitized and blood-type-disadvantaged candidates in the US.





BOS_18_14 IMPACT OF CIT AND ITS INTERACTION WITH DONOR VARIABLES ON KIDNEY GRAFT SURVIVAL

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Background: Changes to the kidney allocation policy (KAS) has led to increase in cold ischemia times (CIT) for a deceased donor kidney transplant. The aim of the study was to evaluate the impact of CIT and its interaction with donor variables on long term kidney allograft survival.

Methods: SRTR data of adult deceased donor kidney transplants from December 12/05/2007 to 12/31/2023 were analyzed. Two-way interactions were explored separately by fitting a multivariate cox regression model with a continuous effect for CIT.

Results: A total of 169,310 kidney transplants were analyzed in our study. They were divided into pre-KAS (n=58,671), KAS (n=73,910) and KAS-250 (n=36,729) eras. The CIT increased from 16 to 17 and 19.5 hours, respectively during these eras. In multivariate cox regression analysis, CIT (reference 12-16 hours vs 8-12 hours, HR 0.949, p=0.0004; vs 20-24 hours, HR 1.034, p=0.0258; vs 24-28 hours, HR 1.043, p=0.0173), allocation type (local vs region and national, HR 1.050, P=0.0008 and HR 1.071, p<0.0001, respectively) and use of machine perfusion (vs cold storage HR 0.969, p=0.0023) were the only modifiable variable that impact graft survival. Donor variable-CIT interactions that adversely affect 5-year allograft survival are male donor gender (p=0.0133), local vs regional/national allocation (p=0.0248), organs from hepatitis C positive (HCV) (p=0.0249) and donation after circulatory death donors (DCD) (p=0.0288) (figure 1)

Conclusions: Kidney allocation policies are regularly changed to improve equity in access to kidney transplantation. CIT increased as an effect of these policy changes. Worse graft survival can be observed if the CIT exceeds 20 hours. Certain donor variable-CIT interaction can adversely affect graft outcomes. Future policy changes should be made to expedite kidneys for allocation from male donors, regional /national allocation, organs from HCV positive and DCD donors.

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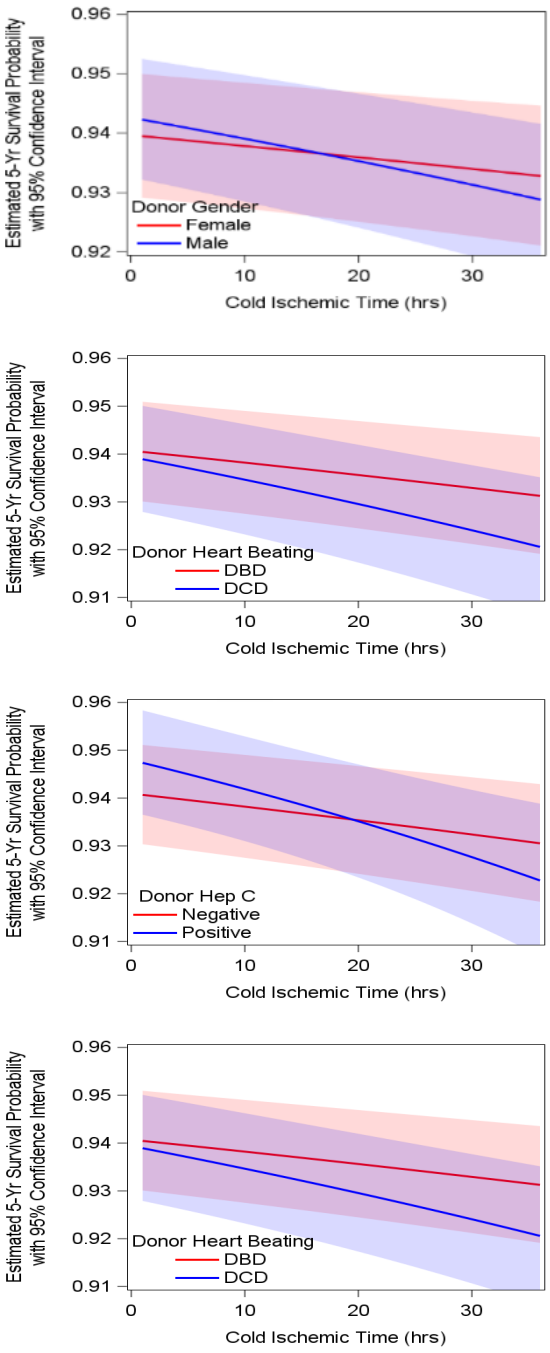

Figure 1: 5-Year Survival Probabilities from the Main Effects Model with the Interaction of Interest

BOS_18_15 3-STEP MODEL OF INFORMED CONSENT FOR LIVING KIDNEY DONATION: PRELIMINARY STAKEHOLDER FEEDBACK

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Background: The 3-Step Model of Informed Consent for Living Kidney Donation aims to ensure equitable living donor (LD) decision-making opportunities. It includes a prompt question sheet and a knowledge assessment questionnaire for prospective donors, and a structured conversation checklist for healthcare professionals (HCP). These tools serve to standardize informed consent, provide comprehensive education, tailor information to individual needs, and, ultimately, to enable shared decision-making (SDM). This study gathered stakeholder feedback to refine these tools before clinical testing.

Methods: An anonymous online survey was disseminated via the DESCaRTES and EKITA networks to HCPs and non-healthcare stakeholders (e.g. LDs, donor advocates, patient representatives) involved in kidney transplantation. Participants rated items in each tool on a 5-point Likert scale (0 = not at all important to 4 = extremely important) and provided qualitative feedback to identify areas for improvement.

Results: Fifty-eight responses from sixteen European countries, primarily from nephrologists (32/55.2%) and nurses (8/13.8%), highlighted strengths/weaknesses of the tools. Highly rated items in the prompt question sheet addressed short- and long-term risks, potential effect on pregnancy and medical conditions. The questionnaire received high ratings regarding donor withdrawal rights, and LD outcomes. Checklist items about withdrawal rights, explanations of donation consequences, life-long follow-up, and understanding donor motivations were highly rated. Qualitative feedback suggested addressing financial, psychosocial, and recipient considerations. Stakeholders emphasized also addressing post-donation expectations. Overly complex tools were identified as barriers (**Figure 1**).

Conclusions: The 3-Step Model tools were generally well-received as a standardized approach to informed consent. Stakeholder feedback highlighted their utility and identified areas for refinement, particularly financial, psychological, and logistical considerations. These insights will guide tools' optimization before clinical testing, ensuring ethical donor care that supports SDM.

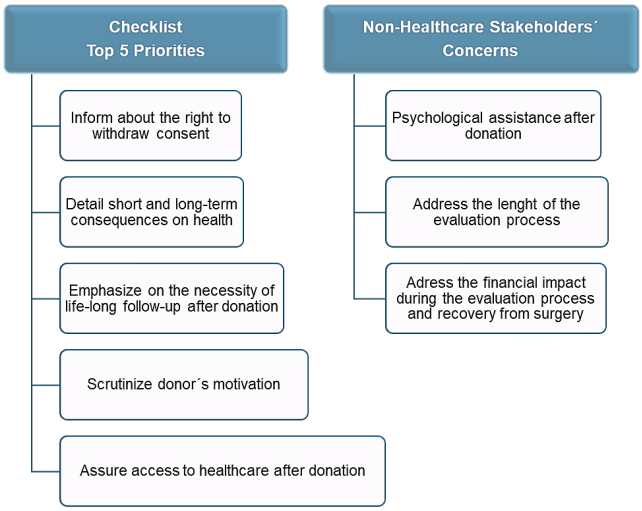

Figure 1. 3-Step Model Checklist Top 5 Priorities and Non-Healthcare Stakeholders' Concerns

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BOS_19_1 BKPYV-SPECIFIC T CELL EXHAUSTION IN KT: TARGETING INHIBITORY RECEPTORS IMPROVES THEIR FUNCTIONS

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Background: BK polyomavirus-associated nephropathy (BKPyVAN) is a significant complication of kidney transplantation associated with high levels of BKPyV replication in plasma and poor graft survival. It is currently treated by reducing immunosuppression to restore the immune response.

Methods: We analyzed circulating T cells from 28 kidney transplant recipients with BKPyV-DNAemia. All had a significant reduction of immunosuppression. We evaluated BKPyV-specific T-cell functionality and phenotype and assessed graft outcomes prospectively.

Results: BKPyV-DNAemia were rapidly controlled in 13 patients (controllers, C-group), whereas 15 presented sustained viral replication and were considered to have not responded to immunosuppression modification (non-controllers (NC-group)). The induction and maintenance therapies used were similar in the C- and NC-groups. The slope of renal function decline tended to be worse in NC-group than in C-group (p<0.055). The NC-group displayed a loss of BKPyV-specific T-cell functions (T-cell proliferation, cytokine secretion) relative to the C-group. This functional impairment was associated with an overexpression of several inhibitory receptors (IR) (PD1, TIGIT, or TIM3), highlighting an exhausted-like phenotype of BKPyV-specific CD4 and CD8 T-cells in the NC-group. BKPyV-specific CD8 in the NC-group were expressing more frequently 2 or 4 IR than those in the C-group (p<0.05). single blocking antibody against IR did not overcome T-cell inhibition, whereas a combination of anti-PD1 and anti-TIM3 antibodies significantly restored BKPyV-specific CD8 T-cell functions (p<0.05).

Conclusions: Sustained BKPyV-DNAemia was associated with an exhausted phenotype of BKPyV specific T-cells despite reduction of immunosuppression in kidney transplant recipients. We show that anti-BKPyV-specific CD8 functions can be restored *ex vivo* by blocking the PD1 and TIM3 pathways, paving the way for new treatment strategies.

BOS_19_2 GLOBAL BURDEN OF INFECTIONS IN PEDIATRIC SOLID ORGAN TRANSPLANT RECIPIENTS IN THE FIRST YEAR AFTER TRANSPLANTATION

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Background: Infections are a leading cause of morbidity and mortality in pediatric solid organ transplant recipients (SOTr). Comprehensive data on the incidence and types of infections in this population remains limited.

Methods: We prospective included pediatric SOTr aged 0-18 years with at least one year of follow-up after transplantation enrolled in the Swiss Transplant Cohort Study (STCS) from 2008 to 2022. We evaluated all clinically relevant infections (infections) using standardized definitions and characterized them by organ type, age, site and type of infection. Incidence rates were calculated, and associations with age, organ type, and rejection episodes were assessed using Poisson generalized linear models and multivariable regression analyses.

Results: A total of 285 pediatric SOTr were included, with kidney (41%) and liver (37%) transplants being the most common. During the first-year post-transplant, 53% (151/285) of patients experienced at least one infection, totaling 360. The overall incidence was 1.36 infection/person/year. Viral infections predominated (53%), followed by bacterial (41%) and fungal infections (6%). Patients receiving liver and lung transplants had higher infection rates (1.91 and 2.53 per person-year, respectively). In univariate analysis younger age, male sex, and liver or lung transplantation were associated with a higher risk. In multivariate analysis type of transplant and male sex remained associated with increased risk of infection. No significant association was found between rejection episodes and infection. Viral infections were overrepresented in younger recipients, while bacterial infections were most frequent in the first three months post-transplant. Opportunistic and vaccine-preventable infections were infrequent.

Conclusions: Pediatric SOT recipients face a substantial burden of infection during the first-year post-transplant, particularly younger male children, liver and lung transplant recipients. Targeted interventions, including optimized prophylaxis and immunization, remain crucial to reducing infection-related morbidity and mortality in this vulnerable population.

BOS_19_3 CIRCULATING SPHINGOSINE, SPHINGOSINE-1-PHOSPHATE AND LONG-TERM MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Kidney transplant recipients (KTR) still face high mortality rates, often due to lethal infections. Sphingosine-1-phosphate (S1P), derived from sphingosine, plays a crucial role in inflammation regulation and cell survival. Elevated circulating S1P levels are linked to reduced severity of infections. Circulating very long-chain saturated fatty acids (VLSFA), which are positively associated with peanut intake and inversely associated with infectious disease mortality in KTR, might contribute to circulating S1P levels. This study aimed to explore associations between plasma sphingosine, S1P, VLSFA, and long-term mortality in KTR.

Methods: The study included 680 outpatient KTR with a functional graft of 1 year. Plasma sphingosine and S1P were measured with liquid chromatography–mass spectrometry. VLSFA were measured with gas chromatography coupled with a flame ionization detector. Univariate and multivariable linear regression analyses were used to assess the association between sphingosine, S1P and potential determinants. Cox regression analyses were used to prospectively study the associations of sphingosine and S1P with all-cause and cause-specific mortality.

Results: VLSFA were among the top predictors of S1P (std. beta=0.13, p=0.001 in multivariable adjusted analyses). During a median (interquartile range) follow-up of 5.4 (4.8–6.1) years, 141 (21%) KTR died with 39 (28%) deaths due to severe infections. Circulating sphingosine was positively associated with infectious disease mortality, with a hazard ratio (HR) (95% confidence interval) per doubling of 1.63 (1.08–2.47), p=0.02, while S1P was inversely associated with all-cause and infectious disease mortality, with a HR per doubling of 0.54 (0.31–0.93), p=0.03 and 0.17 (0.06–0.48), p<0.001, respectively, all independent of adjustment for potential confounders. S1P mediated 12% (p<0.01) of the association between VLSFA and infectious disease mortality.

Conclusions: Circulating sphingosine was positively associated with infectious disease mortality. S1P was positively associated with VLSFA and inversely associated with all-cause and infectious disease mortality. Further studies are needed to assess the effect of VLSFA-containing foods on circulating S1P and on the risk of (fatal) infections in KTR.

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BOS_19_4 THE IMPACT OF RECIPIENT HIV STATUS ON KIDNEY TRANSPLANT OUTCOMES

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Background: Despite increasing literature on kidney transplantation in people with HIV, previous studies have largely overlooked the confounding impact of ethnicity and social deprivation. This study aimed to assess post-transplant outcomes in HIV positive versus negative recipients, adjusting for ethnicity and deprivation status.

Methods: Population-cohort study of single kidney alone transplant recipients (2006-2022) including all 23 UK kidney transplant centres, using the prospectively maintained UK Transplant Registry. The primary outcome was 12-month eGFR (eGFR of 10 for graft failures), with secondary outcomes of delayed graft function and graft survival. Multivariable regression models adjusting for a wide range of donor and recipient characteristics assessed the impact of recipient HIV status on transplant outcomes. Multiple imputation and restricted cubic splines were used for missing data and non-linear modelling.

Results: This study included 30013 kidney transplant recipients: 20517 deceased donor (200 HIV positive recipients) and 9496 live donor (44 HIV positive recipients). In the deceased donor group, HIV-positive recipients had significantly lower 12-month eGFR compared to HIV-negative recipients (adjusted difference = -4.78 (95%CI -7.89 to -1.67), p=0.003). This was not significant in the live donor cohort (adjusted difference = -2.94 (-8.92 to +3.05), p=0.34). Recipient HIV status was not associated with delayed graft function, graft survival (Figure 1) or patient survival in both deceased and live donor cohorts. By contrast, HIV positive recipients were more likely to experience acute rejection within 12 months in both deceased (aOR= 1.79 (1.15 to 2.81), p=0.01) and live (aOR = 3.81 (1.70 to 8.55), p=0.001) donor cohorts.

Conclusions: When adjusting for ethnicity and social deprivation status, recipient HIV status was not associated with graft survival, patient survival or delayed graft function in kidney grafts from either deceased or live donors. However, HIV positive recipients were more likely to experience acute rejection and have inferior eGFR at 1 year.

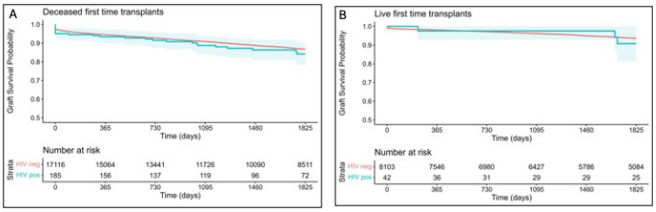

Figure 1 – Kaplan-Meier plot displaying graft survival rates in both first time transplant HIV positive and HIV negative recipients in the deceased donor group (A) and the live donor group (B)

BOS_19_5 RESPIRATORY SYNCYTIAL VIRUS IMMUNITY IN SOLID TRANSPLANT RECIPIENTS COMPARED TO HEALTHY CONTROLS

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Background: Solid organ transplant recipients are at increased risk of respiratory syncytial virus (RSV) infections with severe disease and serious outcome due to inadequate humoral and cellular immune responses. Until now, knowledge of general RSV-specific immunity in SOT recipients compared to healthy controls is limited.

Methods: In this cross-sectional study, 71 healthy controls as well as 105 kidney and 48 lung transplant recipients were recruited from April 2024 to January 2025. RSV-specific IgA and IgG were quantified by ELISA and RSV-specific CD4 and CD8 T cells were analysed using flow cytometry.

Results: Overall, 94% of all individuals had detectable RSV-specific IgG with no difference in IgG levels between the groups (p=0.279). RSV-specific IgA levels were largely below the detection limit and similarly low in all patient groups (p=0.110). While more than half of all healthy controls (58%) and kidney transplant recipients (54%) had specific CD4 T cells above detection limit, significantly less lung transplant recipients (29%) had detectable RSV-specific CD4 T cells (p=0.0045). Accordingly, despite generally low percentages, RSV-specific CD4 T-cell levels among healthy controls (0.03 (IQR 0.05)%) and kidney transplant recipients (0.03 (IQR 0.04)%) were significantly higher than in lung recipients (0.02 (IQR 0.03)%, p=0.0021). Overall, 70% of all individuals had no RSV-specific CD8 T cells, with no difference between groups (p=0.58).

Conclusions: Lung- and kidney transplant recipients had similarly high RSV-specific IgG levels as compared to healthy controls, whereas IgA and CD8 T-cell levels were low in all groups. In contrast, kidney transplant recipients and healthy controls were more likely to have detectable RSV-specific CD4 T cells with significantly higher levels compared to lung transplant recipients. These data provide knowledge on natural immunity as a basis to evaluate immunogenicity of RSV-vaccines in transplant recipients.

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BOS_19_6 MARIBAVIR USE IN MANAGING CYTOMEGALOVIRUS INFECTION AMONG UK KIDNEY TRANSPLANT RECIPIENTS

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Background: Refractory CMV is defined as an infection that does not respond well enough to usual treatments (an increase in 1 $\log_{10}$ in CMV viral load after 2 weeks of therapy). Refractory CMV encompasses CMV infection resistant to first line treatments, with UL97 gene mutations being resistant to valganciclovir and ganciclovir. However, current options to treat these strains of CMV are limited to intravenous therapies, which often require an inpatient stay and can be nephrotoxic, requiring close monitoring with careful dose adjustments. UL54 gene mutations confer multidrug resistance, limiting therapeutic options. Maribavir is an oral antiviral for treatment for refractory CMV infection following solid organ or haematopoeitic stem cell transplantation, approved by NICE in January 2023.

Methods: Members of the UK Renal Pharmacy Group compiled real-world data for patients who have received maribavir in the UK prior to January 2025.

Results: Eight UK centres reported maribavir use in 18 patients, succeeding inadequate response to first line therapies. 12 patients (67%) successfully cleared CMV but reactivated following treatment cessation. Six patients required maribavir re-initiation with one of these patients requiring 3 courses. In total 25 courses of maribavir were completed.

Conclusions: Maribavir is an effective and well tolerated oral option to treat refractory CMV in an outpatient setting, avoiding the associated costs of hospital facilities and reducing the need for nephrotoxic or myelotoxic alternatives. The average treatment duration reflects reports from the SOLSTICE trial, however real-world data highlights high reactivation rates post treatment, and strengthens the importance of close PCR monitoring following treatment cessation. Reported adverse effects were similar to the trials, but demonstrates the need for pre-emptive tacrolimus dose alterations to avoid toxicity and its associated nephrotoxicity.

Table 1: data from completed maribavir courses

Average duration since transplant to positive CMV PCR	473.8 days
Average CMV PCR level upon initial treatment initiation	103,199
Average CMV PCR on maribavir initiation	141,693
Average duration of maribavir therapy	57.6 days
Patients with negative CMV IgG	14 (78%)
Indication	Number of patients
Confirmed resistant CMV	13 with UL97 (1 also with UL54)
Refractory CMV/suspected resistance	4
Recurrence of resistant CMV	7
Contraindicated to other treatments	1
Reason for stopping maribavir	Number of patients
CMV not detected	19
CMV not resistant	1
Rising CMV PCR levels	1
Low level CMV PCR beyond 8 week treatment	2
Adverse effects	1
Patient died	1
Adverse effects experienced	Reported cases
Metallic taste in mouth	7
Interaction with tacrolimus	15
Headache	2
Drowsiness	2

BOS_19_7 IMPACT OF UPPER TRACT BARBOTAGE ON RECURRENT URINARY TRACT INFECTIONS AND CLINICAL DECISION IN TRANSPLANT/ESRD PATIENTS

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Background: Many transplant patients experience recurrent UTIs (rUTIs) refractory to conservative measures often related to non-functioning native or transplant kidneys. We include a GA cystoscopy, retrograde studies and barbotage of all accessible native and transplanted kidneys to try to localize the potential source of rUTIs and where appropriate instill antibiotic locally. We review our use of this novel diagnostic and therapeutic strategy as part of a "bundle of care" for rUTIs.

Methods: Retrospective review of transplant and pre-transplant patients with rUTI who underwent retrograde studies (Jan to Dec 2019) +- antibiotic instillation of non-functioning transplants or native kidneys/stumps.

Results: 36 patients in a 12-month period. Six patients needed repeated antibiotic instillation to maintain response. A third of patients needed alternate urology intervention for rUTIs (bladder outlet surgery, Deflux or Botox). One patient only eventually needed transplant nephrectomy (side directed by barbotage). One comorbid patient was indicated but very high risk for nephrectomy and yearly RG instillations safely avoided the nephrectomy. In most patients, the "bundle of care" together with RG and barbotage helps prevent rUTIs. We are analyzing 5 year follow-up data.

Conclusions: Barbotage+-antibiotics may change the armamentarium of management of rUTIs in transplant patients. In our experience this is effective and may reduce interventions (eg nephrectomy of non-functioning kidneys) and may direct towards a unilateral native or transplant nephrectomy. This may prevent risks of surgery in high-risk patients and reduce long-term costs.

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BOS_19_8 THE FAVORABLE IMPACT OF HBCAB POSTIVE GRAFTS ON LIVER TRANSPLANTATION FOR HBV-RELATED LIVER CANCER

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Background: The utilization of marginal grafts may help alleviate the demand mismatch. However, strategies to optimize the use of hepatitis B core antibody (HBcAb) positive grafts still requires further investigation.

Methods: The study retrospectively analyzed 5351 patients undergoing liver transplantation in 8 centers between January 2015 and December 2020, of which 1406 (26.3%) received HBcAb positive grafts. Propensity score matching (PSM) was used to form comparable groups.

Results: The prognosis of recipients with HBcAb positive grafts were better than those with HBcAb negative grafts before and after PSM (7-year patient survival rate: 72.0 % vs. 68.3%; 72.1% vs. 65.9%, P<0.01). In the subgroup of hepatitis B virus (HBV)-related patients, recipients with HBcAb positive grafts exhibited superior patient survival compared to those with HBcAb negative grafts (7-year patient survival rate: 75.3% vs. 66.0%, P<0.01), while no significant difference was observed in non-HBV related patients. Moreover, in the subgroup of HBV-related hepatocellular carcinoma (HCC) patients, recipients with HBcAb positive grafts had better recurrence-free survival than those with HBcAb negative grafts (7-year recurrence-free survival rate: 63.0% vs. 45.1%, P<0.01), with no significant difference noted in HBV-related non-HCC patients. Cox regression analysis revealed that HBcAb positive graft was an independent protective factor for recurrence-free survival of HBV related HCC patients (hazard ratio: 0.798, 95% confidence interval: 0.670-0.950, P=0.011), and a nomogram was established accordingly with a good predictive efficacy (AUROC=0.740, C-index=0.691). Interestingly, recipients with HBcAb-positive grafts showed improved outcomes compared to those with HBcAb-negative grafts in the subgroup of HBV-related HCC patients with detectable HBV DNA.

Conclusions: HBcAb positive grafts can be safely used for liver transplantation in patients with end-stage liver disease. The utilization of HBcAb positive grafts in HBV-related HCC patients, especially those with active HBV status, had a favorable impact on their prognosis compared to those receiving HBcAb negative grafts.

BOS_19_9 PREDICTION OF BKPYVAN BY NEPHROVIR METHOD IN KIDNEY RECIPIENTS WITH BKPYV-DNAEMIA

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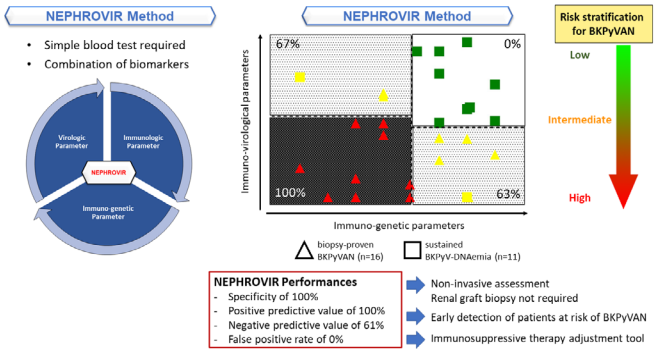
Background: BK Polyomavirus (BKPyV) remains a significant complication after kidney transplantation. Due to BKPyV intra-graft replication, biopsy-proven BKPyV-associated nephropathy (BKPyVAN) affects nearly 10% of patients and causes graft loss in more than 50% of cases. Impaired BKPyV-specific T cell response plays a crucial role in the BKPyVAN pathophysiology. Several teams, including ours, have demonstrated a profound impairment of BKPyV-specific T cells during BKPyVAN. Immunovirological monitoring allows an individual assessment of viral reactivation risk based on the anti-viral immune response.

Methods: To assess the risk of BKPyVAN occurrence, our group has developed the NEPHROVIR method. This non-invasive biological method is based on the innovative combination of biomarkers, including BKPyV load, BKPyV-specific T cell response, and histocompatibility between donor and kidney graft recipient (patent FR1855342).

Results: In our proof-of-concept, the NEPHROVIR method allows the identification of 3 BKPyVAN risk levels: low, intermediate, and high. Based on the assessment of 27 kidney transplant recipients (KTRs) with sustained BKPyV-DNAemia, KTRs with a weak combination of immuno-virological and immuno-genetic parameters (n=9, 33%) were all patients with biopsy-proven BKPyVAN (lower left-hand quadrant). Conversely, KTRs with a potent combination of immuno-virological and immuno-genetic parameters (n=7, 26%) had sustained BKPyV-DNAemia without biopsy-proven BKPyVAN (upper right-hand quadrant). The figure below shows the BKPyVAN risk stratification index obtained from the NEPHROVIR method, with associated test performance.

Conclusions: The NEPHROVIR method is an innovative immunovirological surveillance method for predicting the risk of biopsy-proven BKPyVAN occurrence. Characterizing individual BKPyVAN risk levels could help in the individualized follow-up and management of immunosuppression in KTRs. The long-term objective would be to diagnose very early, or even anticipate, the occurrence of BKPyV-DNAemia and to allow early readjustment of the immunosuppressive treatment.



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BOS_19_10 HLA-E GENOTYPE, LMP-1 VARIANTS, AND DEVELOPMENT OF PTLD IN PRIMARY EBV-INFECTED TRANSPLANT RECIPIENTS

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Background: Epstein-Barr virus (EBV) primary infection is a major risk factor for post-transplant lymphoproliferative disorder (PTLD), which significantly reduces survival rates in solid organ transplant recipients (SOTR). Vietzen et al. recently described their important finding of an association of human leukocyte antigen (HLA)-E*0103/0103 and EBV latent membrane protein 1 (LMP-1) variants GGDPHLPTL and GGDPPLPTL with PTLD. Important findings require independent replication. Therefore, we evaluated HLA-E genotypes and LMP-1 variants in a cohort of 33 SOTR with primary EBV infections in our center, eight of which developed PTLD during the first 18 months after transplantation.

Methods: Stored whole blood samples of SOTR, with active primary EBV infections were selected for investigating the HLA-E genotype and the LMP-1 variant. A targeted PCR test was used for determining the HLA-E alleles, and Sanger sequencing of the LMP-1 fragment was carried out as described previously.

Results: In the entire study population, prevalences of HLA-E0101/0101, HLA-E0103/0103, and HLA-E0101/0103 were 27%, 33% and 40% respectively. Among the PTLD group (N=8), the HLA-E0103/0103 genotype was predominant, observed in 75% of cases, while HLA-E0101/0103 was present in 25%. No PTLD cases were seen in patients with the HLA-E 0101/0101 genotype. In contrast, within the non-PTLD group (N=25), HLA-E0101/0101 was seen in 28%, HLA-E0103/0103 in 20%, and HLA-E0101/0103 in 52%. LMP-1 sequencing showed that the GGDPHLPTL sequence was the most common variant in the transplant population (50% of total). All PTLD cases were infected with EBV carrying this LMP-1 variant.

Conclusions: Our results independently replicated the findings of Vietzen et al., supporting the potential of high risk HLA-E genotypes as well as high risk LMP-1 variants. Both markers, which can be easily detected in a clinical setting, could provide an attractive way to individualize follow-up protocols as well as pre-emptive treatment of EBV infections, with a view to reducing PTLD development.

BOS_19_11 HHV8-RELATED DISEASES IN SOLID ORGAN TRANSPLANTATION: A CASE SERIES

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Background: HHV-8/Kaposi Sarcoma herpesvirus has been associated with a large spectrum of diseases in solid organ transplant (SOT) recipients. In this setting, primary donor-derived infection may manifest with a severe and rapidly fatal non-neoplastic disease called Kaposi-Sarcoma Inflammatory Cytokine Syndrome (KICS). Despite this, HHV-8 serostatus is not routinely screened among donors and recipients.

Methods: In this case series we describe adult SOT recipients diagnosed with a HHV-8 related disease at our center from 2016 to 2023. Data on demographic features, type of SOT (liver, kidney, heart or lung), date of transplantation, HHV-8 infection and serostatus, date of HHV-8 related disease diagnosis, HHV-8-DNA (if available), clinical manifestations and disease severity, immunosuppression regimen were collected. All analyses were descriptive.

Results: We included twelve SOT recipients (7 liver, 3 kidney, 1 combined liver and kidney, 1 heart). Of them (table 1), six had negative serology at the time of transplantation. Serostatus was unknown for all donors except for one (positive). Median age of individuals was 60.5 years (IQR [55.5 – 66]). Infections were characterized by seven (58%) non-neoplastic HHV-8 disease, all compiling criteria for KICS and eight (67%) neoplastic disease (seven Kaposi-Sarcoma, KS, one Multicentric Castleman Disease, MCD). Three patients (25%) had both neoplastic and non-neoplastic disease. Median time from SOT to HHV-8 related disease was shorter for KICS comparing to KS. In nine (75%) patients' immunosuppressive regimen was switched from mycophenolate mofetil or calcineurin inhibitors to mammalian target of rapamycin inhibitor. Among non-neoplastic disease, 5/7 (71%) patients received antiviral treatment (ganciclovir or cidofovir), tocilizumab was administered in 4/7 patients (57%). Among neoplastic disease, chemotherapy was prescribed in 6/8 (75%) patients, mainly with doxorubicin. Overall, 9/12 (75%) patients were hospitalized, 3/12 patients (25%) died and 8/12 (67%) showed remission, 1/12 (8%) relapsed.

Conclusions: HHV-8 related diseases are rare but potentially fatal events complicating SOT course. In high prevalence areas, active serostatus screening could identify high-risk patients to implement surveillance preventive strategies.

Case n°	Age	Sex	SOT type	SOT year	Serostatus	HHV8 disease	Time tpx-disease	Viral load	IL-6 (nv <6.4 pg/mL)	Clinical manifestations/Localization	IS management	Antiviral	CHT	Other medications	Outcome
1	61	M	LT	11/16	D+/R-	KICS	4 m	54900	4741	Sierositis, uveitis	FK→mTOR	GCV, CDF	None	TOC	Remission, on FU
2	57	M	HT	02/18	Dna/R-	KICS+KS	14 m	183673	1402	Lymphnodes	FK→mTOR	GCV, CDF	DOXO	None	Remission, on FU
3	27	M	KT	02/18	Dna/Rna	KS	19 m	503	NA	Lymphnodes	MMF→mTOR	None	DOXO	None	Remission
4	60	M	LT	09/19	Dna/Rna	KICS	13 m	114740	1276	Sierositis, nephropathy	FK→mTOR	CDF	None	TOC	Relapse of KICS + visceral and cutaneous KS
5	66	M	LT	04/21	Dna/Rna	KICS	10 m	204850	>4794	Sierositis, anemia	None	None	None	None	Death
6	50	M	LT	09/22	Dna/R-	KICS + KS	5 m	$>10^7$	772.6	Sierositis, fever	FK→mTOR→ stop	GCV, CDF	None	TOC	Remission, on FU
7	66	M	LT	02/23	Dna/R-	MCD+KICS	7 m	$>10^7$	332.4	Sierositis, fever	FK→mTOR	GCV, CDF	RTX+DOXO	TOC	Death
8	74	M	KT	03/23	Dna/Rna	KS	10 m	Neg	<6.4	Cutaneous	MMF→stop	None	None	Laser	Remission, on FU
9	64	F	LT	06/23	Dna/R-	KS	11 m	5977	<6.4	Cutaneous, GI, lymph nodes	FK→mTOR	None	DOXO →GCT	None	On FU
10	75	M	KT	06/23	Dna/Rna	KS	8 m	Neg	<6.4	GI, cutaneous	MMF→mTOR	None	DOXO	None	On FU
11	54	F	LT	10/23	Dna/R-	KS	8 m	Neg	<6.4	GI, lymphnodes	FK→mTOR	None	DOXO	None	On FU
12	57	F	LT/KT	11/23	Dna/Rna	KICS	6 m	$>10^7$	NA	Sierositis, lymphnodes	None	None	None	None	Death

Table 1.

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BOS_19_12 A REAPPRAISAL OF THE EPIDEMIOLOGY OF HERPES ZOSTER IN KIDNEY TRANSPLANT RECIPIENTS

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Background: As a vaccine against herpes zoster (HZ) is now available for immunocompromised patients, it is useful to reassess the epidemiology of this disease in kidney transplant recipients (KTRs).

Methods: Cases of HZ were identified from the digital medical records of 1144 patients who received a kidney transplant in our center between 2004 and 2015. Patients were followed-up until 2017, graft failure or death. Incidence rates (IR) of HZ were determined in separate subgroups defined by the age range of the recipient at the time of the transplantation (10-years ranges) and compared with data from the general population available the literature. Factors associated with HZ were determined using frailty models.

Results: Over a follow-up of 6702 patient-years (py), 99 cases of HZ were identified, corresponding to an IR of 14.8/1000 py, to be compared with 3.4/1000 py in the general population. Even below 30 years old at the time of transplantation the IR was 7.99/1000 patient-year [1.79 – 16.9], approximately at the same level as in people between 60 and 70 years-old from the general population. In multivariate analysis, the factors associated with HZ were the age at the time of transplantation (HR = 2.3 [1.2—4.4] between 43 and 58 years old, HR = 2.7 [1.4—5.2] after 58 years old, compared with KTRs younger than 43 years, p=0.012), class II HLA mismatches (HR = 1.4 [1.2—1.7] per mismatch, p=0.047), induction using anti-lymphocyte globulins (HR = 1.64 [1.1—2.5], p=0.02). The risk of HZ was reduced in KTRs with MMF/MPA in their maintenance treatment (HR = 0.36 [0.18—0.73], $p=3.4\times10^{-4}$).

Conclusions: KTRs have a high risk of HZ especially after 43 years. Even below 30 years of age, this risk is of the same magnitude as in people over 60 years from the general population, for whom vaccination is recommended. These results are an argument in favor of the vaccination of all the kidney transplant recipients.

BOS_19_13 T-CELL EXHAUSTION IMPACTS SPECIFIC ADAPTIVE RESPONSES AFTER VACCINATION IN SOLID ORGAN TRANSPLANT

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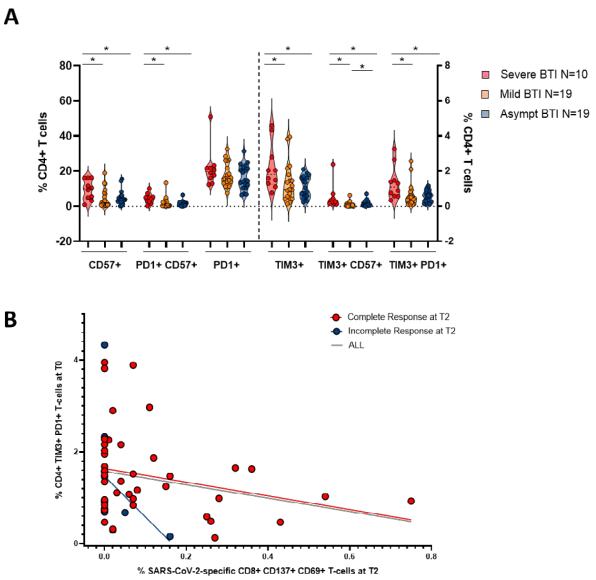
Background: T-cell exhaustion is a dysfunctional state characterized by a progressive loss of effector function that has been classically associated to repeated exposure to foreign antigens such as viral infections or organ transplantation. While such immune hyporesponsiveness could minimize allograft rejection, it can negatively impact on protective immunity after viral infection and vaccination.

Methods: Here, we investigated the impact of baseline T-cell exhaustion/senescence in 80 SOT recipients and their capacity to achieve protective adaptive immunity after SARS-CoV-2 vaccination. Multiple exhaustion and senescent markers in CD4 and CD8 T cells were assessed at baseline and at different time points after vaccination using flow cytometry. Different functional assays detecting antigen-specific neutralizing antibodies (Nab), memory B cells (mBc) (Fluorospot) and Th1/Th2 cytokine-producing cells (Elispot) to depict immune protection were monitored. Also, activation-induced cell markers (AIM) with flow cytometry was done to functionally confirm hyporeactivity.

Results: We first confirmed a wide range of functional immune responses at all memory compartments, serological and cellular among SOT. High percentages of CD57+, CD57+PD1+, PD1+ and CD57+TIM3+ exhausted/senescent CD4 T-cells at baseline, independently predicted incomplete adaptive immune response despite three vaccine doses (p<0.05), regardless the type of SOT, immunosuppressive regimen, recipient age and time after transplantation. Most importantly, such high percentages of baseline CD57+, CD57+PD1+ and CD57+TIM3+ CD4+ T cells predicted subsequent severe COVID-19 breakthrough infections (**Fig. 1A**). Notably, non-responder patients showing high proportion of exhausted/senescent T cells displayed significantly lower T-cell activation after SARS-CoV-2 peptide stimulation in vitro (**Fig. 1B**).

Conclusions: Our study adds new insight in the implications of T-cell exhaustion/senescence driving unsuccessful protective immunity after booster vaccination in SOT and may have relevant implications in different anti-viral immunization.



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BOS_19_14 IMMUNE SIGNATURES IN BKPYVAN: IMPLICATION OF B LYMPHOCYTES AND MACROPHAGES

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Background: BKPy virus (BKPyV) associated Nephropathy (BKPyVAN) is a major complication in kidney transplantation leading to graft loss in 50% of cases. BKPyVAN is associated with immune cell infiltration of the graft in contact with infected cells. This study aimed to characterize this infiltration.

Methods: To characterize the cellular infiltration in BKPyVAN, a transcriptome training (GSE47199) dataset of kidney BKPyVAN biopsies was processed through unsupervised and supervised analyses with immune cell deconvolution, and machine learning. The BKPyVAN signature was validated on a second dataset (GSE72925), and then molecular signatures were confirmed by immunohistochemistry (IHC, OPALE).

Results: The training dataset confirmed a immune infiltration in BKPyVAN, mainly composed of antigen-presenting cells, memory/naïve/class-switched memory B-cells (B-L), effector-memory/naïve CD4+ T cells (T-L), naïve/central memory CD8+ T-L, and Monocyte/Macrophage M1. This analysis shows Inflammatory/immune-activated signatures mainly formed by network of chemokines/receptors interactions involved in the chemotaxis process and compatible with high immune infiltration. The second dataset validated the overexpression of CXCL13 gene and the B-L signature in BKPyVAN. With IHC, we showed a higher frequency of B-L in BKPyVAN than in control kidney ($p<0.0043$) or kidney with TCMR ($p<0.0087$). In addition, CXCL13 expression was more frequently observed in BKPyVAN than in control kidney ($p<0.0152$). Colocalization of CXCL13 with immune cells markers was only positive for CD68 among our panel suggesting the involvement of Lymphocytes B and macrophage in the physiopathology of BKPyVAN.

Conclusions: Transcriptomic analysis as well as IHC suggested an important role of macrophages and B cells in BKPyVAN in addition to the T cell infiltration. CXCL13 secreted by macrophages may participate in the recruitment of B Cells in BKPyVAN. Further studies would be required to evaluate the role of the different cells in BKPyVAN.

BOS_19_15 IMMUNOGENICITY OF RESPIRATORY SYNCYTIAL VIRUS VACCINATION IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Respiratory syncytial virus (RSV) prefusion F-based vaccines have recently been authorized to prevent infections among immunosuppressed individuals and elderly. Knowledge on the use of these vaccines in solid organ transplant (SOT) recipients is limited. Therefore, vaccine-induced immunogenicity and reactogenicity were analyzed in SOT recipients.

Methods: In this observational study, 27 kidney (KTx) and 13 lung (LuTx) transplant patients receiving the protein-based vaccines RSVPreF3-AS01$_E$ or RSVpreF were included. RSV-specific antibodies as well as vaccine-induced CD4 and CD8 T cells including their phenotype and functionality were analyzed before and 14 days after vaccination. Reactogenicity was self-reported using a questionnaire.

Results: Patients mainly received RSVPreF3-AS01$_E$ (LuTx: 76.9%, KTx: 93.3%). RSV-specific IgA levels were mostly below detection limit with no difference after vaccination, while 84.6% LuTx and 92% KTx patients had detectable IgG levels prior to vaccination. Vaccination led to a significant induction of RSV-specific CD4 T cells in KTx ($p<0.0001$) with no difference between RSV-A and RSV-B specific T cells indicating substantial cross-reactivity, while LuTx showed no significant induction of CD4 T cells ($p=0.109$). Likewise, CD8 T cells were not induced. Vaccine-induced CD4 T-cell levels in KTx patients were significantly higher than in LuTx patients ($p=0.0007$). RSV-specific CD4 T cells were predominantly polyfunctional, co-expressing IFNγ, IL-2 and TNF. In line with recent antigen encounter, their CTLA-4 expression level was significantly higher than on polyclonally activated T cells. Vaccination was well tolerated with either no adverse events (KTx: 24%, LuTx: 82%) or mainly pain at the injection site (KTx: 64%, LuTx: 18%).

Conclusions: A single dose of an RSVpreF-based vaccine was well tolerated in transplant recipients. Vaccine-induced CD4 T cells cross-reacted between RSV-A and B and their levels were higher in KTx than in LuTx recipients

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BOS_20_1 FOSTERING NEXT GENERATION OF TRANSPLANT PROFESSIONALS: IMPACT OF A 4 DAY COURSE ON MEDICAL STUDENTS

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Background: Despite the critical role of transplant surgery in modern healthcare, medical students often lack exposure to this subspecialty. Early learning opportunities are key to shaping interest in any field, however, few transplant-focused learning opportunities exist at the undergraduate level. We developed a 4 day teaching series, aiming to improve students' knowledge, skills, motivation, and perceptions of transplant surgery.

Methods: In a scoping survey, 55/61 (90%) UK medical students were 'interested' or 'very interested' to learn about transplantation, 95% felt they did not receive any formal teaching or clinical exposure in transplantation. Also, 53/61 (87%) felt 'underconfident' or 'very underconfident' in their surgical skills. Our course included lectures covering core topics, from organ retrieval to all solid organ transplants, and practical workshops teaching basic and advanced suturing techniques (e.g., simple interrupted to vascular anastomoses). Pre- and post-course questionnaires assessed knowledge, skills, motivation, and perceptions via Likert-scale questions, with responses analysed using Wilcoxon Signed-Rank Tests to assess changes in participants' responses.

Results: An average of 46/52 UK medical students attended each day of the series. 44 delegates (52% Female, 63% clinical years) completed both questionnaires. Significant improvements emerged across multiple domains. Perceptions regarding gender-friendliness (3.16 to 2.48, $p<0.001$) and workplace culture (2.80 to 2.02, $p<0.001$) improved, though concerns about work-life balance persisted. Knowledge scores regarding career-path understanding also rose ($p<0.001$). Skills domains showed improvement (e.g. confidence in performing end-to-end vascular anastomosis,1.48 to 3.82, $p<0.001$). Motivational factors shifted positively, with more interest to organise electives or taster days in transplant surgery (3.36 to 3.75, $p<0.01$).

Conclusions: Early exposure in a student-led transplant course positively improved motivation, perception and skills, and helped alleviate some misconceptions of transplantation. We believe introducing such initiatives, earlier in medical training can improve some of the difficulties currently faced by the transplant surgeons regarding recruitment and retention.

Table 1: Structured timetable of our undergraduate transplant surgery teaching series

Day	Lecture topics	Workshop topics	Total In-person Attendance
Day 1	Principles of transplantation Liver Transplantation Heart and Lung Transplantation	Basic suturing: How to perform a simple interrupted suture, instrument knot tie and vertical mattress Aortic Anastomosis: How to perform end-to-end vascular anastomosis	49
Day 2	Organ Retrieval Uterus Transplantation Corneal Transplantation	Hand tying: how to do a one-handed reef knot and surgeon's knot Advanced suturing: How to do a subcutaneous and subcuticular suture	46
Day 3	Kidney Transplantation Pancreas Transplantation Surgical Pathway to become a transplant surgeon in the UK	Microsurgery workshop: How to perform a simple interrupted suture using microsurgical tools Low-Bench Kidney transplant simulation workshop: How to perform an end-to-side vascular anastomosis	44
Day 4	Intestinal transplantation Hand and Upper Limb transplantation Future of Transplantation	Aortic Anastomosis: How to perform end-to-end vascular anastomosis How to perform an end-to-end intestinal anastomosis	43

Figure 1: Some photos of partcipitants and workshop leads at the practical workshops

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BOS_20_2 VALIDATING THE KDPI AND DEVELOPING AN IMPROVED GRAFT-SURVIVAL PREDICTION SCORE FOR DECEASED KIDNEY DONORS

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Background: Estimating kidney graft survival remains challenging in Europe, as a reliable predictive score has yet to be established. The KDPI, used in the US since 2014, combines donor factors to assess graft survival risk but lacks extensive validation in Europe. This study evaluates KDPI's applicability and proposes the Deceased Kidney Donor Graft Survival Index (DKD-GSI) to improve predictive accuracy for European cohorts.

Methods: We conducted a retrospective analysis of adult kidney transplant recipients in the Netherlands (January 2004–June 2024). Receiver Operating Characteristic (ROC) curves and Kaplan-Meier survival analyses validated KDPI, with death-censored graft survival as the primary outcome. Uni- and Multivariate Cox regression (on 80% of the data) identified variables influencing graft survival. The new DKD-GSI was developed and validated using the remaining 20%.

Results: Data from 6,350 deceased donor kidney transplants were analyzed. Distinction between DCD and DBD was not statistically significant in the long term, contradicting KDPI assumptions. KDPI achieved AUCs of 60.3 and 63.5 for five- and ten-year predictions, respectively. Stratification into KDPI groups (0-20, 20-50, 50-90, 90-100) showed significant differences in survival risk ($p < 0.001$). Cox regression identified factors positively (serum albumin, eGFR, male-to-male donation) and negatively (age, smoking, diabetes) affecting graft survival. The DKD-GSI yielded AUCs of 61.5 and 66 for five- and ten-year predictions and showed significant discrimination in stratified groups (0-1.5, 1.5-3, 3-5, 5-8; $p < 0.001$).

Conclusions: This study highlights DKD-GSI as a promising alternative to KDPI for predicting kidney allograft outcomes. Though preliminary, its implementation could enhance clinical decision-making across Europe, providing better donor-recipient matching through more comprehensive data.

BOS_20_3 EVALUATION OF FOUR INITIAL DOSES OF ENVARSUS IN RENAL TRANSPLANT .OVERDOSE MUST BE AVOIDED

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Background: Envarsus is a new prolonged release formulation of tacrolimus with increased bioavailability. The summary of product characteristics recommends an initial dose of 0.17 mg/kg/day, which we consider may be excessive. We aimed to compare the pharmacokinetics of four different initial doses of Envarsus: 0.15 mg/kg/day (group 1), 0.12 mg/kg/day (group 2), 0.10 mg/kg/day (group 3), and 0.08 mg/kg/day (group 4).

Methods: Induction therapy consisted of thymoglobulin, sirolimus, and prednisone, with initiation of Envarsus when serum creatinine was below 3 mg/dL. We estimated the area under the curve (AUC) and trough concentration at 72 hours, considering the therapeutic window to be between 6 ng/mL and 8 ng/mL. People with trough concentrations above 8 ng/mL had their Envarsus treatment reduced or temporarily suspended (for one day). We evaluated kidney function at three months post-transplant. In total, 176 recipients were enroled but only 168 completed the study (44 in group 1, 38 in group 2, 42 in group 3, and 44 in group 4). The groups were balanced in participant characteristics

Results: Groups 3 and 4, compared with groups 1 and 2, had significantly lower mean trough concentration (8.72 ng/mL and 7.53 ng/mL versus 11.84 ng/mL and 12.02 ng/mL, respectively), mean AUC (324.12 ng·h/mL and 294.93 ng·h/mL versus 440.81 ng·h/mL and 438.95 ng·h/mL, respectively), proportion of patients with supratherapeutic drug levels (50.0% and 36.4% versus 72.1% and 71.1%, respectively), and proportion of patients with a suspendeddose (14.3% and 15.9% versus 31.8% and 34.2%, respectively). Kidney function was similar in all groups at three months

Conclusions: the lowest initial dose of Envarsus (0.08 mg/kg/day) resulted in adequate trough concentration and AUC, and a decrease in dose suspensions. This group had the largest proportion of patients within the therapeutic window

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BOS_20_4 PREVALENCE AND RISK FACTORS OF URETERAL STENOSIS IN KIDNEY TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW

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Background: Following kidney transplantation surgery, recipient morbidity may compromise graft outcomes and survival. Among urologic complications, ureteral stenosis is the most frequently encountered issue. However, the risk factors of post-transplantation ureteral stenosis remained unclear. Therefore, we reviewed the prevalence and potential risk factors associated with ureteral stenosis in kidney transplants recipients.

Methods: Literature searching was systematically performed in PubMed, SCOPUS, and Cochrane Library for all English language articles according to PRISMA standards. The study protocol was registered at PROSPERO. We used specific keywords, such as “ureteral stenosis/stricture”, “renal transplantation”, “prevalence”, and “risk factor”. Each selected study will be extracted and assessed using Newcastle-Ottawa Scale for cohort studies.

Results: A total of 127 relevant studies were initially found for further screening by reviewers. We included five retrospective studies that meet our inclusion criteria involving a total of 5,769 kidney transplant recipients, all categorized as high-quality. The reported prevalence of ureteral stenosis among kidney transplant recipients ranged from 1.2 to 7.6%. Significant risk factors identified include older age, kidney donor with more than two arteries, delayed graft function, prolonged warm ischemic time, hospital readmissions, ureter-bladder anastomosis technique, bladder outlet obstruction, and urinary lithiasis. These factors contribute to ureteral ischemia, which subsequently results in ureteral stenosis.

Conclusions: The prevalence of ureteral stenosis among kidney transplant recipients ranged from 1.2 to 7.6%. The main risk factors are old recipient age, kidney with multiple arteries, and delayed graft function. For patients at higher risk of developing ureteral stenosis, the placement of ureteral stent is recommended as a preventive strategy. We suggest further prospective studies to confirm our findings.

BOS_20_5 MOLECULAR ASSESSMENT OF ANTIBODY-MEDIATED REJECTION CATEGORIES BASED ON BANFF 2022

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Background: A recent Banff 2022 update reclassified antibody-mediated rejection (AMR) based on the presence of microvascular inflammation (MVI), C4d positivity, and donor-specific antibodies (DSA). The role of molecular assessment in biopsies with active and/or chronic AMR features remains unexplored.

Methods: 755 kidney allograft biopsies from 2 European centers were assessed by the Molecular Microscope Diagnostics system (MMDx®) at two independent MMDx laboratories in Portland, USA, and Prague, Czech Republic. We identified 171 cases with AMR (active AMR, n=48, chronic-active AMR, n=97, chronic AMR, n=26), 64 DSA-negative/C4d-negative MVI, and 91 probable AMR cases. MMDx sign-outs, archetype clusters, and molecular scores were compared. DSA cut-off was 500 MFI.

Results: MMDx identified pure molecular AMR in 64% of chronic-active AMR, 52% of active AMR, and 47% of DSA-negative MVI cases, compared to 18% in probable AMR and only 4% in chronic AMR (p<0.001) (Figure 1). Molecular rejection, ABMR, glomerulitis, and peritubular capillaritis scores were highest in MVI, active AMR, and chronic-active AMR, compared to probable AMR and chronic AMR (p<0.001). Acute kidney injury (AKI) and inflammation molecular scores peaked in MVI and active AMR groups (p<0.001). When AMR cases were subclassified by active and/or chronic histologic lesions (cg>0), molecular AMR was most frequent in cases with both active and chronic features (53%) and active-only features (35%). Chronic-only AMR was rare (4%). Among molecular AMR cases, early-stage AMR (EABMR) was most common in active AMR (73%). Cases with active and chronic features showed a distribution of EABMR (36%), fully developed AMR (FABMR, 52%), and late-stage AMR (LABMR, 12%).

Conclusions: MMDx identifies molecular AMR in a relevant proportion of the new Banff 2022 sub-categories, including DSA-negative MVI and probable AMR, while chronic-only AMR shows minimal molecular evidence of rejection. The molecular archetype scores may provide additional and more comprehensive information on activity and chronicity in AMR.

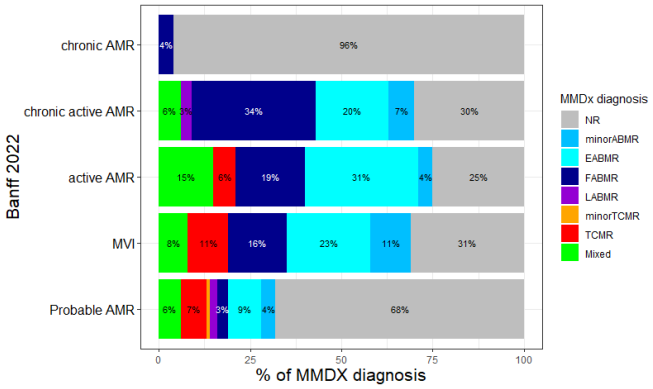

Figure 1. Differences among AMR histology subcategories in the proportions of MMDx diagnoses.

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BOS_20_6 USE OF THE BOVINE PERICARDIUM PATCH IN KIDNEY TRANSPLANTATION FROM A LIVING DONOR: RESULTS OF 70 CASES

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Background: Kidneys with multiple renal arteries (MRAs) pose a challenge to the kidney transplant surgeon. In order to ensure successful renal transplantation, these kidneys often require the performance of complex pre-transplant vascular reconstructions before the organ is viable for implantation, especially in kidneys from living donors, given the absence of an aorta patch. Among the many pre-transplant vascular reconstruction techniques, the use of bovine pericardium patch (BP) is increasingly widespread in the transplantation setting, after early experiences in the oncological field. We report our experience of using BP in the reconstruction and/or creation of a unitary patch for the purpose of living-donor renal transplantation in 70 cases

Methods: From December 2015 to May 2024, 145 patients underwent living donor kidney transplantation at our institution; In 70 cases, the bovine pericardium patch was used for the reconstruction of the arterial patch. Latero-terminal suture with detached stitches or semicontinuous 6-0 prolene sutures were performed on the bench table, depending on the caliber of the vessels. Multiple renal arteries and single arteries with reduced caliber were considered for grafting onto BP patches, up to a diameter of 2 mm. The primary outcomes were the incidence of the development of delayed graft function and/or a vascular or urological complication within 12 months of transplantation.

Results: Seventy living transplant recipients were evaluated. Two renal arteries (RAs) were found in 20 kidneys (28.6%); three renal arteries in 11 allografts (15.7%); single small-to-medium caliber RAs in 39 (55.7%). Renal artery reconstruction was performed in 48.2% (70/145) of patients. None of the patients developed DGF or postoperative vascular or infectious complications

Conclusions: The use of bovine pericardium for the creation of a single renal artery ostium/patch and for renal graft anastomosis from living donor kidney transplantation with single or multiple arteries offers better results in terms of functional outcome, without significant increase in warm ischemia time, and without increased risk of postoperative vascular or infectious complications

BOS_20_7 EARLY GRAFT DYSFUNCTION REQUIRING VA ECMO FOLLOWING DCD HEART TRANSPLANTATION IMPACT ON SURVIVAL

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Background: Clinical DCD heart transplantation (HTx) was established in the UK in 2015 and now accounts for > 30% of UK HTx. Early graft dysfunction (EGD) post-transplant requiring veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) support is more common in DCD heart recipients. There is paucity of data on the impact of early graft dysfunction requiring (VA-ECMO) on recipient survival in DCD HTx.

Methods: This is a single-centre retrospective study of consecutive DCD HTx performed between February 2015 and July 2024. Multi-organ transplants were excluded. The recipients were divided in two groups according to those with and without EGD post-transplant. Donor and recipient characteristics, duration of ICU and hospital stays were compared using logistic regression. Post-transplant survival was assessed with Kaplan-Meier analysis and compared with log-rank test.

Results: There were128 DCD HTx of which 27 (21.1%) developed EGD and required VA-ECMO support. Baseline characteristics are summarised in Table1. EGD post-transplant was associated with longer ICU stay (5 vs 18.5 days, p<0.001) and hospital stay (20 vs 42 days, p<0.001). Survival free of re-transplantation was significantly worse in the EGD group at 90 days (74.1% vs 99% ys, p <0.001). However, long-term conditional survival of recipients who survived the first 90 days post-transplant was similar (Figure1).

Conclusions: In this study, DCD heart recipients who developed EGD requiring VA-ECMO support after HTx had longer ICU and hospital stays and lower survival. However, EGD recipients who survived the first 90 days post-transplant, their long-term survival was comparable to those without EGD. Further studies are needed to identify modifiable risk factor for the development of EGD following DCD HTx to improve outcomes.

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BOS_20_8 PORTAL VENOUS PRESSURE MEASUREMENTS FOLLOWING ISLET AUTROTRANSPLANTATION

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Background: Total pancreatectomy (TP) is a therapeutic option in patients with chronic pancreatitis suffering from intractable pain where all other management options have failed. The addition of an islet autotransplant (TPIAT) where the patient's own islets are infused into the portal vein mitigates and potentially abrogates the inevitable complete loss of endocrine function following the pancreatectomy. The use of the umbilical vein is a safe and reliable technique for intraportal islet infusion.

Methods: Patients undergoing TPIAT at our institution undergo a comprehensive evaluation by a multidisciplinary team. During surgery, the umbilical vein is routinely used for islet infusion which allows for the monitoring of portal pressures and the performance of portal venography if required. For this study portal pressures were recorded intra and postoperatively using an externalised umbilical vein catheter. Data analysis involved descriptive statistics and comparative measures for trends in portal pressure and venous oxygen consumption.

Results: Seventy-six patients underwent TPIAT. Thirty-seven received an islet infusion via the recanalised umbilical vein, and 7 patients had portal pressures assessed post-operatively. Portal pressures increased transiently post-infusion, peaking on days 3 and 6, before returning to baseline by day 7. Venography confirmed patency in all patients, with no evidence of portal vein thrombosis. One patient required an alternative infusion route due to prior surgery obliterating the umbilical vein. No complications arose from use of the umbilical vein.

Conclusions: Use of the recanalised umbilical vein for islet infusion is a safe and effective technique which facilitates subsequent portal venous monitoring. Accurate portal pressures and portal venous oxygenation can be assessed, and use of the umbilical vein additionally allows portal venography to be performed. This study confirms that the increased perioperative portal pressure is transient and that the intraportal route is suitable for islet cell infusion.

BOS_20_9 COMPARISON OF OUTCOMES OF ISLET AUTOTRANSPLANTATION IN GENETIC AND NON-GENETIC CHRONIC PANCREATITIS

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Background: Total pancreatectomy with islet autotransplantation (TPIAT) is an effective surgical option for patients with debilitating chronic pancreatitis (CP). CP of differing aetiologies, such as alcoholic, idiopathic and genetic origins, often results in distinct disease patterns and patient outcomes. This study investigates and compares the outcomes of TPIAT in patients with genetic and non-genetic CP from a single specialist unit in the United Kingdom (UK).

Methods: A retrospective analysis was conducted on all patients who underwent TPIAT from 1994 – 2024 inclusive. Patients were categorised based on the aetiology of CP, either alcoholic, idiopathic or genetic. Patient demographics, operative characteristics, and outcomes of these 2 groups was compared. One-way analysis of variance tests was used to compare categorical data.

Results: 76 patients were included, 60 patients with an alcoholic or idiopathic and 16 patients genetic induced CP. Genetic CP patients were younger with less co-morbidity. Operative duration was longer in the genetic CP cohort (11 hours vs. 8 hours), although estimated blood loss (EBL) was similar in both cohorts. There were less complications and shorter length of stay in the genetic CP cohort (15 days vs. 20 days). Islet yield was significantly lower in the genetic CP cohort (24743 IEQ) compared with alcohol CP cohort (142935 IEQ).

Conclusions: This study highlights the differences in outcomes between patients undergoing TPIAT for genetic and non-genetic CP. Whilst genetic CP patients were younger, experienced fewer complications, and had a shorter hospital stay, they also had lower islet cell yields compared with those with alcoholic CP. These findings suggest that the aetiology of CP significantly influences both the perioperative course and post-surgical outcomes.

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BOS_20_10 EVALUATING POST-TRANSPLANT OUTCOMES IN ELDERLY LIVER RECIPIENTS: A COMPARATIVE STUDY OF PATIENTS AGED OVER 70

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Background: The increasing average age of the population leads to a higher percentage of elderly patients awaiting liver transplantation. However, advanced age has been considered an independent risk factor for candidates. This study aims to evaluate post-transplant outcomes in patients over 70 years, traditionally viewed as an age limit.

Methods: We performed a retrospective analysis of 584 liver transplant recipients at our center from January 2018 to November 2023, dividing them into two groups: under 70 years (n=548) and over 70 years (n=36). Categorical variables were reported as numbers and percentages, while continuous variables were presented as medians and interquartile ranges (IQR).

Results: The median age was 58 years (IQR 52-63) for the younger group and 71 years (IQR 70-72) for the older group (p<0.001). Both groups were homogeneous in sex and BMI (p>0.05). No significant differences were observed in cirrhosis complications (ascites, encephalopathy, portal hypertension, jaundice, coagulopathy, esophageal varices, hepatocellular carcinoma; p>0.05). The MELD score was lower in patients over 70 (12.5, IQR 9-17) compared to those under 70 (15, IQR 10-23) (p=0.032). Post-operative complications, including early allograft dysfunction, hepatic artery thrombosis, or biliary and cardiac complications, showed no significant differences (p>0.05). The Comprehensive Complication Index was similar between groups (30, IQR 21-49 for under 70 vs. 29.6, IQR 21-38.35 for over 70; p=0.519). The median hospital stay was shorter for patients over 70 (14.5 days, IQR 12-17) compared to younger patients (16 days, IQR 11-29) (p=0.032). The 90-day readmission rate was not significantly different (p>0.05).

Conclusions: The results indicate that patients over 70 years can achieve post-liver transplant outcomes comparable to younger patients, suggesting that advanced age should not be an exclusive criterion for disqualifying candidates from liver transplantation.

BOS_20_11 GRAFT AND DONOR WEIGHT IN PEDIATRIC LIVER TRANSPLANTATION - A HIGH-VOLUME SINGLE CENTER EXPERIENCE

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Background: Pediatric liver transplantation (PLT) is a well-established treatment for end-stage liver disease in children. However, it still presents significant challenges, such as optimizing graft selection based on the recipient's size. The preoperative graft-to-recipient weight ratio (GRWR) is a predictor of outcomes in living donor liver transplantation (LDLT), but the optimal GRWR remains a topic of debate especially in small children with a body weight below 10 kg.

Methods: This retrospective single-center cohort study analyzed 57 pediatric liver transplants using left lateral segments (2019–2024) to evaluate the impact of recipient weight (<10 kg vs. ≥10 kg), donor type (LDLT vs. deceased (DDLT)), and GRWR on outcomes, including survival, complications, graft function, and rehospitalisation.

Results: Recipients < 10 kg (n = 34) had similar overall (88.2%) and graft survival (88.2%) as those ≥10 kg (n = 23, 95.7% and 100%). Despite a higher GRWR in smaller recipients (4.9% vs. 2.4%, p < 0.05), concerning biliary and vascular complications were comparable. However, acute cellular rejection (56.5% vs. 11.8%, p < 0.05) and 90-day rehospitalisations (56.5% vs. 26.5%, p = 0.022) were more frequent in larger recipients. Living-related donation was significantly more common in recipients weighing <10 kg (61.8% vs. 8.7%, p < 0.05). The LDLT group had lower recipient weight (7.1 kg vs. 11.8 kg) and higher GRWR (4.6% vs. 3.4%, p < 0.05). Vascular complications such as arterial (13% vs. 0%, p < 0.05) and portal vein thrombosis (21.7% vs. 2.9%, p < 0.05) were more frequent in LDLT, but there were no differences in biliary complications, readmissions, or overall survival.

Conclusions: These findings confirm the safety and efficacy of higher GRWR in low-weight recipients. Higher GRWR, did not increase rejection or biliary complications. Survival and graft function remained similar. PLT recipients < 10 kg achieve comparable outcomes to larger recipients. While vascular complications were more frequent in LDLT, they did not impact long-term results. DDLT achieved comparable results to LDLT.

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BOS_20_12 CONSENSUS GUIDELINES FOR THE CLASSIFICATION OF BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION

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Background: Injury to the bile ducts during liver retrieval and the transport process can lead to the development of biliary complications (BC) following orthotopic liver transplantation (OLT). Consistency in how to diagnose and report post-OLT BC is currently lacking and therefore clinical studies are often non-comparable, hampering advances in the field. Thus, a consensus on how to define, grade, report and monitor post-OLT BC is urgently needed to guide future clinical trial design and improve post-OLT outcomes.

Methods: The reporting guidelines and grading of BC presented here were established after a consensus meeting held in Innsbruck, Austria, on 14th and 15th December 2023, followed by rounds of online voting according to a modified Delphi method.

Results: After the in-person meeting, three rounds of online-voting and a subsequent online discussion, the panel agreed on recommendations for classifying, grading and reporting post-OLT BC. BC not affecting the anastomotic area should be classified as hilar or intrahepatic post-transplant cholangiopathy. BC affecting the anastomotic area should be classified as anastomotic stricture/leakage. BC should be graded according to a modified Clavien Dindo classification into grade I to V. BC rates should be assessed 12 months post-OLT. ERCP/MRCP is the gold standard for diagnosing post-OLT BC, however, no protocol ERCP/MRCP is needed.

Conclusions: The established guidelines provide clarity on the definition, grading, monitoring and reporting of post-OLT BC aiming to facilitate future clinical trial development.

BOS_20_13 POOR ONE-YEAR OUTCOMES FOLLOWING HEPATIC ARTERY THROMBOSIS AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: Hepatic artery thrombosis (HAT) after pediatric liver transplantation (pLT) is a severe complication that can lead to acute graft failure, often requiring urgent re-transplantation. Despite its significance, the outcomes of HAT after pLT remain poorly characterized. This study aimed to determine the one-year incidence of graft loss and mortality and to identify associated risk factors in patients who develop HAT after pLT.

Methods: We analyzed data from patients who developed HAT after pLT from the HEPatic Artery Stenosis and Thrombosis after Liver Transplantation in Children (HEPATIC) registry. This registry includes data from 24 centers across 20 countries and six continents, spanning a 20-year period during which 8,469 pLTs were performed. Clinical characteristics were examined at three timeframes: pre-transplant, immediate post-transplant, and following HAT diagnosis. Risk factors for graft loss and mortality after HAT were identified through multivariate Cox regression analyses, with model assumptions verified using Schoenfeld residuals.

Results: HAT occurred in 3.4% of patients (n=287, 53% female, median age 1.8 years). Following the diagnosis of HAT, the cumulative incidence of graft loss was 44% (95% CI 38–49) at one month and 56% (95% CI 50–62) at one year. Mortality rates were 15% (95% CI 11–19) and 23% (95% CI 18–28) at these respective timepoints. Multivariate Cox regression analysis identified three independent risk factors for one-year graft loss after HAT: aspartate aminotransferase (AST) ≥ 1000 U/L, an international normalized ratio (INR) ≥2, and dialysis at HAT diagnosis (each p <0.05). Independent risk factors for one-year mortality included non-cirrhotic primary diseases, living donor pLT, AST ≥ 1000 U/L, INR ≥ 2, and dialysis at HAT diagnosis (each p <0.05).

Conclusions: Patients with HAT after pLT experience notably high rates of graft loss and mortality, particularly within the first month following diagnosis and with signs of graft and multi-organ failure. Risk stratification according to risk factors identified at HAT diagnosis underscore the critical need for strategies to prevent graft loss and mortality after HAT.

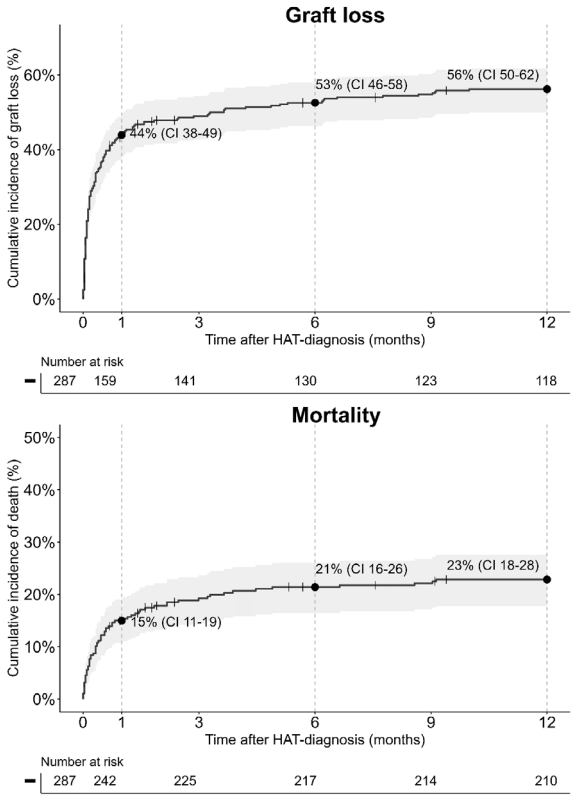

Figure 1. Kaplan-Meier curves displaying the overall cumulative incidence of graft loss and mortality within the first year after diagnosis of HAT.

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BOS_20_14 PROGNOSTIC ROLE OF THYROID HORMONES IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE

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Background: Acute-on-chronic liver failure (ACLF) is characterized by systemic inflammation, organ dysfunction, and high mortality. Thyroid hormone dysregulation, commonly observed in critical illnesses, may impact outcomes in ACLF. This study evaluates the prognostic significance of thyroid hormones (TSH, fT3, fT4) in predicting survival in ACLF patients, particularly in the context of liver transplantation (LT).

Methods: A retrospective analysis of 95 ACLF patients was conducted. Thyroid hormone levels (TSH, fT3, fT4) were analyzed in relation to survival and mortality post-LT. Statistical comparisons between survivors and non-survivors employed the Mann-Whitney U test, while correlations between thyroid parameters and clinical scores (MELD, CLIF-C ACLF) were assessed using Spearman's correlation. A p-value < 0.05 was considered significant.

Results: Non-survivors exhibited significantly lower fT3 levels compared to survivors (mean: 2.28 vs. 2.76 pg/mL, p = 0.002), while fT4 levels were also reduced in non-survivors (mean: 12.28 vs. 14.16 pmol/L, p = 0.032). TSH levels did not differ significantly between groups (p = 0.973). Correlation analysis revealed an inverse relationship between fT3 and CLIF-C ACLF scores (r = -0.338, p = 0.003), as well as between fT4 and both CLIF-C ACLF scores (r = -0.352, p < 0.001) and MELD scores (r = -0.398, p < 0.001). These findings suggest that decreased fT3 and fT4 levels are associated with disease severity and worse prognosis in ACLF.

Conclusions: Low fT3 and fT4 levels are significant predictors of mortality in ACLF and correlate with established severity scores. The lack of a significant role for TSH suggests that peripheral thyroid hormone conversion may be more relevant in this context. Assessing thyroid hormone levels could enhance prognostic models in ACLF, particularly in identifying high-risk patients for LT. Prospective studies are needed to confirm these findings and explore the mechanistic role of thyroid hormones in ACLF pathophysiology.

BOS_20_15 ISCHEMIC CHOLANGIPATHY AFTER DCD LIVER TRANSPLANTATION:INSIGHTS FROM A HIGH-VOLUME SINGLE-CENTER STUDY

Aamir Nawaz[1], Amir Ali[2], Rhiannon Taylor[3], Maria Jacobs[4], Annalisa Dolcet[5], David Wallace[6], Buddhika Uragoda Appuhamilage[7], karen mercer[8], Stephen Gregory[9], Pauline Kane[9], Alberto Sanchez-Fueyo[9], Miriam Cortes Cerisuelo[10], Hector Vilca Melendez[9], Nigel Heaton[11], Wayel Jassem[12]

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Background: In some centers, massive era-specific improvements have been observed in the survival of recipients who have received a liver donated following circulatory death (DCD). However, a huge international concern still exists over the impact of ischaemic cholangiopathy (IC) in these patients. We used the Kings College Hospital (KCH) DCD database to evaluate both the incidence and risk factors of IC between 2001 and 2024.

Methods: We identified all elective adult recipients of a DCD liver at KCH. IC was defined using clinical and radiological criteria. Univariate and adjusted logistical regression techniques were used to identify factors that influenced whether or not patients developed ischaemic cholangiopathy. Multiple imputation methods were used to account for missing data.

Results: During the study period, 767 DCD LTs were performed and of these 62 livers received normothermic machine perfusion (NMP). Overall, 44 (5.7%) recipients developed IC of which 20 patients 45% were diagnosed within six months of transplantation. Eight patients 18% developed biliary stricture, two of whom required surgical biliary reconstruction. Seven patients (28%) lost their grafts due to IC and had to be retransplanted. In univariate analysis, older donors, prolonged cold ischaemic time, and donors with shorter hospital stays were risk factors for developing IC. In multivariate analysis, the retrieval unit (odds ratio [OR], 3.71; p<0.01) was strongly associated with a higher rate of post-transplant IC. There was no difference in the rate of IC between recipients whose organs had or had not received NMP.

Conclusions: Despite era-specific improvements in DCD liver transplantation IC remains an early post-transplant threat to graft survival. Irrespective of machine perfusion technology, careful donor and recipient selection, safe and efficient technique of organ DCD procurement and the operative process can help to reduce the rate of IC and increase confidence in the use of DCD livers.

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BOS_21_1 EXPLORING PROTEOMICS SIGNATURES OF LIVER VIABILITY DURING NORMOTHERMIC MACHINE PERFUSION FOR BIOMARKER DISCOVERY

Meryl Copray, **Martin Pabst[1], Marieke Klijn[2], Jeroen De Jonge[3], Marcel Ottens[2]**

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Background: Normothermic machine perfusion (NMP) facilitates real-time functional assessment of donor livers by simulating physiological conditions. However, current biomarkers, such as lactate clearance and bile production, demonstrate limited diagnostic accuracy, emphasizing the need for more reliable indicators to enhance viability assessment and predict post-transplant outcomes.

Methods: This study used 24 donor livers assessed during the DHOPE-COR-NMP protocol, covering a wide range of viability. Blood-based perfusate samples were collected at four timepoints: COR-T-1 (baseline), NMP-T60, NMP-T150 (decision moment), and NMP-Tend. A total of 72 samples were subjected to mass spectrometry-based shotgun proteomics, enabling comparison between transplanted (n=12) and non-transplanted (n=12) livers during NMP.

Results: Functional enrichment analysis (FDR ≤ 0.05) revealed that transplanted livers exhibited greater metabolic activity during NMP, involving wound healing, defence, and immune responses. Non-transplanted livers showed a gradual increase of metabolic activity between NMP-T60 and NMP-T150. At NMP-T150, 960 proteins were detected, with 191 upregulated and 1 downregulated in non-transplanted livers ($p < 0.05$, fold change ≥ |1.5|) compared to transplanted livers. Notably, the regulation of activated PAK-2p34, a promoter of programmed cell death, and the KEAP1-NFE2L2 pathway, associated with hepatoprotection against lipotoxicity, were over-represented in non-transplanted livers, indicating unfavourable conditions. Mitigating PAK-2p34 activity and lipotoxicity may be critical for improving clinical practices.

Conclusions: Proteomic analysis revealed distinct metabolic signatures differentiating transplanted and non-transplanted livers, identifying wound healing, defence, and immune responses as potential markers of transplantation suitability. Targeted strategies to reduce PAK-2p34 activation and lipotoxicity may advance liver transplantation outcomes.

BOS_21_2 GENETIC MODIFICATION OF PIGS FOR XENOTRANSPLANTATION

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Background: Gene editing of the genome of pigs has enabled the generation of an unlimited supply of human-compatible xenograft donor organs for transplantation. While inactivation of the α1,3-galactosyl transferase gene resulted in the elimination of hyperacute rejection (HAR), knockout of additional targets, including CMAH knockout and Beta4Gal knockout, has addressed further aspects of innate immunity, while knockout of the growth hormone receptor gene has allowed the generation of smaller human-sized donor pigs. In addition, multiple genetic modifications are required to address inflammation, and coagulation dysfunction resulting from delayed xenograft rejection (DXR).

Methods: Incorporation of efficacious combinations of human complement inhibitor genes (CD46, DAF), anti-inflammatory genes (HO1), immunomodulators (CD47), and anti-coagulant genes (TBM, EPCR), through utilization of multi-cistronic vectors, has facilitated the production of pigs with ten (10) genetic modifications (4 knockouts + 6 human genes) allowing co-expression and co-segregation of the “stacked” transgenes. By applying transgenic interventions to address both innate immunity and inflammation via overexpression of cytoprotective and immunosuppressive transgenes, in combination with mitigation of coagulation dysfunction, cells and organs from these multi-transgenic pigs have the potential to address virtually all levels of xenograft incompatibility.

Results: Significant progress in this area has resulted in further extension of survival times of multi-transgenic xenograft kidney, heart, and lungs in preclinical non-human primate (NHP) models. In addition, 10GE hearts and kidneys have been tested in preclinical human decedent models and demonstrated full functionality for 3-7 days without rejection. Over the past two years, hearts from our 10GE pigs have been transplanted into 2 patients under a compassionate-use eIND at University of Maryland, and Revivicor xenokidneys transplanted into another two patients at NYU.

Conclusions: In all cases, there was prolonged survival which allowed learnings that will facilitate human clinical trials planned for 2025.

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BOS_21_3 RECOVERY OF RAT HEARTS AFTER COLD STORAGE WITH ACID SENSING ION CHANNEL INHIBITOR HI1A VARIES BY SEX

Sanjay Dutta[1], Jeanette Villanueva[2], Ling Gao[3], Aoife Doyle[2], Nathan Palpant[4], Glenn King[4], Peter Macdonald[2]

[1]Victor Chang Cardiac Research Institute; Cardiac Transplantation, [2]Victor Chang Cardiac Research Institute, [3]Victor Chang Cardiac Research Intitute, [4]The University of Queensland

Background: Most heart transplants rely on cardioplegia and cold static storage (CSS) for preservation, however long ischaemic times result in poor outcomes. Supplementation of cardioplegia improves post-transplant organ function and Hi1a, an acid sensing ion channel (ASIC) 1a inhibitor derived from funnel web spider venom, reduces ischaemia-reperfusion injury. Women are underrepresented in cardiovascular research, and oestrogen has been shown to decrease ASIC1a expression in other tissue types. We investigated if the cardiac functional recovery following CSS with cardioplegia supplemented with Hi1a differed based on sex.

Methods: Hearts were isolated from male (M) and female (F) Wistar rats (300-570g, n = 6-10/group) perfused ex-vivo with Krebs-Henseleit buffer at 37°C, and baseline haemodynamic measurements of aortic flow (AF) were obtained. Hearts were arrested with Celsior (Cel) cardioplegia either alone, or supplemented with 10nm Hi1a. Following 6-hour CSS (4°C), hearts were re-perfused ex-vivo. Haemodynamic measurements were obtained, and recovery expressed as percentage of pre-storage baseline (mean ± SEM).

Results: Compared to unsupplemented Celsior (AF 14± 5.0%), male hearts stored in Celsior supplemented with 10nM Hi1a had significantly improved recovery (AF 55± 10%, P = 0.026). Female rat hearts stored in unsupplemented Celsior (AF 24±5.8%) had improved recovery compared to male hearts, however supplementation with 10nM Hi1a did not significantly improve recovery (AF 31±9.8%, P = 0.89). Two-way ANOVA revealed significant interaction between supplementation with Hi1a and sex (P = 0.047), with supplementation resulting in improved recovery overall (P = 0.007) with no significant impact of sex (P = 0.412).

Conclusions: Supplementation of Celsior with Hi1a improves cardiac recovery following 6 hours CSS in male but not female rats, showing that its benefit as a preconditioning agent is influenced by sex. Further work is needed to examine reasons for differing efficacy between sexes. ASIC1a inhibitors may improve acceptable ischaemic times for organ transplantation however sex of donors may need to be considered.

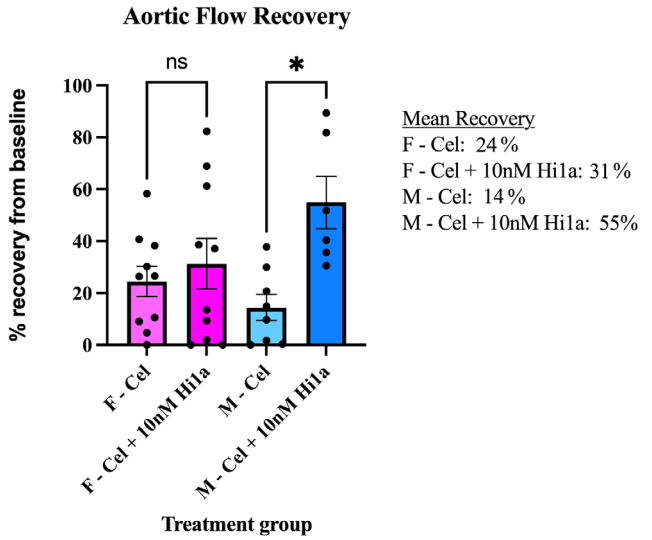

Figure 1: Mean myocardial functional recovery following 6hrs CSS, expressed as a percentage of baseline aortic flow. Error bar represents standard error of the mean.

BOS_21_4 GENETIC ENGINEERING OF PORCINE AND HUMAN ORGANS DURING EX VIVO PERFUSION: A PROOF OF CONCEPT

Avery Fortier[1], Matthew Holzner[2], Yichen Zhong[3], Kimberly Feeney[4], Huong Pham[5], Leona Kim-Schluger[6], Sander Florman[3], Yizhou Dong[3], Daniel Puleston[3], Leonie Van Leeuwen[7], Zeeshan Akhtar[8]

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Background: Amidst the donor organ scarcity, normothermic machine perfusion (NMP) has emerged as a method to evaluate and preserve grafts prior to transplantation. Genetic engineering of these organs may offer the next frontier: beyond assessment to treatment. Here, we integrated lipid nanoparticle (LNP) technology with liver and kidney NMP to deliver xenogeneic mRNAs encoding luciferase and IL-10. Our proof of principle establishes an opportunity for groundbreaking organ repair using machine perfusion.

Methods: Porcine and human organs were perfused for up to 40 hours with continuous monitoring of blood gas values. At 1 hour of NMP, LNPs containing either firefly luciferase or mouse IL-10 mRNA were administered to the organ arterially. Luciferase production was assessed with whole organ imaging and tissue immunohistochemistry. IL-10 production was quantified by protein analysis of perfusate.

Results: Luciferase expression was widespread throughout the liver parenchyma (Fig. 1A-B). Significant IL-10 overexpression was measured in the liver after 6 hours and in the kidney after 4 hours (Fig. 1C-D). Organs demonstrated stable flows (Fig. 1 E-H). Livers showed effective lactate clearance (Fig. 1 I-K). One paired kidney had sustained urine production during NMP (Fig. 1L).

Conclusions: Our findings demonstrate the feasibility of targeting mRNA delivery to donor organs during NMP. The successful expression of IL-10 and luciferase across organ type and model shows the potential of this approach for both immunomodulation and functional protein production. This work will enable further optimization of mRNA-based perfusion therapies, potentially expanding the organ pool and improving patient outcomes.

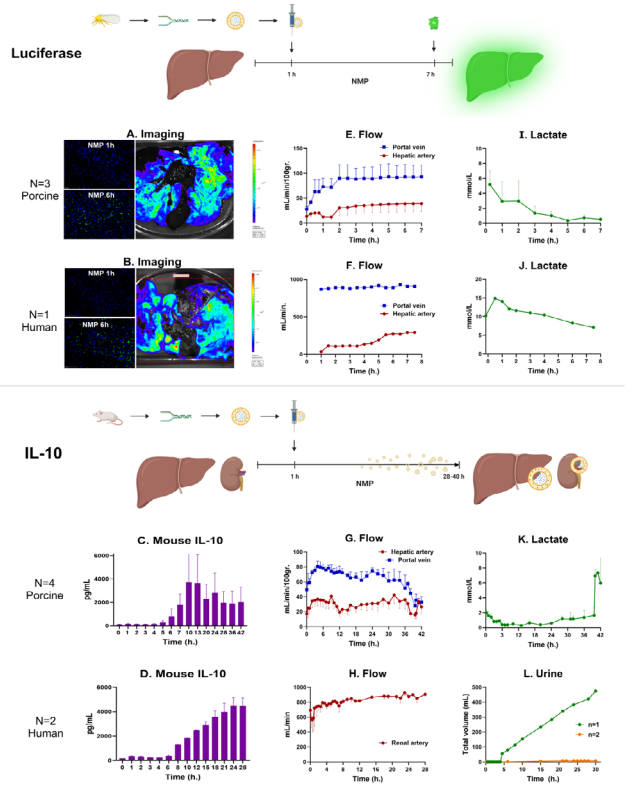

Figure 1: LNP-mediated gene editing during NMP. **A-B:** Immunohistochemical and whole organ imaging of luciferase expression in the liver. **C-D:** Protein expression of IL-10 in the kidney and liver. **E-G:** Hepatic artery and portal vein flow rates of the liver. **H:** Renal artery flow rate of the kidney. **I-K:** Lactate clearance of the liver. **L:** Cumulative urine production of the kidney. All data shown as mean ± SEM. Created with Biorender.com and GraphPad Prism 10.3.1.

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BOS_21_5 SEQUENTIAL HYPOTHERMIC AND NORMOTHERMIC LIVER MACHINE PERFUSION WITHOUT A PERFUSION SOLUTION SWITCH

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[1]University Medical Center Groningen; Umcg; Surgery, [2]Umcg; Umcg; Surgery, [3]University Medical Center Groningen; University Medical Center Groningen, [4]University Medical Center Groningen, [5]University Medical Center Groningen; Umcg Comprehensive Transplant Center; Hpb Surgery and Liver Transplantation

Background: Liver transplantation is a critical treatment for patients with end-stage liver disease, but a shortage of donor organs necessitates the use of extended criteria donor (ECD) livers. Current protocols assess ECD liver viability via normothermic machine perfusion (NMP). At our center, ECD livers undergo dual hypothermic oxygenated perfusion (DHOPE), followed by controlled oxygenated rewarming (COR) to normothermic conditions. However, switching perfusion solutions between DHOPE and COR introduces additional cold ischemia time and logistical challenges. In this study we investigated the feasibility of sequential DHOPE-COR-NMP without a fluid switch.

Methods: Eighteen porcine livers subjected to 30 minutes of warm ischemia were randomly assigned to one of three groups: the standard DHOPE-COR-NMP protocol with a perfusate switch (Switch), continuous DHOPE-COR-NMP with red blood cells (RBCs) added during COR (RBC-COR), and continuous DHOPE-COR-NMP with RBCs introduced during DHOPE (RBC-DHOPE). Additionally, human livers donated for research were tested under conditions matching the RBC-COR group. Hepatocyte and cholangiocyte viability, along with injury markers, were evaluated using histology and standard diagnostic techniques.

Results: Portal and arterial flows remained stable across all porcine groups, although the RBC-DHOPE group required higher pressures during DHOPE (Figure 1). Biochemical and histological parameters were comparable across groups, with stable perfusate pH and increased liver weight post-perfusion. Bile production was adequate, and hepatocyte injury markers decreased during NMP. Hemolysis occurred only in the switch group. Findings from human liver experiments aligned with the results from the porcine model.

Conclusions: Continuous perfusion within the DHOPE-COR-NMP protocol is both feasible and safe, yielding comparable hepatobiliary viability and injury outcomes regardless of a solution switch.

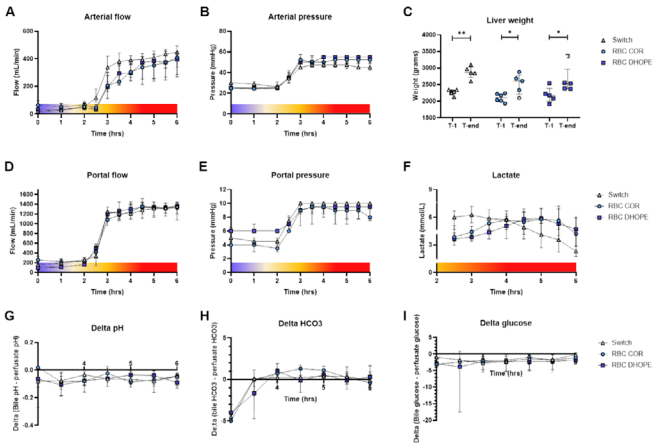

Figure 1. Machine perfusion characteristics and viability criteria during porcine perfusion

BOS_21_6 TANSPLANT EDERLY KIDNEYS INDUCES SENESCENCE IN YOUNG RECIPIENTS IN A RAT MODEL

Elisenda Banon-Maneus[1], Marta Lazo[2], Jordi Rovira[3], Maria Jose Ramirez-Bajo[4], Enrique Montagud-Marrahi[5], Fritz Diekmann[6], Josep M Campistol[7]

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Background: Kidneys are essential for homeostasis and survival, and the prevalence of kidney disease increases with age. In organ transplantation, age classification of donors and recipients expands the donor pool, and then donor-recipient age disparities exist. Kidneys from elderly donors have a higher risk of chronic allograft nephropathy (CAN), linked to cellular senescence, a process involved in regeneration failure and fibrosis. Older organs accumulate senescent cells, which may induce senescence in younger recipients. During transplantation, donor cells are transferred, leading to a microchimeric state. We hypothesize that transplanting old organs into younger recipients could promote senescence due to increased SAPS-factor release.

Methods: An experimental renal transplant isogenic model in rats was used. Donors and recipients were categorized as young (Y-3m), old (O-10m), and elderly (E-18m), resulting in 7 donor/recipient groups. Animals were sacrificed 6 weeks post-transplantation. Tubular damage scores and bulk RNAseq were performed on graft kidneys, liver, brain, lymph nodes, intestines, heart, lung, adipose tissue, muscle, testis, and spleen. Kidney pro-inflammatory cytokines, regulated necrosis, ferroptosis, necroptosis, apoptosis, senescence, and SASP were assessed using Real-Time PCR. Biochemical parameters of iron metabolism were measured in blood and tissue.

Results: Elderly organs contained more senescent cells, although significant increases in SASP components at the mRNA level were not observed. Gene expression analysis of SASP components showed that Tgfβ1 was over-expressed in all grafts, irrespective of age. IL6 and PAI-1 were over-expressed in elderly grafts compared to younger ones, while CTGF was down-regulated. The BCL-2 apoptosis resistance factor was conserved. Blood parameters showed no significant differences between groups. Preliminary RNAseq analysis indicated that senescence may be triggered by transplanting elderly organs.

Conclusions: Preliminary results suggest that transplanting elderly kidneys induces senescence in recipients. Further analysis is needed to determine whether this is a systemic phenomenon or affects only specific organs.

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BOS_21_7 APOLIPOPROTEIN L1 GENETIC RISK VARIANTS IN AN AMSTERDAM MULTI-ETHNIC COHORT

Emma van Schijndel[1], Nienke Manson[2], Bart Ferwerda[3], Henrike Galenkamp[4], Marc Hilhorst[5], Frederike Bemelman[6]

[1]Amsterdam University Medical Center; Amc, [2]Amsterdam Umc; Location Amc; Nephrology, [3]Amsterdam Umc; Public Health and Clinical Epidemiology, [4]Amsterdam Umc; Public and Occupational Health, [5]Amsterdam Umc; Nephrology, [6]Amsterdam Umc; Amsterdam University Medical Center; Department of Nephrology

Background: Apolipoprotein L1 (APOL1) genetic risk variants are found almost exclusively in individuals of African descent. Carriers of two risk variants (G1, G2 or a combination) are predisposed to chronic and end-stage kidney disease. Carriage of the APOL1 p.N264K allele protects individuals with two APOL1 risk variants, making the risk of kidney disease comparable to one or no APOL1 risk variants. In kidney transplantation, deceased donor kidneys with a high risk APOL1 genotype show reduced allograft survival. In living donors, a high risk genotype is associated with lower kidney function in donors both pre- and post-donation. The aim of this study was to determine the prevalence of APOL1 risk variants in our multi-ethnic Amsterdam population.

Methods: We included 10 630 participants from Dutch (n= 3567), African Surinamese (n= 2238), Moroccan (n= 3194) or Ghanaian (n= 1631) ethnicity utilising the Healthy Life in an Urban Setting (HELIUS) cohort. The APOL1 risk variants were determined by either PCR or a TaqMan Assay. Primary outcome was the prevalence of APOL1 risk variants in the ethnic groups. A secondary outcome was the prevalence of the protective p.N264K allele in a representative subgroup.

Results: The prevalence of APOL1 risk genotypes within the entire cohort was 6.5%. Of the African Surinamese participants, 10.0% had two risk variants and 40.4% had one (figure 1). In the Ghanaian group, 28.8% had two risk variants and 46.4% had one. In a subgroup of 5 967 participants, heterozygosity for the protective p.N264K APOL1 variant was found in 12.7% of the participants with two APOL1 risk variants.

Conclusions: In conclusion, APOL1 high-risk alleles are prevalent in the African Surinamese and Ghanaian population of Amsterdam. The protective p.N264K allele was present in a substantial part of the high-risk participants in the subgroup. This is a first step in assessing the impact of APOL1 risk variants on our Amsterdam cohort. Clinical consequences are currently analysed.

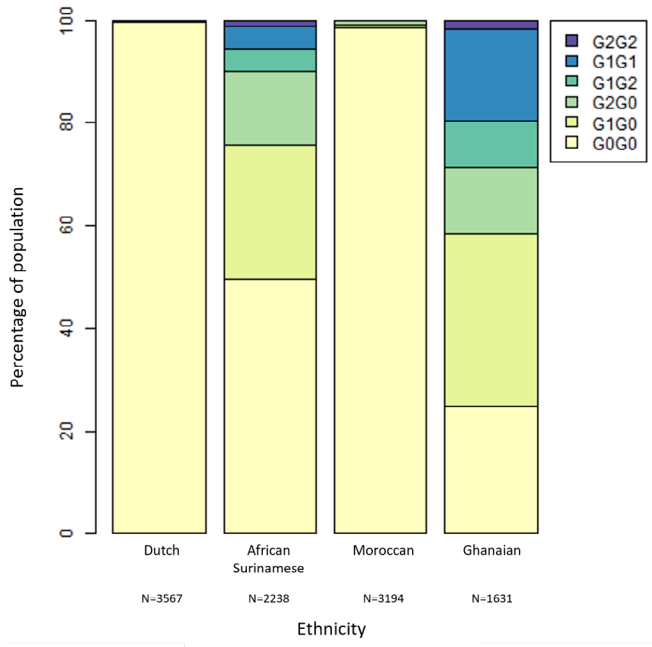

Figure 1: Prevalence of APOL1 genotypes in the ethnic groups.

BOS_21_8 GINSENOSIDE RG3 MITIGATES ISCHEMIA-REPERFUSION RENAL INJURY BY ENHANCING AMPK AND AUTOPHAGY

Jae Wan Jeon[1], Seongyeop Jeong[2], Heyrim Park[3], Kyungho Park[4], Eu Jin Lee[5], Young Rok Ham[6], Ki Ryang Na[5], Yoon-Kyung Chang[7], Dae Eun Choi[8]

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Background: Ginsenoside Rg3 (Rg3) has demonstrated various renal-protective effects, but the mechanisms underlying its role in autophagy and its protective efficacy against renal ischemia-reperfusion injury (IRI) remain unclear. This study aims to investigate the induction of autophagy flux by Rg3 and its impact on mitigating renal cell death in IRI.

Methods: C57BL/6 mice were categorized into the following groups: sham, sham treated with Rg3, IRI treated with saline, and IRI treated with Rg3. Kidney and blood samples were collected 24 hours after the surgical procedures, including sham and ischemia-reperfusion (IR) operations. Evaluations encompassed renal function, histological analysis of kidney tissue, and protein expression of autophagy markers.

Results: IRI mice showed elevated levels of blood urea nitrogen (BUN) and serum creatinine (s-Cr) compared to the sham group. Treatment with Rg3 significantly reduced these levels in IRI mice. Furthermore, Rg3 treatment attenuated renal injury, as indicated by reduced tubular cell detachment and necrosis scores compared to saline-treated IRI mice. Rg3 also decreased oxidative stress and enhanced autophagy, evidenced by increased levels of LC3 and Beclin-1, decreased p62, and elevated ATP6E levels. Additionally, Rg3 promoted AMPK phosphorylation in the kidneys of IRI mice.

Conclusions: Ginsenoside Rg3 enhances AMPK-mediated autophagy flux, reduces oxidative stress, and mitigates renal cell death in acute renal injury caused by ischemia-reperfusion.

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BOS_21_9 METABOLIC BALANCE OF HUMAN LIVERS DURING LONG-TERM NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) is used to preserve and assess the viability of (extended criteria) high-risk donor livers. Long-term NMP (LT-NMP; ≥24h) is emerging as a method to improve or repair livers initially deemed unsuitable for transplantation. This study investigated metabolism during LT-NMP, focusing on hepatic energy consumption and nitrogen and electrolyte balances to have a better perception of long-term perfusion requirements.

Methods: Human livers donated for research purposes underwent LT-NMP using a modified Liver Assist (XVIVO, Groningen, the Netherlands) perfusion device, including adjusted oxygenators and gas mixer, continuous renal replacement therapy, and continuous monitoring. In this study, we measured oxygen consumption ($\dot{V}O2$) and carbon dioxide production ($\dot{V}CO2$) to determine the energy expenditure of 14 human livers during LT-NMP for 7 days. Additionally, hepatic balances of glucose and lactate, as well as of nitrogen and electrolytes were determined.

Results: Initial high metabolic rates during the first day of LT-NMP decreased and stabilized by nearly 50% on day 3, suggesting a quiescent state until day 7 (Figure). Most of the energy used by the livers during LT-NMP was derived from glucose (75-88%) (Figure). Continuous amino acid supplementation was essential to maintain an anabolic state, whereas livers without supplementation became catabolic. While net electrolyte balances were close to zero, significant uptake and release of electrolytes occurred throughout LT-NMP.

Conclusions: During LT-NMP, livers reached a metabolically quiescent state after 3 days with decreased energy consumption. Tailoring perfusate composition and supplementation protocols to the specific needs of the liver could enhance organ preservation and potentially expand the pool of viable donor livers after LT-NMP.

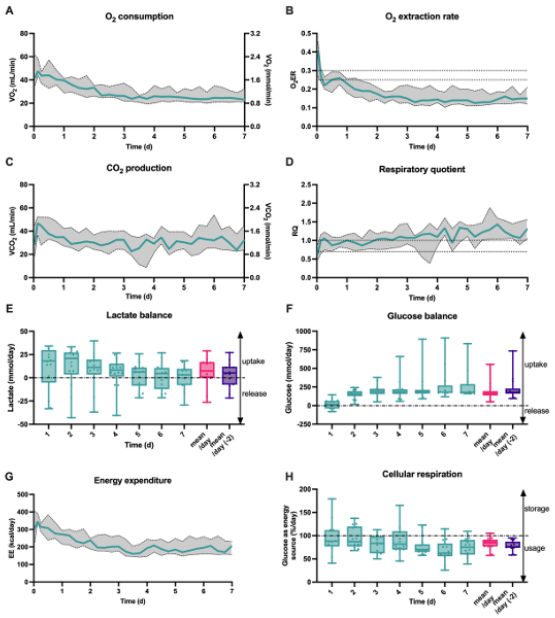

Figure: Energy utilization by the livers during NMP

Panel A-D: The oxygen consumption (VO_2), extraction ratio (O_2ER), carbon dioxide production (VCO_2), and respiratory quotient (RQ) of all 14 livers during 7 days of NMP expressed as median with interquartile range. The VO_2 and O_2ER demonstrate a decrease till day 3 with subsequent stabilization. During perfusion, VCO_2 remained constant, and RQ slightly increased. The horizontal dotted black lines describe the range of humans at rest. **Panel E-F:** The hepatic balance of lactate and glucose per day of all 14 livers, including the mean per day. The mean of days 3-7 (purple) is also shown because the last five days demonstrate a quiescent state. The use of lactate as an energy source decreases during the week, mainly because the lactate production is minimized during the perfusion. The use of glucose as energy is low on the first day of perfusion, possibly due to the use of lactate, but increased and stabilized from day two onwards. **Panel G-H:** The energy expenditure (EE), in the median with interquartile range, displays the same pattern as the VO_2. The cellular respiration reaches values below 100% from the third day, indicating the use of glucose as an energy source instead of storage. Because cellular respiration remained far above 50%, most energy was produced from glucose.

BOS_21_10 TRANSCRIPTOMIC SIGNATURES OF PROLONGED DELAYED GRAFT FUNCTION IN HUMAN KIDNEYS UNDERGOING NORMOTHERMIC MACHINE PERFUSION

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Background: Prolonged delayed graft function (PDGF), the clinical manifestation of severe ischaemia-reperfusion-injury (IRI), remains an unmet challenge in kidney transplantation (KT). Normothermic machine perfusion (NMP) aims to resuscitate organs but did not prevent incidences of PDGF in a randomised controlled trial (RCT). This study aimed to further explore the transcriptomic signatures and cellular landscape underpinning IRI and PDGF in human kidneys undergoing NMP.

Methods: Bulk RNAseq of tissue biopsies taken at end NMP from immediate graft function (IGF;n=10) and PDGF (n=10) kidneys perfused in the aforementioned RCT was performed. Curated kidney cell population signatures from scRNAseq data were used to deconvolute bulk RNAseq. Small RNAseq was performed for urinary extracellular vesicles (uEVs) from paired urine samples obtained during NMP. An external cohort of NMP kidneys with low acute tubular injury (ATI;n=7) versus high ATI (n=7) scores, histologically similar to IGF and PDGF kidneys respectively, were used to validate tissue-centric transcriptomic findings.

Results: Gene Set Enrichment Analysis (GSEA) of differentially expressed genes (DEGs) confirmed enrichment of pro-inflammatory pathways in PDGF-versus-IGF kidneys during NMP. GSEA on significant DEGs revealed a core signature of *TNFalpha via NFkB signalling*, *Inflammatory Response* and *Allograft Rejection* driving IRI in PDGF kidneys. Deconvolution of bulk RNAseq data showed enrichment of transcriptomic signatures associated with mononuclear phagocytes type-A&B (pro-inflammatory innate immune cells/macrophages), fibroblasts and myofibroblasts. Relative depletion of tubular epithelial cell signatures was also seen. GSEA findings and cell identity signatures were recapitulated in the validation high-vs-low ATI cohort. Small RNAseq of uEVs revealed macrophage-specific miRNA in the urine of PDGF kidneys during NMP.

Conclusions: We identified and validated a core signature of IRI during NMP in kidneys developing PDGF and in kidneys with severe ATI, and highlighted the role of pro-inflammatory innate immune cells in this process. We identified a uEV macrophage miRNA signature in PDGF kidneys requiring further validation.

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BOS_21_11 GWAS IDENTIFIES DONOR GENETIC RISK LOCI LINKED TO NON-ANASTOMOTIC BILIARY STRICTURES AFTER LIVER TRANSPLANTATION

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Background: Non-anastomotic biliary strictures (NAS) affect up to 30% of liver transplant recipients, with a threefold higher incidence in livers donated after circulatory death (DCD) compared to brain-dead donors (DBD). NAS results from ischemia-reperfusion injury, bile salt toxicity, and immune processes. We hypothesized that genetic variants in bile salt transporter genes of the donor liver predispose to NAS after liver transplantation.

Methods: This observational cohort study included liver transplant recipients from DBD and DCD donors without machine perfusion. We performed genome-wide analyses (GWAS) to identify loci associated with NAS, stratified by graft type (DBD and DCD). Logistic regression models adjusted for donor age, sex, and principal components 1–3. Risk loci (p<1x10-5) were prioritized with FUMA, incorporating functional annotations and gene expression data from GTEx. Targeted gene analyses focused on bile salt transporter genes and on SNPs previously linked to biliary tract disorders.

Results: A total of 649 DBD liver and 127 DCD liver recipients were included. NAS incidence was 9% (n=59) in the DBD group and 28% (n=35) in the DCD group. In the DBD group, GWAS and subsequent prioritization identified novel risk loci with eQTL effects on the genes G Protein-Coupled Receptor 180 (GPR180) and Lipolysis Stimulated Lipoprotein Receptor (LSR). These genetic variants, with minor allele frequencies of 20% (GPR180) and 8% (LSR) in our DBD cohort, significantly increased NAS risk, with combined loci amplifying risk (hazard ratios up to 9.70; Figure 1). Bile salt transporter and other targeted gene analyses revealed no strong associations with NAS.

Conclusions: Our analyses implicate systemic processes such as vascular remodeling and fibrosis (GPR180) and lipid metabolism (LSR), but not bile salt transport, in the pathogenesis of NAS. Integrating genetic and clinical data could improve NAS risk prediction and help personalize management strategies.

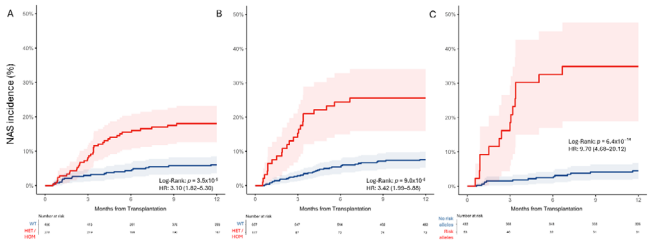

Figure 1. Kaplan Meier curves depicting NAS incidence across different GPR180 and LSR genotypes.

Panel C compares NAS incidence for individuals carrying a combination of risk alleles from both GPR180 and LSR eQTL SNPs to those with no risk alleles.

NAS, non-anastomotic biliary strictures; WT, wildtype; HET, heterozygous; HOM, homozygous

BOS_21_12 NECROPTOSIS IN KIDNEY ISCHAEMIA REPERFUSION INJURY AND THE EFFECTS OF A RIPK1 INHIBITOR IN A PRECLINICAL MODEL

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Background: Ischaemia-reperfusion injury (IRI) is inevitable in transplantation, affecting kidney post-transplant outcomes, particularly in those with donation after circulatory death (DCD). Necroptosis is a form of cell death in IRI and phosphorylation of RIPK1 (pRIPK1) is a key in this pathway. The aims of this study were: 1. to investigate RIPK1 phosphorylation in clinical kidney transplantation, 2. to assess efficacy of a novel RIPK1 inhibitor, GNE684, in two pig models of kidney IRI.

Methods: First, the extent of phosphorylation of RIPK1 in DCD human kidneys was assessed using immunohistochemistry of biopsies post-retrieval (n=6) and 1h after transplantation (n=7) scored for pRIPK1 by a pathologist. Secondly, effects of GNE684 were assessed in a preclinical kidney IRI model using either static cold storage (SCS) or hypothermic machine perfusion (HMP). After 1h warm ischaemia pig kidneys were retrieved in pairs. In the SCS model (n=6), pairs were randomised to UW+GNE684 (5μM) delivered via the renal artery or control. Kidneys then underwent 7h SCS in UW±GNE684, followed by 4h ex vivo normothermic reperfusion with whole blood (NR). In the HMP model (n=6 pairs), kidneys were randomised to HMP alone or HMP with UW-MPS+GNE684 (5μM) for 12h, followed by 8h NR. Injury markers and cytokines (AST, LDH, IL-6), necroptosis markers (pRIPK1, pRIPK3 and pMLKL) and tissue GNE684 concentrations were assessed.

Results: Clinical DCD kidney biopsies presented a significant increase in pRIPK1 after transplantation (p=0.034, Figure-1A). The preclinical kidney IRI models showed increasing levels of IRI markers during NR with no differences between groups. HMP led to higher GNE684 tissue concentrations post-preservation (p<0.0001) and during NR (p=0.013) compared to SCS. GNE684 in both models reduced pRIPK1 at 1h NR (p=0.032 SCS and 0.036 HMP) and at 4h NR in the HMP model (p=0.034) (Figure-1A, B). Reduction of pMLKL at 1h NR (P=0.01), pRIPK3 at 1h (p=0.019) and 8h NR (p=0.03) were also observed in the HMP model.

Conclusions: This study assessed phosphorylation of RIPK1 in a large animal kidney IRI model and clinical transplant biopsies. pRIPK1 was increased in IRI and its levels were reduced by GNE684, identifying this as a potential therapeutic strategy to reduce necroptosis. HMP was a superior method of delivery compared to SCS.

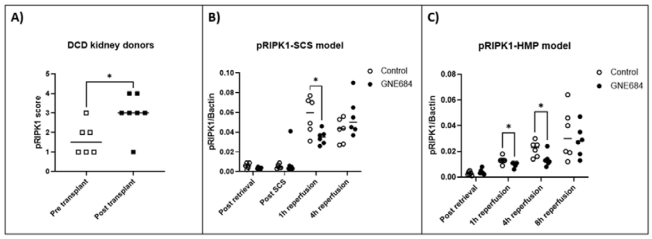

Figure1) pRIPK1 in clinical samples and in a preclinical model of ischaemia reperfusion injury (IRI). Panel A) pRIPK1 scores of clinical kidney biopsies taken immediately post-retrieval from donors after circulatory death (DCD, n=6) and 1h after transplantation (n=7).
Panels B and C) pRIPK1 levels in two pig kidney models of IRI. Panel B shows results for the SCS model where GNE684 was delivered to the retrieved kidneys via renal artery, followed by 7h static cold storage in UW+GNE684. Kidneys were then normothermically reperfused with whole blood (NR) for 4h. Panel C shows results for the HMP model where GNE684 was delivered to the kidneys during 12h hypothermic machine perfusion and then kidneys underwent 8h NR. Results are shown as mean and individual kidneys.

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BOS_21_13 TRANSLATIONAL METHOD OF SEX MISMATCHED LUNG TRANSPLANT AND HORMONAL TREATMENT OF BRAIN DEATH FEMALE RAT DONORS

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Background: Studies have identified the influence of sex mismatch in lung transplant outcomes. Showing that the combination of female donors and male receptors present the worse outcome, with higher risk. Immunological responses differ between sexes. One aspect that could be highlighted is the role of female sex hormones, especially estradiol, in the regulation of the inflammatory response. As such, we have developed a lung transplantation method that allows the analysis of sex mismatch and treatment of the brain-dead donor.

Methods: Female Wistar rats with high estradiol concentration (proestrus and estrus) and male Wistar rats were separated in 3 groups: M/M – lung of male donors were transplanted to male recipients; F/M - lung of female donors transplanted to male recipients; FE2C/M – female donors received continuously treatment with 17β-estradiol (E2 - 50µg/mL i.v. 2mL/h), their lungs were transplanted to male recipients. Donors were submitted to brain death and maintained for 6h and lungs were maintained for 4h in the recipient, afterwards blood and lung tissue were sampled. Serum will be analyzed for inflammatory mediators' concentrations and lung for histopathological analysis.

Results: Preliminary data analysis indicate that FE2C/M group have promising results as the lungs of treated groups presented higher success, with more animals surviving the reperfusion and improved macroscopic aspect. Future analysis of lung and systemic inflammation could further reveal estradiol positive results in transplant prognosis.

Conclusions: This new method enables research of sex effects in the lung transplant outcomes. Bringing the possibility of different combinations and the extension of observation time, therefore future analysis with new treatments in males and females, as well as short- and long-term analysis after transplant. Grant 2023/12247-2, 2021/13020-6, São Paulo Research Foundation (FAPESP).

BOS_21_14 TRANSCRIPTOME REGULATION OF MIR-210 DURING ISCHAEMIA IN GLOMERULAR ENDOTHELIUM

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Background: During transplantation, the kidney is subjected to ischemia reperfusion injury (IRI). Biopsies taken from transplant kidneys after reperfusion demonstrate significant fibrin deposition and microthrombi formation in the glomeruli. This suggests that the highly specialised glomerular endothelium is damaged during renal IRI. We therefore assessed the glomerular endothelial transcriptomic response, both microRNA and mRNA, to ischemia in order to identify both injurious and protective responses.

Methods: Primary human glomerular endothelial cells (HGEnCs) were cultured in 1% oxygen for 4 (acute hypoxia) 12 and 24hours (chronic hypoxia). Total RNA was extracted and parallel sequencing for both miRNA and mRNA was conducted with the aim of uncovering the miRNA-mRNA regulatory network. miRNA and mRNA sequencing data analysis was carried out using R. Cells were transfected with miR-210-3p mimic and control to assess cellular bioenergetics by extracellular flux assays.

Results: Cells subjected to acute hypoxia express a distinct transcriptome profile without any significant changes in miRNA expression, whereas cells subjected to chronic hypoxia showed enrichment in miRNA processing and maturation, with significantly high miR-210-3p expression **Fig1A**). By integrating the sequencing data, we further identified Hypoxia inducible factor (HIF1A) and transferrin receptor 1 (TFRC) as putative targets of miR-210-3p in glomerular endothelial cells under hypoxic conditions. Transfection of glomerular endothelial cells with miR-210-3p mimic resulted in a decrease in HIF1A (p=0.0326) and TFRC (p=0.0326) expression (**Fig1 B&C**). Finally, when HGEnCs over-express miR-210-3p, they show an increase in glycolytic capacity but unaltered mitochondria function, providing a potential compensatory mechanism for maintenance of ATP in hypoxia to limit cellular damage.

Conclusions: The glomerular endothelial expression of miR-210-3p in hypoxia modifies the expression of key proteins that regulate cellular responses and increase glycolytic pathway capacity. Exploiting this pathway during organ preservation could prevent and reduce allograft injury and improve the outcomes.

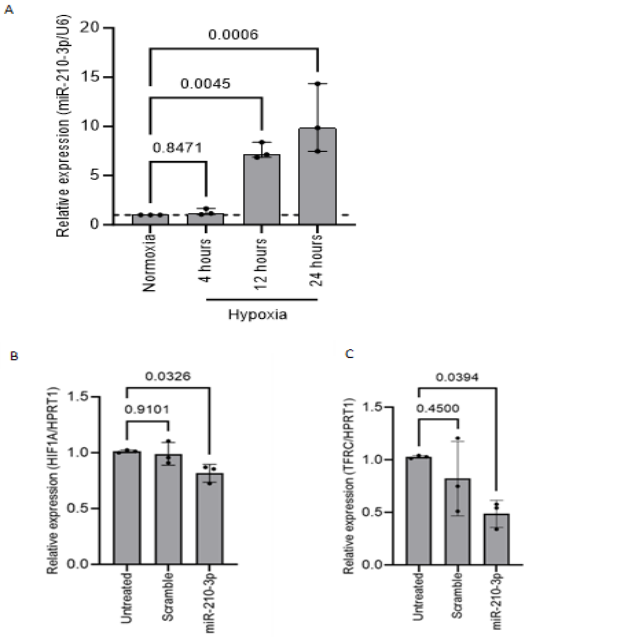

Figure 1: A) miR-210-3p upregulation in human glomerular endothelial cells when cultured during hypoxia. Cells were cultured in 1% oxygen for 4 hours, 12 hours and 24 hours. miR-210-3p expression was normalised to U6. Data shown as mean ± SD of n=3 biological replicates. Statistical analysis was performed using One-way ANOVA with Holm- Šídák post-hoc test.

Transfection of glomerular endothelial cells with miR-210-3p mimic shows a significant downregulation whereas scramble control showed unaltered B) HIF1A and C) TFRC expression. Data shown as mean ± SD of n=at least 3 replicates. One-Way ANOVA with Dunnett's post-hoc test was performed.

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BOS_21_15 CARDIAC REGENERATION FROM WHARTON'S JELLY AND MONONUCLEAR STEAM CELLS IMPLANT IN MYOCARDIUM INFARCTION OF RATS

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Background: Cardiovascular diseases (CVD) are the most common cause of mortality worldwide. Myocardial infarction (MI) can result in irreversible damage to the heart. For patients with severe post-MI sequelae, options in regenerative medicine were studied using cell therapy and biomaterials, such as Wharton's Jelly (WG), which have become a promising option in myocardial regeneration. WG protects the umbilical cord it is a membrane rich in components of the extracellular matrix and it can be used in the context of tissue healing.

Methods: To evaluate the effect of the implantation of stem cells and Wharton's jelly in myocardial infarction (MI) with left ventricular dysfunction in an animal model, 70 male Wistar rats aged 2 to 3 months were subjected to MI through left coronary occlusion. After seven days, the animals underwent echocardiography: animals with LVEF < 50% (n=48) were separated into four groups, randomly selected and submitted to a sternotomy and intramyocardial application of 0.9% sodium chloride (control group, n=12), Wharton's jelly implant (GW, n=11), bone marrow mononuclear stem cells (CT, n=10) and the association of Wharton's jelly with stem cells (GW+CT, n=15), in the region of the MI. After 30 days, a new echocardiography and histopathological analysis were performed.

Results: Regarding LVEF analysis, the animals were considered homogeneous seven days after MI (p=0.434). Thirty days later, an improvement in LVEF was identified in the GW+CT group in relation to the control group (p=0.002) and in the GW+CT group versus the CT group (p=0.001). Regarding histological analysis, it was identified that the GW and GW+CT groups had a smaller infarct area compared to the control group (p<0.001).

Conclusion: Decellularized Wharton's jelly associated with bone marrow stem cells has therapeutic potential, as it demonstrated functional improvement and reduction in the infarct area, thirty days after experimental MI in an animal model.

Bridging oncology and transplantation

BOS_22_1 IMPACT OF TRANSPLANT PROGRAM ON THE PROBABILITY OF CONVERSION AFTER IMMUNOTHERAPY FOR HEPATOCELLULAR CARCINOMA

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Background: The ability of noncurative intent systemic immunotherapy to convert patients with hepatocellular carcinoma (HCC) to curative treatments (curative conversion) remains controversial. This study aimed to take a reliable epidemiological snapshot of response patterns to Atezolizumab plus Bevacizumab (AB) therapy, focusing on curative conversion rates.

Methods: Patients with HCC receiving first-line Atezolizumab plus Bevacizumab (AB) between 2019 and 2023 were included using centre-level aggregate data from a large international consortium. The primary end-point was the curative conversion rate, distinguishing potential conversion (PC) - when objective response (OR) resulted in a consistent decrease of tumour burden and alpha-fetoprotein levels - from actual conversion (AC) when OR resulted in curative treatment. Under-conversion (UC) was defined as PC - AC]/OR) rates. A meta-analytic approach was used to analyse aggregate data.

Results: Data from 46 international centres encompassing 1,413 patients treated with AB were analysed. A significant discrepancy was observed between PC (16%, 95% CI 13-20) and AC rates (3%, 95% CI 1-5). For patients treated with AB, the presence of a liver transplant program, as well as the proportion of patients >70 years old or with metastases, significantly influenced AC rates. UC rates were consequently high (40%, 95% CI 28-52) despite high OR rates (29%, 95% CI 24-34). The presence of a transplant program consistently decreased the risk of UC in AB patients. Diabetes and ALBI> 1 were additional factors affecting UC risk

Conclusions: Despite promising advances, actual conversion rates remain low, underscoring a worrisome UC phenomenon in real-world practice, even with novel immunotherapy-based combinations. The significant role of transplant programs in improving conversion rates highlights the critical importance of referring patients to expert centres, where multidisciplinary teams can evaluate complex cases using a multiparametric approach to optimise outcomes.

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BOS_22_2 LISTING PATIENTS WITH HEPATOCELLULAR CARCINOMA FOR LIVER TRANSPLANTATION: ONTARIO & REVISED CRITERIA

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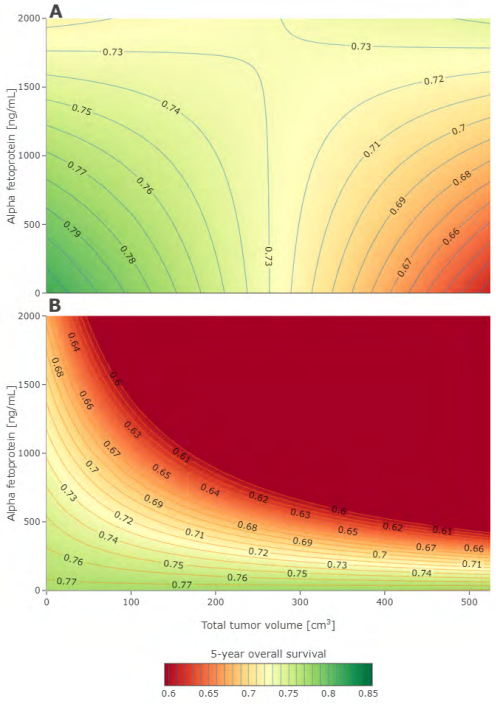
Background: Liver transplantation (LT) is a curative treatment option for hepatocellular carcinoma (HCC). We aim to validate the existing waitlisting exception points of the Ontario criteria (OC) (total tumour volume [TTV] ≤ 145cm3, alpha fetoprotein [AFP] ≤ 1 000ug/L, no macrovascular invasion, no extrahepatic spread), and to re-assess the parameters cutoff values.

Methods: Patients with HCC were selected from the United Network for Organ Sharing registry, with complete tumor variables at waitlisting. Overall survival (OS) analysis was performed and assessed using estimates (% and median OS) and effect sizes. Multivariable a priori Cox proportional hazard regression modelling was employed to account for potential confounders. Competing risk for HCC-related deaths was evaluated with subdistribution hazard rate (SHR).

Results: The 29 086 patients had a median age of 60 years (IQR: 55,, 64), 22 303 (77%) were male, with a median Model of End-stage Liver Disease score of 10 (IQR: 8, 14). Compared to traditional Milan Criteria, this cohort encompassed a net of +380 (1.3%) patients classified as within OC. Patients within OC reached a 5-year OS of 76% (95%CI: 75, 76), median OS 13.5 years (95%CI: 13.2, 13.9). Being within OC compared to beyond OC significantly decreases the risk of HCC-related deaths (SHR 0.43; 95%CI: 0.36, 0.53). To reassess TTV and AFP cutoffs in patients transplanted between 2013 and 2016 (contemporary era) ; (n=6 592), a multivariable prediction of 5-year OS was performed and presented in contour survival plots (Figure 1). Modelled acceptable outcome (5-year OS > 60%) was reached in four categories: small tumors (TTV 0 - 85 cm3 & AFP ≤1 500 ng/mL), moderate tumors (TTV 86 – 160 cm3 & AFP ≤ 1 000 ng/mL), large tumors: (TTV 161 – 250 cm3 & AFP ≤ 750 ng/mL), and very large tumors (TTV 251 – 415 cm3 & AFP ≤ 500 ng/mL). These revised Ontario criteria were associated with an observed 5-years OS of 76% (95%CI: 75, 76).

Conclusions: The patients within OC have excellent outcomes. Extension of these criteria are feasible in statistical models. Incorporating AFP allows for improved risk stratification, compared to morphometric cutoffs alone.



BOS_22_3 CANCER RELATED MORTALITY AFTER SOLID ORGAN TRANSPLANT IN ENGLAND: THE EPCOT STUDY

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Background: Post-transplant cancer is a leading cause of mortality. However, published literature is dated, heterogenous and/or provides conflicting mortality rates. Our aim was to analyse post-transplant cancer mortality using national record-linked transplant registry data.

Methods: Epidemiology of Cancer after solid Organ Transplantation (EpCOT) linked UK Transplant Registry data (held by NHS Blood & Transplant), cancer data (previously held by Public Health England), and administration and mortality data (held by NHS England) between 1985-2015 with outcomes to 2023. In this analysis, cancer-related mortality for 2001-2022 was assessed using standardized mortality ratios (SMR) and confident intervals (CI).

Results: Our cohort included 40,267 solid-organ transplant recipients, accounting for 448,071 person-years (median years follow-up 10.9, interquartile range 7.8-15). We observed 14,576 (36.2%) deaths, with 2,648 (18.2%) attributed to cancer. Transplantation was associated with increased cancer-related mortality; SMR 1.95 (95% CI: 1.87-2.05) for men and 2.18 (95% CI 2.04-2.32) for women. Considerable differences were seen stratified by graft type. For example, liver transplant recipients have increased SMR for cancer-related death; 3.12 (95% CI 3.04-3.61) for men and 2.78 (95% CI: 2.43-3.18) for women, whilst simultaneous kidney-pancreas transplant recipients showed no increased SMR; 1.18 (95% CI: 0.86-1.6) for men and 1.44 (95% CI: 0.96-2.17) for women. Transplantation was associated with increased mortality for most cancers, notably non-Hodgkin lymphoma, liver and kidney, whilst the inverse appears to be true for prostate cancer (SMR 0.43 95% CI: 0.33–0.56).

Conclusions: Transplant recipients in England have increased cancer-related mortality but this isn't uniform. EpCOT aims to provide detailed epidemiological analyses to inform clinical practice to reduce the burden of post-transplant cancer.

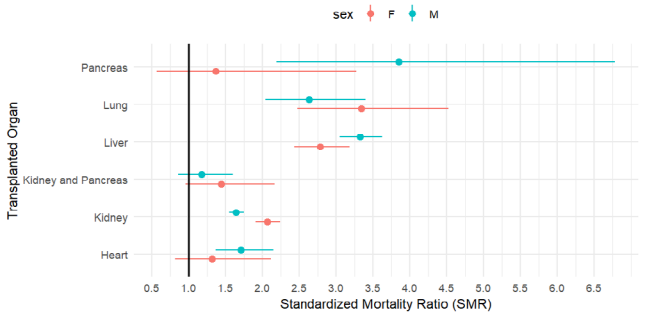
Table 1 - Characteristics of solid organ transplant recipients in England 2001-2015 (first transplants only)

Characteristics	Heart N (%)	Kidney N (%)	Liver N (%)	Lung N (%)	Pancreas N (%)	SPK N (%)	Total* N (%)
Total	1,856 (4.6)	26,904 (66.8)	7,503 (18.6)	1,741 (4.3)	232 (0.6)	1,576 (3.9)	40,267 (100.0)
Sex							
F	564 (30.4)	10,339 (38.4)	3,003 (40.0)	756 (43.4)	145 (62.5)	643 (40.8)	15,669 (38.9)
M	1,292 (69.6)	16,565 (61.6)	4,500 (60.0)	985 (56.6)	87 (37.5)	933 (59.2)	24,598 (61.1)
Age at first transplant							
0-17	405 (21.8)	1,516 (5.6)	898 (12.0)	85 (4.9)	0 (0.0)	3 (0.2)	3,034 (7.5)
18-35	318 (17.1)	5,212 (19.4)	873 (11.6)	327 (18.8)	36 (15.5)	381 (24.2)	7,242 (18.0)
36-50	464 (25.0)	8,800 (32.7)	1,981 (26.4)	402 (23.1)	126 (54.3)	935 (59.3)	12,820 (31.8)
51-65	644 (34.7)	8,727 (32.4)	3,266 (43.5)	898 (51.6)	66 (28.4)	253 (16.1)	13,968 (34.7)
>65	25 (1.3)	2,649 (9.8)	485 (6.5)	29 (1.7)	4 (1.7)	4 (0.3)	3,203 (8.0)
Ethnicity							
Asian	169 (9.1)	3,451 (12.8)	795 (10.6)	43 (2.5)	4 (1.7)	95 (6.0)	4,598 (11.4)
Black	55 (3.0)	1,794 (6.7)	279 (3.7)	18 (1.0)	3 (1.3)	59 (3.7)	2,219 (5.5)
Chinese/Oriental	9 (0.5)	240 (0.9)	72 (1.0)	1 (0.1)	0 (0.0)	5 (0.3)	328 (0.8)
Mixed	13 (0.7)	100 (0.4)	14 (0.2)	1 (0.1)	0 (0.0)	3 (0.2)	132 (0.3)
Other	20 (1.1)	331 (1.2)	89 (1.2)	4 (0.2)	2 (0.9)	12 (0.8)	463 (1.1)
Unknown	5 (0.3)	165 (0.6)	7 (0.1)	4 (0.2)	1 (0.4)	8 (0.5)	190 (0.5)
White	1,585 (85.4)	20,823 (77.4)	6,247 (83.3)	1,670 (95.9)	222 (95.7)	1,394 (88.5)	32,337 (80.3)
Year transplant							
2001-2005	653 (35.2)	6,961 (25.9)	2,254 (30.0)	447 (25.7)	20 (8.6)	237 (15.0)	10,733 (26.7)
2006-2010	531 (28.6)	8,977 (33.4)	2,321 (30.9)	541 (31.1)	99 (42.7)	646 (41.0)	13,238 (32.9)
2011-2015	672 (36.2)	10,966 (40.8)	2,928 (39.0)	753 (43.3)	113 (48.7)	693 (44.0)	16,296 (40.5)

Abbreviation: SPK, Simultaneous pancreas and kidney transplant

* Includes other solid organ transplants including heart & lung transplants and multi-visceral.

Figure 1 - Forest plot of SMR for post-transplant cancer-related mortality



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BOS_22_4 GLYCA AND ALL-CAUSE MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS: RESULTS OF THE TRASPLANTLINES BIOBANK AND COHORT STUDY

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Background: Despite the benefits of kidney transplantation compared to dialysis, life expectancy in kidney transplant recipients (KTR) remains 25-30% lower than that of age-matched peers in the general population. Chronic inflammation is a key contributor to poor outcomes in KTR. GlycA is a composite biomarker of systemic inflammation associated with all-cause mortality in general population studies, but there are no data on GlycA concentrations and outcome in KTR.

Methods: This prospective study was performed using data of stable outpatient KTR participating in the TransplantLines Biobank and Cohort Study. GlycA concentration was measured by nuclear magnetic resonance spectroscopy. We performed multivariable linear regression to analyze the association between concentrations of GlycA and conventional biomarkers of inflammation. To test for the association between GlycA concentration and all-cause mortality, Cox regression was used.

Results: We had data of 909 KTR, mean age 56 (± 13) years, 557 (60.9%) males, and GlycA concentration 435 (± 92) µmol/L. During a median follow-up of 5.5 [Interquartile range=4.0-6.7] years, 196 (21.4 %) KTR died. After adjusting for sex, age, and body mass index, GlycA was positively associated with log-transformed high sensitivity C-reactive protein (hsCRP) (standardized B coefficient (std B) = 0.68, P<0.001) and negatively with albumin (Std B= -0.25, P<0.001). With strengths of associations expressed per standard deviation change, GlycA was more associated with all-cause mortality than hsCRP (Hazard ratio (HR) = 1.56, 95%CI 1.41-1.73, P<0.001 vs. HR = 1.25, 95%CI 1.16-1.39, P<0.001 respectively). After adjusting for age, sex, and estimated glomerular filtration rate the respective HR were 1.46, 95%CI 1.30-1.64, P<0.001 and 1.19, 95%CI 1.09-1.29, P<0.001. After adjusting for hsCRP GlycA was associated with all-cause mortality (HR= 1.55, 95%CI 1.30-1.84, P<0.001). hsCRP was not associated with all-cause mortality after adjusting for GlycA (HR=0.92, 95%CI 0.76-1.12, P= 0.40).

Conclusions: In KTR, GlycA showed an independent association with an elevated mortality risk. GlycA was more strongly associated with all-cause mortality than hsCRP. Further research is warranted to evaluate whether GlycA values could be relevant to improving clinical outcomes in KTR.

BOS_22_5 KIDNEY ALLOGRAFT REJECTION UNDER IMMUNE CHECKPOINT INHIBITORS

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Background: Immune checkpoint inhibitors (ICI) have significantly improved cancer survival, but solid organ transplant recipients are excluded from clinical trials due to the risk of allograft rejection (AR). Retrospective studies report rejection rates around 42%, with kidney transplant recipients (KTR) showing the highest rates. Early AR, often resistant to standard immunosuppression, can lead to graft loss in 65–80% of cases. A comprehensive characterization of AR in this context might elucidate the underlying mechanisms and guide clinical decision-making. Here, we present a case series of 14 KTR who developed AR during ICI treatment.

Methods: The *Immune Checkpoint in Renal Transplant Recipients (ICIR)* study collects retrospective and prospective data on KTR treated with ICI. For this case series, we identified patients who developed AR during ICI therapy. Baseline demographic data, treatment regimens, and outcomes were analyzed.

Results: Among 14 KTR, 15 AR episodes were observed. The median time to rejection was 64 (IQR 15-205) days. All patients stopped ICI therapy, received corticosteroids, and one received intravenous immunoglobulins, yet 6 required urgent transplantectomy. Seven patients remained dialysis-dependent. Histological analysis revealed severe tubulointerstitial inflammation and arteritis, indicating T-cell mediated rejection. Five patients had antibody-mediated rejection (ABMR) with C4d positivity, but only one had detectable donor-specific antibodies (DSA). Microvascular inflammation (MVI) (g + cpt ≥ 2, without circulating DSA and with negative C4d staining) was seen in 6 patients. In terms of cancer outcomes, 8 patients achieved complete response (CR), 1 had stable disease, and 4 showed disease progression. The 6-month survival rate was 30%, with 7 deaths, 4 due to cancer progression.

Conclusions: In this vulnerable population of KTR with advanced cancer, AR following ICI therapy was severe, leading to significant graft loss. However, tumoral response was impressive with 57% having a CR. Even in the absence of DSA, histological findings pointed to MVI that could be driven by cytotoxic T cells and/or NK cells. Further cellular and molecular analyses of graft infiltrates are needed to clarify the mechanisms of ICI-mediated rejection and optimize management strategies.

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BOS_22_6 VIGILANCE DATA IN ORGAN DONATION AND SOLID ORGAN TRANSPLANTATION IN GERMANY 2016-2023: DONOR-TRANSMITTED CANCER

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Background: The transmission of a malignant tumor from the donor to the recipient is a risk that results in high morbidity and mortality for the recipient(s). The evaluation of serious adverse events (SAE) and serious adverse reactions (SAR) reports may help to better assess the risk for the transmission of donor-transmitted cancer (DTC). The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is assigned by the German Federal Ministry of Health to manage and monitor SAE and SAR.

Methods: A special team of qualified physicians of the DSO analyzed all incoming SAE and SAR reported from January 1st 2016 to December 31st 2023 related to a potential malignant disease. The assessment of imputability as proven or probable (P/P) transmission was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC). A DTC was defined as a malignant tumor that was already present in the donor organ at the time of transplantation and was either proven or probable (P/P) transmitted to one or more recipients.

Results: From January 1st 2016 to December 31st 2023, 9771 donors donated post-mortem organs to 27919 recipients. During this period 163 malignancy related reports were registered. In 114 cases a malignant tumor was histopathologically confirmed (114/9771; 1,1%). In 20 of 114 (17,5 %) cases, a P/P transmission of the tumor to 28 recipients was determined after detailed investigation. The tumor transmission rate for donors was 20/9771 (0,20%), for recipients 28/27919 (0,10 %). The mortality for the recipients was high (14/28; 50 %). The DTC cases included three adenocarcinomas, two lymphomas, two melanomas, two renal cell carcinomas, two urothelial carcinomas, two neuroendocrine lung cancer, one non-small cell lung cancer, one pleural mesothelioma, one squamous cell carcinoma, one angiosarcoma, one choriocarcinoma, one Kaposi sarcoma and one carcinoma of unknown primary (CUP). None of the DTC were known in the donor.

Conclusions: In organ donation and transplantation, a DTC is a rare event. In the event of transmission, the morbidity and mortality rate for the recipient is high. A detailed and careful analysis of SAE and SAR cases may help to improve donor assessment and develop strategies to reduce the risk of transmitting donor disease to transplant recipients.

BOS_22_7 TABELECLEUCEL FOR EBV PTLD AFTER FAILURE OF RITUXIMAB+/- CHEMOTHERAPY POST SOLID ORGAN OR HEMATOPOIETIC CELL TRANSPLANT

Sridhar Chaganti[1], Kris Michael Mahadeo[2], Robert A. Baiocchi[3], Amer Beitinjaneh[4], Sylvain Choquet[5], Daan Dierickx[6], Armin Ghobadi[7], R Dinavahi[8], Aditi Mehta[8], Sarah Nkiforow[9], Roberta Valenti[10], Sandrine Roye[11], Ran Reshef[12], Susan Prockop[13]

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Background: Poor OS in patients with relapsed/refractory EBV$^+$ PTLD (R/R EBV+ PTLD) presents an urgent unmet need for effective therapies. Data from ALLELE (NCT03394365), a phase 3 multicenter clinical trial of tabelecleucel (tab-cel), an on demand, allogeneic cytotoxic T-cell immunotherapy to treat EBV-associated post-transplant relapsed/refractory (R/R) EBV+ PTLD arising after solid organ transplant (SOT) or hematopoietic stem cell transplant (HCT) were previously reported. Here we present updated results from the most recent data cut-off with a focus on the SOT cohort.

Methods: Recipients of all SOT types were eligible. Pts receive tab-cel at $2x10^6$ cells/kg on days 1, 8 and 15 and outcomes were assessed at the end of each 35d treatment cycle. Patients with EBV$^+$ PTLD following failure of rituximab (R) and SOT1 [n=18]) and failure of R+chemotherapy (R+CT) (SOT2 [n=31]) were included.

Results: Analysis as of October 2023 was consistent with previously presented ALLELE data. The overall ORR was 51% (25/49) in SOT overall, 55.6% (10/18) in SOT1, and 48.4% (15/31) in SOT2 (**Table**). For SOT patients, median TTR was 2.0 mo. Median OS was 18.4 mo for the SOT patients (95% CI: 5.0, NE). Responders to tab-cel had a 1-year OS rate of 83.4%. Serious treatment emergent AEs (TEAEs) and fatal TEAEs were reported in 61.2% and 18.4% of SOT pts, respectively. No fatal TEAEs were treatment related. The safety profile was favorable a consistent with previous data, with no reports of tumor flare reaction, infusion reaction, cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, marrow rejection, or transmission of infectious diseases. No events of graft vs host disease or organ rejection were reported as tab-cel-related.

Conclusions: Updated ALLELE phase 3 data, with a significantly increased number of pts analyzed confirm that tab-cel provides improved ORR translating into higher OS rates in responders, in a difficult to treat population with poor survival and no approved therapies. Tab-cel was well tolerated without evidence of safety concerns.

Efficacy outcomes with tabelecleucel in patients with EBV+ PTLD following SOT

	SOT1 (N=18)	SOT2 (N=31)	ALL (N=49)
Responders			
ORR, n (%)	10 (55.6)	15 (48.4)	25 (51.0)
Best Overall Response, n (%)			
Complete response	6 (33.3)	7 (22.6)	13 (26.5)
Partial response	4 (22.2)	8 (25.8)	12 (24.5)
Stable disease	2 (11.1)	1 (3.2)	3 (6.1)
Progressive disease	3 (16.7)	9 (29.0)	12 (24.5)
Not evaluable	3 (16.7)	6 (19.4)	9 (18.4)
Clinical Benefit Rate, n (%)	12 (66.7)	16 (51.6)	28 (57.1)
Median time to response, months (range)	1.6 (0.9, 3.7)	2.0 (0.7, 4.7)	2.0 (0.7, 4.7)

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BOS_22_8 ANALYSIS OF CLINICAL AND IMMUNOLOGICAL RISK FACTORS IN HEART TRANSPLANT RECIPIENTS WITH MALIGNANCY

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Background: Long-term prognosis after heart transplantation is influenced by complications of immunosuppressive therapy, including malignancies. This study aimed to identify clinical risk factors influencing 5-year survival after cancer diagnosis.

Methods: We included 242 heart transplant recipients from 2008 to 2020 at our center; we collected data on neoplasm diagnosis, immunosuppressive therapy at diagnosis, and main clinical data. As an outcome, we assessed 5-year survival.

Results: Among the patients we included in our study, 50 were diagnosed with 112 malignancies; 24 solid tumors, 83 non-melanoma skin cancers, and 5 hematologic malignancies (PTLD-Post-transplant lymphoproliferative disorder). Patients with solid tumors had a significantly worse 5-year prognosis compared to other types (47.3±14.2% vs 66.6±27.2% PTLD vs 100% skin cancers; P=0.01). Among patients with solid tumors, as expected, the absence of metastases and the possibility of surgical resection influenced the outcome (65.3±15.8% vs 0% and 80.0±11.2% vs 33.3±19.2%, respectively); the choice of a surgical approach was not influenced by the presence or absence of metastases at diagnosis. No cardiovascular complications related to surgical or oncological therapies were observed. Patients who were not on mycophenolate therapy (yes 62.0±15.7% vs no 30.0±23.9%) due to leukopenia, likely an expression of greater immunosuppression, had a worse prognosis. Finally, recipients from donors older than 55 years showed a trend towards a worse prognosis at one year, with similar prevalence of metastatic disease, suggesting a possible role of donor immunosenescence.

Conclusions: Our data, in addition to showing the effect of tumor stage and the possibility of surgical treatment, suggest a potential role of immunosuppression and donor-related immunosenescence. These hypotheses should be confirmed by studies with molecular biology and immunogenetic methods involving both recipient and donor.

BOS_22_9 THE COAST STUDY: POST-TRANSPLANT CUTANEOUS SQUAMOUS CELL CARCINOMA OUTCOMES HAVE NOT IMPROVED

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Background: Cutaneous squamous cell carcinoma (CSCC) is the most common post-transplant malignancy, occurring up to 250 times more frequently than in the immunocompetent population. Historic cohort studies indicate that up to 25% of OTRs will develop a new CSCC within 12 months of their first. However, significant clinical equipoise exists regarding management of first CSCC in solid-organ transplant recipients (SOTR), exemplified by a Delphi panel recently failing to reach a consensus on appropriate management approaches. Despite this uncertainty, few studies have investigated outcomes of CSCC in SOTR in the last 2 decades, particularly given the changing demographics of the SOTR populations and changes in immunosuppressive options available. To address this paucity of evidence, we undertook a multi-centre retrospective cohort study (Contemporary Outcomes After Skin cancer in Transplant, COAST) to assess contemporary management and outcomes of first CSCC in kidney transplant recipients (KTR).

Methods: Adult KTR from 8 centres with a first-ever CSCC between 2016 and 2020 were included. Data was collected using a standardised proforma and anonymized prior to compilation. Outcomes of interest included new CSCC and a composite 'poor outcome' including death from any cause, new CSCC or solid-organ malignancy, CSCC metastasis and graft loss.

Results:136 patients were followed for a median of 37 months. Demographics are shown in Table 1. During this period, 48.5% developed a new CSCC (24.7% in the first 12 months), 29.4% died, and 72.4% overall had a 'poor outcome'. Patients with first-ever CSCC who were male or who presented with a high-risk tumour (Brigham and Women's Hospital tumour stage ≥ T2b), multiple CSCC or previous basal cell carcinoma were at significantly increased risk for further CSCC or a 'poor outcome' (Fig 1). Management after a first CSCC varied widely between centres in terms of modification of immunosuppression and use of topical/systemic chemoprevention.

Conclusions: Given the observation that outcomes were broadly unchanged from historic cohort studies, this study demonstrates the urgent need for prospective studies to establish the most appropriate approach to management after a first CSCC. We propose a risk stratification approach to highlight KTR who may benefit from early management.

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Table 1. Demographics of 136 cases diagnosed with first CSCC

Baseline Characteristics	All patients (n=136)
Age (years)	64 (57-72)
Sex	
Male	102 (75)
Female	34 (25)
Ethnicity	
White	128 (94.1)
Black	2 (1.5)
Asian	1 (0.7)
Not stated	5 (3.7)
Previous non-cutaneous cancer [a]	11 (8.1)
Previous skin cancer [b]	46 (34.1)
Previous actinic keratoses [c]	67 (49.3)
Previous Bowen's/keratoacanthoma [d]	43 (31.9)
Smoking history	
Current	11 (8.1)
Ex-smoker	15 (11)
Never smoker	37 (27.2)
Not recorded/unknown	73 (53.7)
Total number of transplants	
One	107 (78.7)
Two	23 (16.9)
Three	6 (4.4)
eGFR	41 (27-55)
Previous rejection [e]	21 (15.7)
Evidence of DSA prior to CSCC [e]	11 (8.2)
Cumulative lifetime duration of IS (months)	136 (68-204)
Induction therapies [f]	
Basiliximab/equivalent	68 (57.6)
Alemtuzumab	21 (17.8)
ATG/Thymoglobulin	6 (5.1)
Other	4 (3.4)
None	19 (16.1)
Number of IS agents at diagnosis	
One	8 (5.9)
Two	70 (51.5)
Three	58 (42.6)
Calcineurin/MTOR inhibitor	
Tacrolimus	104 (76.5)
Ciclosporin	18 (13.2)
Sirolimus	4 (2.9)
Nil	10 (7.4)
Antiproliferative	
MMF/MPA	59 (43.4)
Azathioprine	46 (33.8)
Nil	31 (22.8)
Corticosteroid	92 (67.6)
Number of CSCC removed at first episode	
Single	127 (93.4)
Multiple	9 (6.6)

Values are expressed as number (percentage) or median (interquartile range), as appropriate.
ATG, anti-thymocyte globulin; CSCC, cutaneous squamous cell carcinoma; DSA, donor specific antibody; eGFR, estimated glomerular filtration rate; IS, immunosuppression; MMF, mycophenolate mofetil; MPA, mycophenolic acid; MTOR, mammalian target of rapamycin.

a 1 case had missing data.

b Previous basal cell carcinoma or melanoma; 1 case had missing data.

c Includes both clinical and histological diagnosis.

d Previous histologically proven Bowen's disease (SCC in situ) or keratoacanthoma; 1 case had missing data.

e 2 cases had missing data.

f 18 cases had missing data

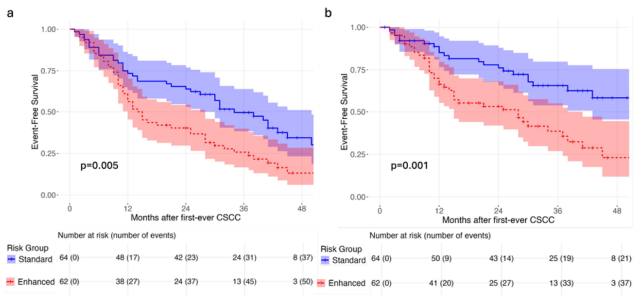

Figure 1:Kaplan-Meir curves showing event-free survival in patients after a first-ever CSCC. Results are presented by risk group for (a) all poor outcomes (further malignancy, metastasis, graft loss or death) and (b) further CSCC. The 'enhanced risk' group includes patients with any of: HR-CSCC, multiple first CSCC, or history of basal cell carcinoma before the CSCC.

BOS_22_10 ISCHEMIA-REPERFUSION INJURY IMPACTS HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) remains the only curative treatment for cirrhosis complicated by hepatocellular carcinoma (HCC). HCC recurrence (HCCr) significantly impairs long-term outcomes and is influenced by pre-LT (tumor morphology and biology) and post-LT factors (immunosuppressive regimens). Emerging evidence suggests that perioperative factors, including ischemia-reperfusion injury (IRI), may also contribute to HCCr.

Methods: We retrospectively analyzed data from 248 patients transplanted for HCC (2009-2021). IRI was considered as severe (Sev-IRI) when combining both occurrence of reperfusion syndrome and IRI-related clinical events (primary non-function, early allograft dysfunction, or ischemic-type biliary lesion). Occurrence of urgent relaparotomy (<48H after LT), prolonged intubation (>12H), reintubation, continuous veno-venous hemofiltration or molecular adsorbent recirculating system defined complicated immediate post-operative evolution. A double-step (univariate then multivariate) regression analysis explored risk factors for decreased disease-free survival (DFS) after LT.

Results: HCCr was observed in 37 patients (14.9%) (mean interval=30.0±33.4 months post-LT). Patients experiencing Sev-IRI demonstrated a higher HCCr rate: 18/58 (31.0%) vs. 19/190 (10.0%) (p<0.001) with a similar Milan-out status at pathology (16/58 (27.6%) vs. 46/190 (24.2%) (p=0.603)). DFS and overall survival were significantly shorter in Sev-IRI subgroup: 55.3±52.3 vs. 77.6±52.4 and 62.0±50.5 vs. 80.2±50.9 months (p<0.001), respectively (mean follow-up=75.9±51.3 months) (Figure 1). After multivariate regression analysis, 5 factors reduced DFS, including Sev-IRI (p<0.05) (Table 1).

Conclusions: These findings suggest that Sev-IRI may increase the risk of HCCr following LT. Further research involving larger patient cohorts is warranted for results validation. If so, strategies to mitigate IRI could play a pivotal role in reducing HCCr rate after LT.

Factor	HR	HR 95%CI	p-value
Charlson comorbidity index	1.22	1.04–1.43	0.015
Microvascular invasion	1.52	1.02–2.29	0.043
Poor differentiation	2.44	1.37–4.02	0.002
Severe IRI	1.89	1.08–3.33	0.026
Complicated post-operative evolution	2.21	1.44–3.40	<0.001

Table 1. Risk factors for decreased DFS after LT for HCC

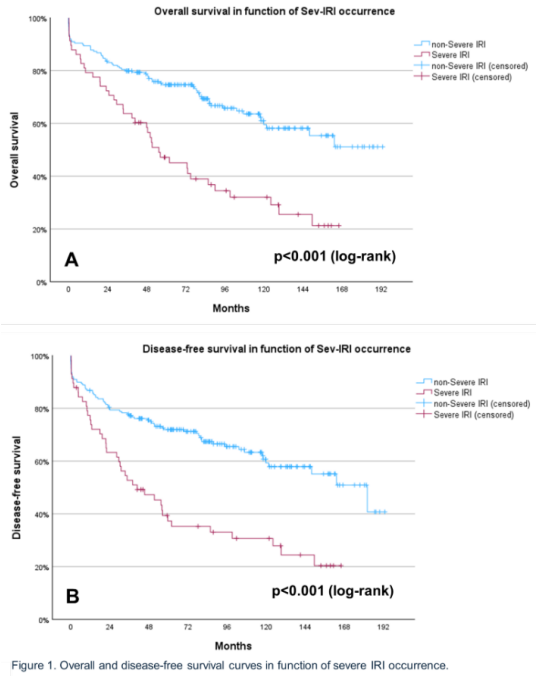

Figure 1. Overall and disease-free survival curves in function of severe IRI occurrence.

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BOS_22_11 MALIGNANCIES IN KIDNEY TRANSPLANT RECIPIENTS WITH BALKAN ENDEMIC/ARISTOLOCHIC ACID NEPHROPATHY

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Background: Balkan endemic nephropathy (BEN) is a chronic tubulointerstitial disease caused by exposure to aristolochic acid. In addition to renal disease, aristolochic acid has been associated with an increased incidence of upper urothelial carcinomas (UUCs). In 2007, our study revealed that BEN patients have an increased risk of UUCs developing after kidney transplantation, a finding that has since guided our research. Herein, we report the long-term outcome of BEN patients after kidney transplantation.

Methods: Patients with BEN who received kidney allografts between October 1973 and December 2023 were included in the investigation. Medical charts and records were retrospectively collected and analyzed.

Results: Out of 2282 patients who underwent kidney transplantation at our institution from October 1973 to December 2023, 44 (average age 55,57 years, 24 male) had BEN as primary kidney disease. Preventive nephroureterectomy was performed in two patients. One-year graft and patient survival were 97.7% and 100%, respectively. Over the observed period, with median follow-up of seven years, thirteen patients developed 20 malignancies. Nine patients developed UCC, with three of them developing panurothelial metastatic cancers. Malignancies were diagnosed at advanced stages despite the regular ultrasound examinations. Other tumors included pancreatic cancer, basocellular skin cancer, colon, lung, and hepatocellular cancer. Plasmocytoma, tricholeucaemia, and posttransplant lymphoproliferative disease were developed by one patient each. Fourteen patients died: five from malignant disease, two from COVID-19, one from sepsis, and another from cardiovascular diseases.

Conclusions: Patients with BEN are at a significantly increased risk for the development of not only UCC but also other malignancies after transplantation. Frequency of UCC and difficult diagnosis underscore the gravity of the problem and the need to perform regular screening for early detection of malignancy in order to improve outcomes.

BOS_22_12 LIVER AUTOTRANSPLANTATION: SAFETY AND EFFICACY IN A HIGH VOLUME CENTER

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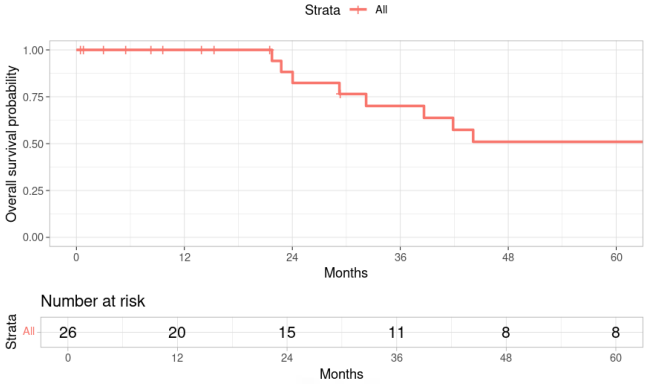
Background: Critically located liver tumors can be resected using liver autotransplantation (LAT). Ex vivo procedures requires complete hepatectomy, followed by tumor resection as a bench procedure and subsequent transplantation of the unaffected liver segments. Ante situm procedure entails anterior rotation of the liver after dissection of the supra-hepatic inferior vena cava (IVC), followed by liver resection and caval reconstruction. Both techniques require parenchymal cooling to reduce metabolic activity. In place of traditional cold flushing, our group described the use of hypothermic machine perfusion (HOPE) to efficiently cool and oxygenate the liver.

Methods: We presents a single-center case series of LAT. Data are expressed as numbers and percentages for qualitative variables and medians with interquartile ranges for quantitative variables.

Results: A total of 28 cases were analyzed: 19 underwent ex vivo and 9 ante situm procedures. Cold perfusion was gravity-driven in 17 cases and HOPE was used in 11. Veno-venous bypass was employed in 24 cases, with IVC replacement or reconstruction performed in 21 cases and preservation in 3. Patients ranged from 49 to 63 years old and were affected by adrenal carcinoma (1), angioma (2), hepatocholangiocarcinoma (1), metastases [colorectal (1), lung (1), pancreatoblastoma (1), neuroendocrine tumors (1)], hepatocellular carcinoma (2), leiomyosarcoma (2), and cholangiocarcinoma (16). Most patients (75%) presented a single large nodule (70–140 mm), and 61% had undergone prior chemotherapy. Median cold ischemia time was 100 minutes (78–147), warm ischemia 25 minutes (13–44),) and the anhepatic phase lasted 129 minutes (109–169). ICU stay averaged 5 days, with a median hospital stay of 21 days. Graft-related complications occurred in 14 patients (54%): bile leakage (27%), liver failure (7%), and bleeding (15%). Non-graft complications included pulmonary issues (38%) and infections (42%). Median CCI was 38 (8.7–63.7), with 3 (10,7%) in-hospital mortalities. Median survival was 29 months (13–67), 5-year survival was 51%.

Conclusions: Ex situ liver surgery is an extremely challenging procedure, but the potential long-term survival benefits justify its risks in carefully selected patients. Patient selection remains critical to optimize outcomes.



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BOS_22_13 THE "YIN-YANG" OF HCC MANAGEMENT: FROM THERAPEUTIC HIERARCHY TO TRANSPLANT BENEFIT

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Background: At first glance, the two innovative concepts of therapeutic hierarchy (TH) and transplant benefit (TB) in managing patients with hepatocellular carcinoma (HCC) might appear conflicting. This study aims to show the close statistical and clinical relationship between these concepts in a large cohort of Italian patients with HCC.

Methods: A large cohort of consecutive patients with HCC (n=2489) from the ITA.LI.CA database 2008-2022 (n=8166) was judged as potentially eligible for liver transplantation (LT) according to the following criteria: age 70 years or younger and absence of relevant extra-hepatic comorbidities, absence of macroscopic vascular invasion or metastases. To assess the correlation between TH and TB, we did a Lasso-Cox multivariable analysis to investigate the independent prognostic power of treatment choice (LT vs liver resection [LR], vs ablation [ABL], vs intra-arterial therapies [IAT], vs systemic therapy [ST]). The treatment effect was described using both hazard ratios and the difference in restricted survival mean between the therapies at 5 years (gain in life months).

Results: Lasso-Cox selected the following covariates as the leading independent survival predictors: alcohol liver disease, Charlson comorbidity index, MELD score, diameter and number of nodules, alpha-fetoprotein level, and treatment choice. Taking LT as the reference, the hazard ratios of LR, ABL, IAT, and ST were 3.0 (2.2-4.0), 3.7 (2.8-4.9), 6.7 (5.0-9.0), and 10.7 (7.3-15.7), respectively, validating the concept of TH. Conversely, the 5-year TB (life-months saved) over LR, ABL, IAT, and ST was 5.4 (3.6-7.2), 6.4 (4.6-8.2), 17.8 (15.5-20.1), and 29.9 (25.2-34.5), respectively.

Conclusions: TH was the main predictor of 5-year TB in a large cohort of transplantable Italian patients with HCC: the lower the first alternative to LT in the TH, the higher the TB. Yin (TH) represents an individual-centred perspective, while Yang (TB) is population-centred.

BOS_22_14 LIVER AUTOTRANSPLANTATION FOR INTRAHEPATIC CHOLANGIOCARCINOMA: SURVIVAL ANALYSIS AND COMPARISON TO SYSTEMIC CHEMOTHERAPY

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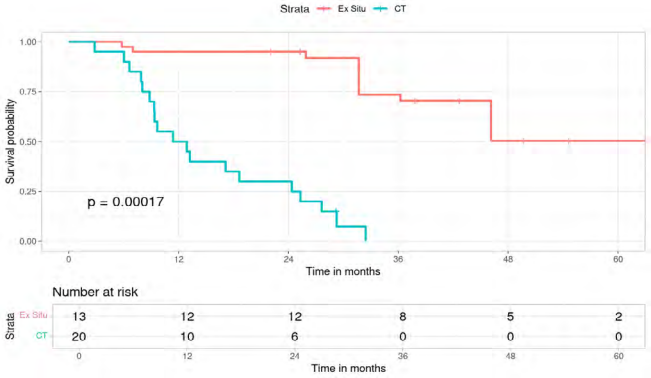
Background: Surgical resection is the standard treatment for intrahepatic cholangiocarcinoma (iCCA). Systemic chemotherapy is the standard care for patients not eligible for surgery. Liver autotransplantation is a surgical technique that could be an effective treatment, increasing the number of patients eligible for surgery.

Methods: This monocentric retrospective study aims to evaluate long-term outcomes in terms of overall survival (OS) and progression-free survival (PFS) and the related prognostic factors in patients affected by iCCA treated with liver autotransplantation or chemotherapy.

Results: The two populations of patients with iCCA, treated with autotransplantation (group S) or chemotherapy (group C), were compared. The first aim was to analyze OS and PFS using survival analysis with the Kaplan-Meier estimator. The second aim was the evaluation of the effect of individual covariates on survival. A propensity score-matching (PSM) analysis was carried out with the matching method "exact" including age, stage, therapy response and Ca19-9. A total of 40 patients were included from 2010 to 2020: 13 patients were in group S and 27 in group C. The group S had a survival benefit and a longer PFS compared to group C: 1-year survival was 84.6% vs 52.1%, with a median OS of 46.1 vs 12.7 months and a median PFS of 23.08 vs 8.03 months, respectively. The 5-year survival was 42.3% vs 0%. Variables that influence patients' survival were the stage of disease, patient's age, Ca19-9 level, and liver function at Cox's regression analysis. The PSM analysis showed that the two populations still have significantly different OS, with a great advantage for surgical population (p=0.00017).

Conclusions: Liver autotransplantation appears to provide longer survival and lower progression probability compared to chemotherapy, despite being technically challenging and associated with high morbidity and mortality. Patients should be carefully selected, considering good performance status, low Ca19-9 level, and liver function. Liver autotransplantation deserves consideration in high-volume hepatobiliary centers with expertise in both hepatic resection and transplant surgery.



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BOS_22_15 HEPATOCELLULAR CARCINOMA RECURRENCE ANALYSIS IN HOPE LIVER TRANSPLANTATION

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Background: Tumor recurrence following liver transplant (LT) is caused by several factors, including ischemia-reperfusion injury (IRI). Hypothermic oxygenated perfusion (HOPE) reduces IRI severity and downstream inflammation. Studies suggest a decreased recurrence rate of hepatocellular carcinoma (HCC) in grafts undergoing HOPE. Our aim was to study tumor recurrence incidence and pattern in HCC transplanted patients with grafts perfused with HOPE.

Methods: 2 groups of HCC adult patients submitted to orthotopic LT between 08/2020 and 10/2023: not perfused and perfused with HOPE (according to the protocol, through portal vein for a minimum of 120 minutes). 100% brain dead donors.

Results: 76 HCC patients were transplanted during the study period. Not perfused group: 24 patients, median age 61 years (IQR 56-66). Donors' age 58.5 years (IQR 54.25-67.75) (0% ≥80years old). Cold ischemia time (CIT) 283.5 minutes (IQR 241.75-336.25). Follow-up of 1082 days (IQR 385-1247.25) with recurrence in two patients (8.3%), both with hepatic recurrence. DFS of 95.8% at one year. At date of analysis, one patient with recurrence died (50%) due to disease progression. HOPE group: 52 patients, median age of 62 years (IQR 56.25-66.75). Donors' age 73 years (IQR 68.25-79) (23.1% ≥80years old). CIT 220.5 minutes (IQR 185.5-255), HOPE time 132.5 minutes (IQR 123-173.5). Reduced IRI severity (p=0.001). Follow-up of 615 days (IQR 438.5-838), with recurrence in four patients (7.7%), only extrahepatic. DFS of 98% at one year. No mortality in patients with recurrence in this group. Recurrence rate (p=1.000) and DFS (p=0.911) were similar between groups, but patients didn't have hepatic recurrence in the HOPE group. In the HOPE group 21.1% of patients had a metroticket result ≤50% and only one of these had HCC recurrence. There was a significant difference in donors' age (p<0.001), as well as in CIT (p<0.001).

Conclusions: In our experience, the use of HOPE appears to reduce hepatic recurrence after LT for HCC. It allowed for use of grafts from donors aged ≥80 years old, improving access to LT for these patients, and significantly reduced the CIT and IRI severity.

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PRINTED POSTERS

Access to transplantation

PP_001 RESURRECTION OF ORGAN TRADING FROM CAMBODIA AFTER THE PANDEMIC

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Background: Singapore has the 7th highest incidence of end-stage kidney disease (337 pmp) and a low kidney transplant rate of 18.7 pmp in 2022. As a result, 526 patients from the Singapore General Hospital (SGH) have travelled to India and China (1979 to 2019) for commercial kidney transplants (CKTX). In 2020, travel for CKTX ceased but resumed in 2021 with Cambodia being the new hub for CKTX. Reports on CKTX from South-East Asia is scarce and this is the first study to report on the characteristics and outcomes of CKTX from Cambodia.

Methods: This was a retrospective audit of 33 patients who had undergone CKTX in Cambodia and were on follow-up at SGH during the period of 1st January 2018 to 31st October 2024. Criteria for CKTX was fulfilled for all under the Declaration of Istanbul framework. Upon return to Singapore after CKTX, all patients seeking further care at SGH were required to be admitted which allowed collection of data from medical reports (when available) and tests performed while inpatient.

Results: The cohort was predominantly male (66%) with a median age of 59 (range 28-77) years and median time on dialysis of 11.3 (0-109.2) months. None of these patients were registered on the Singapore's waiting list and only 22% (n=7/32) had prior evaluation for transplant in Singapore which was not completed. Notably, 10 patients had potential contraindications to transplant that should have been evaluated further prior to CKTX including pre-malignant conditions (n=6) and coronary artery disease (n=4). Handover of care was inadequate with only 47% (n=15) having hand-written memos which did not provide clinical information about the living donor and peri-operative management. Complication rates of CKTX were significantly higher when compared to local kidney transplants (n=87) performed during the same period (surgical complications 19% vs. 6%; infections 28% vs. 7%; non-infective complications 22% vs. 1% and 3-year patient survival 87% vs. 100%).

Conclusions: There is a higher rate of complications from CKT performed in Cambodia due to inadequate evaluation and care. International registries to collect more information about CKT in Cambodia is critically needed to further understand the situation and assist Cambodia to be ethically integrated into the international transplant community.

PP_002 IMPACT OF ADVANCE CARE PLANNING ON THE MENTAL HEALTH OF BEREAVED FAMILIES: A SYSTEMATIC REVIEW

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Background: Decisions regarding end-of-life care, including organ donation, are often made by surrogate decision-makers, such as family members. These decisions can place a significant mental burden on surrogates, especially when the patient's wishes are unclear. Advance care planning (ACP) is a patient-centered process of advanced discussion. This intervention is expected to improve the mental health of surrogates. This study reviewed the evaluations of ACP interventions and examined decision-support approaches, including those related to organ donation.

Methods: This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol is registered with PROSPERO (CRD42022381929). Studies published up to 2024 were identified through comprehensive searches in MEDLINE, EMBASE, PsycINFO, and the Cochrane Central Register of Controlled Trials. Literature selection was conducted independently by two researchers using Covidence Systematic Review software. The inclusion criteria were studies evaluating ACP interventions that met the following conditions: (i) studies reporting bereaved families' mental health outcomes, and (ii) randomized controlled trials (RCTs) or non-RCTs.

Results: A total of 2,906 search results were obtained, and 13 studies met the inclusion criteria, comprising 11 RCTs and two non-RCTs. All interventions involved trained medical professionals facilitating ACP discussions before the patient's death. A scale assessing depression, anxiety, and Post-Traumatic Stress Disorder (PTSD) was used to evaluate mental health. Five studies reported that ACP improved the mental health of family members. Notably, Song et al. (2015, 2016, and 2024) conducted three of these studies.

Conclusions: Depending on the subject and intervention method, pre-death discussions are expected to improve the mental health of bereaved families. ACP may also be a tool for supporting decisions related to organ donation, which is often a mentally stressful process. Implementing ACP could contribute to addressing the shortage of organ donations, a pressing issue in Japan.

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PP_003 OUTCOMES INCLUDING NATIVE LIVER SURVIVAL OF LARGE DUCT PEDIATRIC PRIMARY SCLEROSING CHOLANGITIS

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Background: Natural history of primary sclerosing cholangitis (PSC) in children involves complications related to biliary disease (BD, 28%) and portal hypertension (PHT, 35%) culminating into liver transplantation (LT). Large multicenter study from West has described better outcome with small duct PSC and presence of inflammatory bowel disease (IBD). However, biliary changes of small duct PSC on biopsy are often seen as a spectrum of autoimmune hepatitis (AIH). In the present study, we aimed to study the natural history and outcome of Indian children with large duct PSC.

Methods: Retrospective data analysis of all under-18-year age children with diagnosis of large duct PSC on MRCP. Children with secondary sclerosing cholangitis or small duct PSC with AIH were excluded.Complications related to BD and PHT, outcome in terms of survival with native liver (SNL), death or LT were noted.

Results: We had 32 children (21 males) with a median age at presentation of 12.7 (9.6, 14.9) years. IBD and associated AIH (PSC-Overlap) were present in 13 and 17patients. Median IgG was 22.7 (16.7, 30.1) g/L and auto-antibodies were positive in 23 children (ANA 12, SMA 9, p-ANCA 15). Median PELD/MELD scores and SCOPE index were15 (6, 22) and 6 (5, 7). 26 patients were followed-up over a median duration of 28 (6, 66) months. Complications related to BD, PHT and decompensation developed in 21, 19 and 15; 5 required ERCP interventions. Overall, SNL, death and LT was present in 14, 6 and 6 patients. Poor outcome was related to presence of BD (HR=2.73, p=0.003), esophageal varices (HR=2.45, p=0.014) and ascites (HR=6.14, p<0.001) while presence of IBD was associated with favourable outcome (HR=0.41, p=0.047). Presence of AIH did not affect the outcome of PSC (p=NS).

Conclusions: Outcome of large duct PSC is related to BD and PHT complications but not to AIH. Presence of IBD in PSC indicates a good prognosis.

PP_004 OUTCOMES OF KIDNEY TRANSPLANT CANDIDATES REQUIRING VALVE REPLACEMENT SURGERY

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Background: Patients with valvular heart disease awaiting renal transplantation often undergo pre-transplant valve surgery to optimize cardiovascular function and facilitate transplant eligibility. These patients may however have higher risks of mortality and morbidity post cardiac surgery. This study evaluates the outcomes of ESRD patients who underwent cardiac surgery and their subsequent rates of successful kidney transplantation.

Methods: A retrospective analysis over an 11-year period was conducted of patients with valvular heart disease undergoing cardiac surgery with the intention of being listed for renal transplantation. The primary outcome was successful renal transplantation while secondary outcomes included 30-day mortality, length of stay, postoperative complications, and mortality while on the transplant waiting list.

Results: A total of 20 patients (70% male, average age 57) were included. Half underwent elective surgery, and the other half had urgent procedures. Aortic stenosis (45%) and endocarditis (20%) were the most common diagnoses, with 55% requiring concomitant procedures such as coronary bypass grafting. Follow up ranged from 6 months to 9 years (mean 5.5 years). At follow-up, 6 patients remained on the transplant waiting list, and only 2 were successfully transplanted. Mortality after valve replacement was 60%, with 3 in-hospital deaths, 1 death after redo surgery, and 9 while subsequently waiting for a transplant. Complications included inotropic support (65%), ECMO (1 patient), re-exploration for bleeding (15%), CVVH (90%), pneumonia (20%), AF (25%), and pacemaker placement (2 patients). Two patients developed mediastinitis, with 1 needing wound debridement. The average hospital stay was 36 days (range 6-124 days).

Conclusions: Patients undergoing valve replacement prior to intended renal transplantation represent a high-risk cohort with a guarded prognosis. Despite the intent to optimize patients for transplantation, only 10% achieved this goal. These findings underscore the importance of multidisciplinary decision-making, careful patient selection and setting realistic expectations for outcomes. Given the significant mortality and morbidity associated with this group, a tailored, individualized approach is crucial in managing these complex cases.

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PP_006 PRELIMINARY EVALUATION OF KIDNEY ALLOCATION ALGORITHM CHANGES IN SWITZERLAND

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Background: The allocation of kidneys is severely complicated by the presence of HLA-antibodies. Being a small country, Switzerland has adapted its allocation algorithm for kidneys in a way that HLA-antibodies are decisive for kidney allocation, overruling possible HLA-matches. Still, finding a suitable kidney for a highly immunized patient is posing a challenge. As an alleviation, the responsible group for kidney allocation in Switzerland decided to adapt the allocation algorithm. In order to generate improved chances for highly immunized patients, the allocation rules were changed per 1st April 2024 as to prioritize patients with a calculated Panel Reactive Antibody (abbreviation: cPRA) above or equal to 98%.

Methods: This paper sets out to investigate preliminary results of this change. Data from the national allocation tool encompassing six years is used to investigate the impact on the national waiting list and transplantations. Statistical measures, such as an exact Fisher Test, are applied to compare the amount of transplanted patients with a cPRA above 98% before and after the implantation of this change. In addition, the possibility of future transplantations is analysed as well as the impact on the status of the national waiting list.

Results: Preliminary results show that the amount of transplanted patients with a cPRA above than 98% has significantly risen over the investigated timeframe, even when compared to the larger timeframe before the change. Also, the percentage of highly immunized patients transplanted in the wake of the change has more than tripled in the investigated period, rising from a yearly average of 1.58% to an extrapolated average of 6.81%.

Conclusions: The implemented change has been highly impactful. The chances for patients with a cPRA above 98% to receive a suitable organ have improved with this change and the amount of such patients on the list could be reduced by more than 2%.

PP_007 TRENDS IN KIDNEY TRANSPLANTATION IN ROMA ETHNICITY - A NEGLECTED ETHICAL PROBLEM IN TRANSPLANTATION

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Background: Kidney transplantation is the standard of care for patients with end-stage kidney disease for all patients without contraindications. However, there is little evidence of Roma representation in national cohorts of kidney transplant recipients. We aim to determine the trends in kidney transplantation of the Roma minority in Croatia, their clinical characteristics, complications, and outcomes before and after entering Eurotransplant in 2007.

Methods: In a prevalent cohort of kidney transplant recipients, we retrospectively and from 2012 prospectively collected clinical characteristics and laboratory data from 24 Roma patients, followed up over a median of 140 (range 4-276) months.

Results: Until August 15, 2007, five Roma patients underwent kidney transplantation (cohort 1). Since that time, 19 additional patients received allografts (cohort 2), four of them over the last year. The average age of Cohort 1 was 29.75 years vs. 36,54 years in Cohort 2. The average waiting time was 49.75 (range 10 to 120 months) and 43.73 (range 5 to 92 months) in cohorts 1 and two, respectively. One patient received a kidney allograft from a living unrelated spousal donor, and all others were from deceased donors. Two (8.3 %) patients died, both with functioning allograft, one from heart failure and the other from Aspergillosis. Three patients (12.5%) developed end-stage kidney allograft failure and returned to dialysis, one of them was restransplanted. Two of them lost grafts due to severe acute rejection caused by noncompliance. Two young patients were also non-compliant with immunosuppressive medications, while one autistic patient does not attend controls but is alive with a functioning allograft. The most frequent post-transplant complications were urinary tract infections, sepsis, and NODAT.

Conclusions: The outcomes of Romas are excellent. However, compliance remains a significant challenge that influences their post-transplant outcomes.

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PP_008 THE EFFECT OF INTRODUCING THE PRESUMED BRAIN DEATH REPORTING INDICATOR ON ORGAN DONATION IN KOREA

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Background: The number of individuals awaiting organ transplants in South Korea has steadily increased, reaching 43,421 in 2023. In contrast, brain-dead organ donors have averaged only 443 annually (2021~2023). To address this imbalance between organ transplant demand and brain-dead donors, institutional improvements were deemed necessary. As part of these efforts, the 'number of reports of presumed brain death' indicator was introduced on a pilot basis in Korea's 2023 medical quality assessment. This study aims to examine the impact of this indicator's introduction on organ donation outcomes in Korea.

Methods: The study analyzed data reported to Korea Organ Donation Agency (KODA) on presumed brain death reports, medically eligible cases, and completed organ donations from January to December 2023, comparing them to the same period in 2022. Presumed brain death reports were defined according to the Organ Transplantation Act, medically eligible cases excluding those categorized as "not brain dead" or "not eligible for donation." Completed organ donations referred to successful transplants.

Results: Presumed brain death reports increased by 35%, from 2,163 in 2022 to 2,921 in 2023. The proportion of cases classified as "not brain dead" decreased from 4.6% to 2.8%, while "not eligible for donation" cases rose from 12.6% to 22.1%. Medically eligible cases increased by 22.4%, from 1,791 to 2,193, though their proportion declined from 82.8% to 75.1%. Completed organ donations grew by 19.2%, from 405 to 483. Regionally, presumed brain death reports rose by 36.1% in the Central region, 20% in Chungcheong-Honam, and 43.9% in Yeongnam. Medically eligible cases increased by 20.3%, 12.6%, and 33.8%, respectively. Organ donations rose by 31.5% in the Central region and 12.9% in Yeongnam, with no change in Chungcheong-Honam.

Conclusions: The pilot indicator increased reports, medically eligible cases, and organ donations. However, the proportion of eligible cases declined, and regional variations were observed, indicating the need for systematic brain death management and tailored regional strategies. These institutional improvements have fostered active participation from medical institutions and are expected to contribute significantly to the activation of organ donation.

PP_009 EMPOWERING PATIENTS IN KIDNEY TRANSPLANTATION: DEVELOPMENT OF 'THE NEW US' DECISION AID

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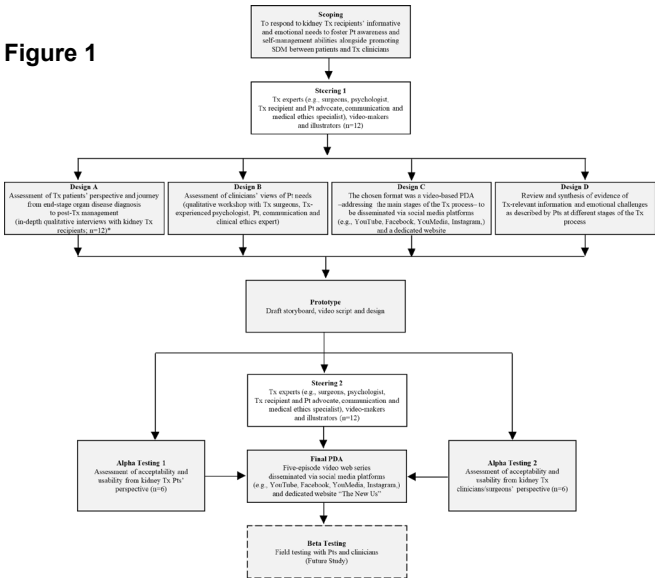
Background: Pre-transplant education is critical to prepare chronic kidney disease (CKD) patients for transplantation. It helps them understand the scope of the process, treatment options with risks and benefits of deceased and living donor transplantation, pre-operative assessments, and prospects for post-transplant care. Shared decision-making (SDM) is the recommended decision-making and educational model in organ transplantation. Patient decision aids (PDA) foster implementation of SDM between patients and clinicians by supporting patient understanding and enabling their active participation in decision-making. We describe the development process of a PDA, titled 'The New Us', targeting CKD patients.

Methods: PDA development followed a structured and systematic approach aligned with the International PDA Standards. These standards recommend that PDAs be carefully designed, user-tested, and open to scrutiny, with all development phases well-documented and systematically applied. They encompass a range of criteria, including scoping the problem, involving a multidisciplinary steering group, designing and developing the content, and conducting iterative testing phases.

Results: Key themes of the transplant journey were identified, emphasizing patient empowerment and holistic support. The chosen format was a video-based PDA to be disseminated via social media and a dedicated website. The PDA prototype was assembled and later assessed by the steering group. The final PDA consisted of a five-episode web series of a CKD patient which was distributed online with an integrated communication plan. Over an 8-month period, it reached over 56,000 viewers, was a top-six selection at an International Social Film Festival, and drove 39,000 users to "The New Us" website. Alpha Testing data collection is in progress at the time of writing (Figure 1).

Conclusions: Leveraging storytelling and accessibility of new technologies, "The New Us" has the potential to empower CKD patients by enhanced understanding, self-management abilities, and successful implementation of SDM between patients and clinicians. Positive viewership suggests a positive response. Future studies will perform Beta Testing to formally assess usability and feasibility from clinicians' and patients' perspectives.

Figure 1



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PP_011 A CLINICAL GOVERNANCE CORE INTO THE TRANSPLANT NETWORK OF THE CAMPANIA REGION

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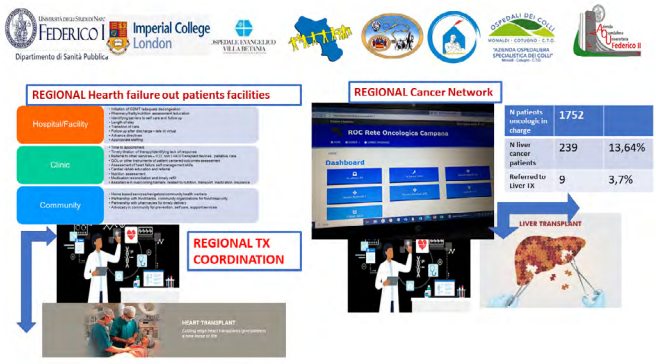
Background: The introduction of practical hospital applications of Evidence-Based Medicine (EBM), related practices (EBP), and a methodology focused on Patient-Reported Outcome Measures (PROMs) bridges the gap between research and clinical practice. This approach plays a central role in organ transplantation from living and cadaveric donors, aiming to reduce disparities in healthcare provision among different regions

Methods: The proposed model introduced in 2024 from regional transplant coordination involves a planning committee composed of professionals from donation and transplantation programs, experts in epidemiology, and institutional governance of healthcare policies within transplant directorates and transplant service desks. The committee analyzed directional data from codified information flows within the regional IT system (Sinfonia) to map hospital pathways, follow-up procedures, and waiting lists. Following the Santander Declaration of 2023, a roadmap for integrating transplantation into routine regional healthcare assistance was developed

Results: The impact areas identified include: Risk factor identification, Outcome analysis and governance, Integrated Care Pathways (PDTA), Screening programs. The committee introduced also options analyzed bridging the gap between cardiac hearth failure and liver tumors patients and the access to transplantation pathways as Obesity and Body Mass Index (BMI) emerged as consistent factors in the analysis of metabolic alterations into regional population (median BMI = 27,3 in abdominal Tx waiting lists and 27,9 in hearth TX waiting list). A network between cardiac regional facilities was built whereas in liver tumor evaluation the referral of a Liver TX center was selected as mandatory consult, given the evidence that, although Liver Tx appears to offer better survival, compared with resection, there are heterogeneity comparing the two strategies, also due the scarcity of organs and out-of-pocket costs.

Conclusions: In line with the Paris Transplant Group, the Campania region coordination in these controversial settings promoted integrated care models, and streamline patient referrals to transplant hubs. This initiative supports inclusivity and provides a more comprehensive mapping of healthcare needs.



PP_013 OUTCOMES FROM EUOPEAN PAEDIATRIC ACCESS TO KIDNEY TRANSPLANTATION (EUPAKT) STUDY

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Background: Kidney transplantation is advocated as the gold standard in optimising health and improving quality of life in children with end stage kidney disease (ESKD). However, multiple factors, including psychosocial and therapy adherence, have been cited to delay transplantation. Moreover, we do not understand how transplantation delays influence the child's quality of life (QoL).

Methods: A multicentre (11 European paediatric nephrology centres) longitudinal registry study was designed to prospectively collect pre-transplant data on all patients receiving paediatric care with ESKD between September 2020 and 2021, followed by 1-year post-baseline data. We collected data on patient demographics, clinician-reported factors delaying transplantation, changes in kidney replacement therapy including transplantation during the study period, patient- and proxy-reported QoL on a 1 to 5 Likert scale, clinician-, patient- and proxy-reported therapy adherence also on a 1 to 5 Likert scale.

Results: Among 167 patient entries, 53 received a transplant during the study period. There were 203 entries describing factors contributing to kidney transplantation delay. The most cited factors were donor-availability (42%), disease-related (24%), size of the child (12%) and psychosocial (11%). Children having "psychosocial factors" delaying their transplant at baseline, were less likely to be among the children who received a transplant (p=0.02). At pre-transplant baseline, there was no difference in clinician-, patient- or carer-reported therapy adherence. Transplanted children were more likely to report a better QoL score at pre-transplant baseline (p=0.03). Although there was no significant difference in therapy adherence (clinician-reported p=0.697, patient-reported p=0.260, carer-reported p=0.765), QoL scores declined after 1 year of waiting for a transplant (patient-reported p=0.006, carer-reported p<0.001).

Conclusion: Children with psychosocial factors delaying transplantation are more likely to experience greater delays in transplantation. There is no difference in therapy adherence between children who receive a transplant and those who experience delays. Children still waiting for transplantation 1-year-on are likely to experience significant decline in their QoL.

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PP_014 SUCCESSFUL KIDNEY TRANSPLANTATION IN FUNCTIONALLY ILLITERATE PATIENTS: CASE SERIES

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Background: Functional illiteracy is still present in certain vulnerable groups, e.g. in Roma minority and in elderly, especially females. Illiteracy imposes challenges on achieving optimal healthcare availability and patient safety. While poor health literacy has been linked to inferior outcomes in kidney transplant recipients, specific data related to functional illiteracy is lacking.

Methods: We present here 2 cases of illiterate ESKD patients who were successfully transplanted.

Results: Both patients were Roma women, aged 61 and 63 at the time of their evaluation for deceased donor kidney transplantation. One had diabetic nephropathy, and the other ADPKD. During the work-up, no medical contraindications were found but during the informed consent it became evident that they were completely illiterate. Illiteracy complicates the very process of decision-making and informing the patient thus potentially undermining the informed consent. It interferes with the self-care of the patient and the opportunity to obtain information independently. In our cases, family support and involvement was crucial. However, as much the family members empower the illiterate patient and ease the healthcare process, the patient's autonomy must be respected. Individual consultations were conducted, followed by joint discussions with a literate family member. The first patient was accompanied by her husband and the second by her daughter, both who continued to come to postransplant follow-up. The first patient was successfully transplanted at 62 years of age, with excellent graft function at 5-year follow-up. The second patient was transplanted at 64 years of age, with good function at 2 years follow-up. There were no adverse events related to health literacy.

Conclusions: illiteracy is not a contraindication for transplantation, but only a barrier which can be overcome through good support and a personalized approach. During follow-up there were no illiteracy associated adverse events confirming the safety of our approach.

PP_015 SURVIVAL BENEFIT OF HLA-INCOMPATIBLE LDKT COMPARED TO DECEASED DONOR WAITLING IN ELDERLY PATIENTS

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Background: HLA-incompatible living donor kidney transplantation (HLAi-LDKT) in elderly patients is challenging issue due to risk of complications associated with pretransplant desensitization and heavy immunosuppression. This study evaluates survival benefit of HLAi-LDKT compared to waiting DDKT in elderly patients to determine the optimal strategy.

Methods: We analyzed 758 patients who registered for KT at their 60 or older in Korean single center. For elderly HLAi-LDKT, outcomes were compared according to HLA antibody strength. To investigate survival benefit, patients who received HLAi-LDKT was 1:5 matched with controls who remained on the waiting list or received DDKT (Waitlist-or-DDKT group), and with those who remained on the waiting list without receiving a transplant (Waitlist-only group).

Results: The 57 HLAi-LDKT group consisted of positive complement-dependent cytotoxicity (CDC) crossmatch (CDC+FC+) (n=12), positive flow cytometric crossmatch (CDC-FC+) (n=30), pretransplant donor-specific antibody only (CDC-FC-DSA+) (n=15). Desensitization protocol targeting DSA consisted of plasmapheresis, intravenous immunoglobulin, and rituximab with/without bortezomib. The number of preoperative plasmapheresis differed significantly among these groups (7.8±2.3, 4.3±1.6, 3.4±2.1, p<0.001). The 5-year graft survival rates were similar (91.7% for CDC+FC+ vs. 88.1% for CDC-FC+ vs. 91.7% for CDC-FC-DSA+, p=0.921) although biopsy-proven rejection was numerically higher in CDC+FC+ and CDC-FC+ than that of CDC-FC-DSA+ (38.1% vs. 30.0% vs. 13.3%, P=0.461). Among matched population, the 10-year patient survival rate was 76.7% for HLAi-LDKT, compared to 62.1% for the Waitlist-or-DDKT group, and 52.6% for the Waitlist-only group, with a statistically significant difference between HLAi-LDKT and the Waitlist-only group (p=0.046).

Conclusions: In patients aged 60 and older, HLAi-LDKT offers survival benefit compared to remaining on the waitlist. HLAi-LDKT with potent desensitization could be a viable option in the elderly patients.

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PP_016 GUIDE: GENERATING UNDERSTANDING IN DISPARITIES AND EQUITY: A PATIENT SURVEY ON HEALTHCARE JOURNEY

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Background: Kidney and liver transplant recipients face unique challenges in their care pathways, influenced by socioeconomic status, treatment management, and care coordination. While clinical aspects are well-documented, patients' perceptions and care disparities remain underexplored.

Methods: A survey was conducted with 693 kidney and liver transplant recipients, using questionnaires available in digital or paper formats. Participants were recruited through healthcare professionals and patient associations. The questionnaires included Likert and Osgood scales as well as single- and multiple-choice questions. Key themes included perceptions of pre- and post-transplant care, quality of information received, relationships with specialists, psychological well-being, and treatment adherence.

Results: Kidney or liver transplant patients expressed a strong need for enhanced support, including respectively, individualized therapeutic education (33.4%-32.3%), psychological support (17.9%-20.9%), and follow-up applications (25.3%-22%) (Figure1). Most patients reported taking anti-rejection medications twice daily and more than 80% feel that they were not offered the option of switching to once-daily regimens despite moderate anxiety about changing their treatment. The findings also revealed significant disparities, mainly linked to socioeconomic status. Surprisingly, the precarious patients were around one third for both kidney and liver. They were more likely to report psychological difficulties, a lower acceptance of the transplant, and greater hesitancy to voice misunderstandings to specialists. Moreover, kidney patients in precarious situations reported an extension of the dialysis period by up to 7.5 months and a more negative perception of this phase (Table 1).

Conclusions: These results emphasize the need to develop educational tools, follow-up applications, and psychological support to reduce disparities and improve the care experience for transplant recipients.

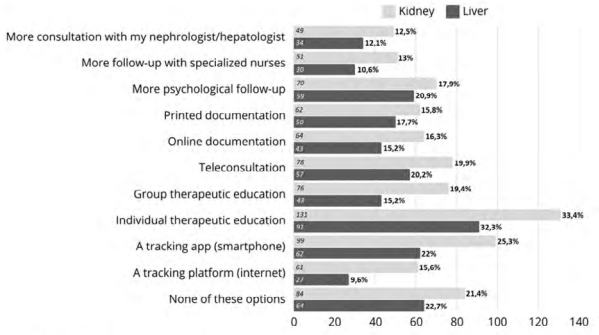

Figure 1: Patients' main expectations regarding their follow-up

	Non precarious	Precarious
[Kidney] Time spent on dialysis (number of months; mean)	21	28,4
[Kidney] In my opinion, this period on dialysis was (Acceptable 1 - Too long 7; mean)	3,6	4,2
I feel I was given enough information about the nutritional guidelines I need to follow with my transplant (Strongly disagree 1 - Strongly agree 7; mean)	5,96	5,45
I feel I was given enough information about the recommended physical activity after my transplant (Strongly disagree 1 - Strongly agree 7; mean)	5,69	5,15
I feel I was given enough information about the nutritional guidelines I need to follow with my transplant (Strongly disagree 1 - Strongly agree 7; mean)	5,71	5,87
I feel I was given enough information about the recommended physical activity after my transplant (Strongly disagree 1 - Strongly agree 7; mean)	5,49	5,6
[Kidney] I sometimes struggle to accept the fact that I have someone else's organ (Strongly disagree 1 - Strongly agree 7; mean)	2,04	2,7
[Liver] I sometimes struggle to accept the fact that I have someone else's organ (Strongly disagree 1 - Strongly agree 7; mean)	1,7	2,07
[Kidney] I sometimes regret having had the transplant (Strongly disagree 1 - Strongly agree 7; mean)	1,44	1,82
[Liver] I sometimes regret having had the transplant (Strongly disagree 1 - Strongly agree 7; mean)	1,79	2,21
Sometimes, I don't dare to tell my nephrologist/hepatologist that their explanations are too complex (Strongly disagree 1 - Strongly agree 7; mean)	2,04	2,6
When I am in consultation with my nephrologist/hepatologist, there are topics I don't dare to bring up (Strongly disagree 1 - Strongly agree 7; mean)	2,57	3,12

Table 1: Main results according to precariousness (Global: non precarious: n= 459, precarious n=234; Kidney: non precarious: n=255 precarious: n=137; Liver: non precarious: n=192 precarious: n=90)

PP_017 IMPLEMENTING A RETRIEVAL TEAM INFORMATION CHECKLIST TO IMPROVE COMPLIANCE - QUALITY IMPROVEMENT PROJECT

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Background: RTI is collected national by every organ retrieval centre in the country and returned to the national central NHS Organ Donation Transpant Information Services, NHS Blood and Transplant to enhance coordination, improve safety and efficiency during complex multi-visceral operations. The RTI forms include vital information on donors, retrieval teams and specific organ transplant details which are crucial for the success, safety, and legality of retrieval efforts. Within Scotland there were higher than expected issues/ non return rate of the RTI forms to address this a standardised checklist was implemented.

Methods: This study employs a pre- and post-intervention design. The intervention consists of the introduction of a standardised checklist system that aims to ensure staff complete and return all the correct paperwork required in the RTI forms.The study was conducted in the Transplant department of the Edinburgh Royal Infirmary, a tertiary centre and teaching hospital. Data were collected through two main methods: RTI form Data and Staff Surveys. Primary outcomes included: The number of incomplete documents. Secondary outcomes included: Staff satisfaction, measured through survey responses using a 5-point Likert scale (1 = Strongly Disagree, 5 = Strongly Agree) regarding the usefulness and clarity of the checklist

Results: The baseline audit looking at pre- checklist implementation identified that between March 2023 and April 2024 a total of 17 RTI forms were missing/awaited and 3 forms had unresolved issues. Following the implementation of the checklist there were no missing/awaited forms with only 1 form having an unresolved issues. This represented a 100% reduction in compliance of missing/awaited forms and 66% reduction in unresolved issues ($p < 0.05$). This indicates a statistically significant improvement in document management following the introduction of the checklist.

Conclusions: This study demonstrates that the introduction of a checklist can significantly reduced the occurrence of lost paperwork and improve document management processes thus reducing administration time. Future research could explore the long-term effects of the checklist intervention and its applicability in other transplant regional settings.

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PP_018 CLINICAL LEADS FOR ORGAN UTILISATION (CLU): A SURVEY TO CAPTURE SUCCESS, CHALLENGES AND FUTURE DIRECTION

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Introduction: The Clinical Leads for Utilisation (CLU) scheme launched in 2020 to identify and reduce barriers to organ utilisation (OU), improve collaboration, and deliver OU improvement strategies. The recent reconfiguration of the leadership team to form the Organ Utilisation Development Team (OUDT), provided an opportunity to refocus on strategy and forward planning.

Methods: An electronic survey was designed and circulated via email to all 54 CLUs. Questions were structured around the following themes: CLU demographics; scheme effectiveness, achievements and reflections; local transplant activity and CLU projects; and perceived barriers and solutions. Results were analysed, and themes identified.

Results: 48 (89%) responses were captured June-July 2024 from adult (64%), paediatric (9%) and combined (28%) CLUs, representing all solid organ types. Key findings from respondents included: • 59% confirmed their CLU role was job planned. • 77% felt the CLU scheme was working effectively. • 68% had noticed a culture change within their transplant centre. The Offer Review Scheme was recognised as a significant achievement with ongoing benefit to OU. All respondents confirmed offer 'decline' meetings were established in their local centres, supporting the delivery of the Organ Utilisation Group recommendations. To inform standardisation of these meetings, participants were asked to comment on optimum frequency of meetings, with results in Figure 1. Identified challenges for CLUs included lack of time, need for sustainable funding, visibility with Trust Boards, and team culture. Looking forward, 95% felt more structured support and guidance would be helpful, with suggested improvements outlined in Table 1.

Conclusion: This community engagement and resulting insight gained has provided grassroots generated renewed direction of focus for OUDT. Some early actions have been identified and implemented and a longer-term improvement action plan is also in progress, to support the future efficacy of the CLU scheme.

Figure 1: Preferred frequency of unit decline meetings

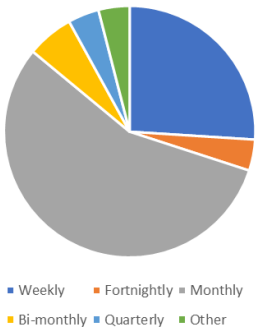

Table 1: CLU generated ideas for delivering improvement

Additional resources required	No. of responses
Business case support	22
Organisational development	18
Stats input	18
Data collection	16
Administrative support	13
Structure & Planning	12
Toolkits	12
Outside support to increase visibility	9
Digital solutions	9
Clinical advice/mentoring	7
External scrutiny from NHSE	1
Funding	1

PP_019 KIDNEY TRANSPLANTATION IN HIGHLY SENSITIZED. WHAT DID WE DO?

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Background: Faced with the problem of a shortage of organs for transplantation and long waiting lists, transplantation in highly sensitized patients is a particular problem.Several alternative options to receive a transplant exist for these patients, including additional priority in regular allocation, special programs based on allocation through acceptable antigens, kidney paired donation programs, desensitization protocols, or a combination of the latter two. Aim: to make an summer of guideline and to share our experience in enabling kidney transplantation in highly sensitized patients.

Methods: Using the guideline from the ESOT working group and KDIGO for management of kidney transplant patients with anti HLA antibodies and comparison of practice across Europe for sensitized patients, we summary the definition of sensitization and strategies for access to kidney transplantation for highly sensitized patients. As the number of patients on our national waiting list for kidney transplants increased, so did the number of patients who developed anti-HLA antibodies. Sensitization was most often due to red blood cell transfusions, pregnancy or previous transplantation. Patients had developed anti-HLA antibodies, determined with the Luminex technique, from Class 1 and 2 , both donor nonspecific and donor specific, as well as consistently positive Complement- dependent cytotoxicity (CDC) crossmatches with potential related and unrelated donors. To improve their organ availability we have implemented the rule to give priority if the cross match was negative.

Results: On several occasions, highly sensitized patients from the waiting list who were eligible for recipients based on blood groups and allowed number of HLA mismatches were called. Four of them, tree women (age 34, 44 and 52) and one men (age 56), with previously positive cross match, have received an organ, from a deceased donor, with a negative cross match befor transplantation. They had successful transplantation and good function of the grafts. No episodes of humoral rejection were noted.

Conclusions: Prioritizing highly sensitized patients on the waiting list for kidney transplantation from a deceased donor, with a negative cros match, may be the only opportunity for organ access and the key to successful transplantation.

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PP_023 VALIDATION OF THE FACIT CALCINEURIN INHIBITOR - NEUROTOXICITY PATIENT REPORTED OUTCOME MEASURE

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Background: There is significant interest in amplifying the patient's voice in drug development, with recent consensus meetings recommending expanded use of patient-reported outcomes (PROs) to better understand the tolerability of immunosuppression. We conducted a psychometric evaluation of the Functional Assessment of Chronic Illness Therapy Calcineurin Inhibitor – Neurotoxicity (FACIT-CNI-NTX), a new PRO measure developed for use in clinical trials to assess levels of side effects of CNIs.

Methods: Kidney transplant recipients were recruited from a major academic transplant centre in the United States and completed baseline and 4-month follow-up surveys to assess longitudinal validity. The surveys included the FACIT-CNI-NTX and other PRO measures to enable validation. The FACIT-CNI-NTX has two scales, Tremors (4 questions) and Cognitive Side Effects (4 questions), both on a 16-point scale.

Results: 198 kidney recipients completed the baseline assessment, with 169 (85%) completing the 4-month follow-up; 37% on a once-a-day tacrolimus formulation, 63% on a twice-a-day formulation. FACIT-CNI-NTX scales had good internal consistency reliability (>0.80). Concurrent and known groups validity was evidenced through moderate to large correlations (range: 0.29-0.64) with other PROs of similar concepts (e.g., quality of life), and by statistically significant differences in scores between known clinical groups (e.g., levels of overall side effect burden). Meaningful change thresholds, reflecting the amount of improvement or worsening patients find meaningful, ranged between 2-3 points for both scales.

Conclusions: Coupled with its previously-demonstrated content validity, these results show that the FACIT-CNI-NTX is fit-for-purpose for CNI clinical trials. The meaningful change thresholds will enable its application as a trial endpoint, helping advance patient-centric drug development among kidney transplant recipients by determining which CNI formulations are most tolerable.

PP_025 APPROPRIATE INDICATIONS FOR LIVER TRANSPLANTATION IN CARRYOVER BILIARY ATRESIA IN JAPAN

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Background: In carryover biliary atresia (BA) patients (PTs) who achieve long-term survival following Kasai procedure, some may eventually require liver transplantation (LT). In cases where a PT is unable to undergo living donor LT (LDLT) due to the unavailability of a donor, such as parents' age or graft size, deceased donor LT (DDLT) is indicated. Current organ allocation in Japan, based on MELD may not sufficiently rescue them. This study aims to clarify risk factors for carryover BA who require LT and to identify the clinical course after liver dysfunction emerges.

Methods: We define "carryover BA" as PTs over age of 16 who have not undergone LT. Data were collected from 34 carryover BA who visited our institute between 1997 and 2023.

Results: Of 34 PTs, 23 (67.6%) were considered to indicate LT due to repeated cholangitis (n=9, 39.1%), liver dysfunction (n=8, 34.8%), portal hypertension (n=4, 17.4%), and hepatopulmonary syndrome (n=2, 8.7%). Of the 23 PTs, 10 (43.5%) underwent LT (6 LDLT, 4 DDLT) at a median age of 22.5 yeas (17.0-34.3). The 5- and 10-year survival rates for LT PTs were both 90%. Of the remaining 13 PTs, 9 (69.2%) died at a median age of 28.9 years (18.8-41.1). The time from the onset of T-bil >10 mg/dl to death was 108.5 days (48-439). Additionally, the time to death after a MELD >28, which is considered the potential threshold for receiving DDLT in Japan, was 31.1 days (0-111). When comparing native liver survivors (n=11) with PTs who either underwent LT or had a poor prognosis (n=23), no significant differences were found in the age at Kasai procedure, frequency of cholangitis, frequency of abdominal surgeries, or presence of bile lakes on CT. Significant predictive risk factors for requiring LT, based on data after age of 12, included peak T-bil values (p=0.0001, AUC=0.91502, cutoff: 1.9 mg/dl), peak AST values (p=0.047, AUC=0.71542, cutoff: 104 IU/L), spleen size (p=0.005, AUC=0.84722, cutoff: 12cm), and presence of an atrophic liver appearance (p=0.014).

Conclusions: In carryover BA PTs, those with splenomegaly >12 cm, liver atrophy, peak T-bil >1.9 mg/dl and AST >104 IU/L should be considered for LT. PTs with persistently high T-bil (>10 mg/dl) without recovery exhibit extremely poor prognosis, suggesting that DDLT should be prioritized in these cases.

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PP_027 TRENDS IN FACTORS AFFECTING ACCESS TO KIDNEY TRANSPLANTATION AND GRAFT SURVIVAL (COLLABORATIVE TRANSPLANT STUDY)

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Background: Univariate Kaplan-Meier analysis of the CTS data shows that graft survival for kidney transplant recipients improved steadily over 20 years before the SARS-CoV-2 pandemic. Three-year overall graft survival rates were 83.4% for patients transplanted 2000–2004, increasing to 83.5%, 84.4%, and 85.5% in the subsequent five-year periods. We aimed to assess trends in commonly known confounding factors during this time.

Methods: We analyzed first deceased-donor kidney-only transplants in Europe from 2000 to 2019 (162 transplant centers; 126,172 transplants), stratified into four periods: 2000–2004, 2005–2009, 2010–2014, and 2015–2019. Kaplan-Meier analysis was used for univariate survival, Cox regression for multivariable three-year overall graft loss, chi-squared test for categorical variables, and Kruskal-Wallis test for continuous confounders.

Results: As shown in Table 1, comparing the first to the last period, mean donor age increased by eight years and recipient age by six years - factors typically associated with lower graft survival. However, cold ischemia time decreased by four hours and patients receiving induction therapy increased - trends reported to favor graft survival. Also, steroid usage among recipients decreased. Other analyzed factors did not show clear trends. Figure 1 presents the hazard ratios (HR) for 3-year overall graft loss. While the number of HLA mismatches increased, their negative impact remained constant over time with HRs between 1.07 and 1.08 (1A). In contrast, the risk of graft loss with pre-transplant panel-reactive antibodies (CDC PRA) decreased steadily, with hazard ratios dropping from HR=1.32 in the first to HR=1.07 in the last period (1B).

Conclusions: The average number of HLA mismatches increased, but their negative impact on graft survival remains significant with similar hazard ratio. On the other hand, the detrimental effect of HLA pre-sensitization has decreased probably due to refined antibody detection methods with more specific exclusion of incompatible antigens and to wider use of induction therapy.

Confounder	00-04 (N=33,041)	05-09 (N=33,273)	10-14 (N=31,448)	15-19 (N=28,410)	P
Donor age					<0.001
Mean (SD)	46.0 (17.0)	49.4 (17.0)	52.6 (16.9)	54.0 (17.2)	
Recipient age					<0.001
Mean (SD)	47.7 (15.0)	50.1 (15.0)	52.6 (15.1)	53.4 (15.2)	
Number of HLA-A+B +DR mismatches					<0.001
0–1	4,536 (15%)	3,837 (13%)	2,670 (10%)	1,817 (8%)	
2–4	21,470 (72%)	20,449 (69%)	18,678 (70%)	16,192 (69%)	
5–6	3,706 (12%)	5,145 (17%)	5,349 (20%)	5,468 (23%)	
Pre-Tx CDC PRA (%)					<0.001
0	23,704 (86%)	23,301 (90%)	18,399 (86%)	13,987 (86%)	
>0	3,775 (14%)	2,715 (10%)	2,966 (14%)	2,200 (14%)	
Cold ischemia time					<0.001
Mean (SD)	17.6 (7.18)	15.8 (6.04)	14.5 (5.43)	13.8 (5.46)	
Steroids					<0.001
No	1,631 (6%)	2,549 (9%)	3,699 (13%)	3,858 (15%)	
Yes	28,021 (94%)	27,356 (91%)	24,402 (87%)	21,356 (85%)	
Induction therapy					<0.001
No	19,477 (66%)	15,023 (50%)	13,111 (47%)	12,421 (49%)	
Yes	10,175 (34%)	14,882 (50%)	14,990 (53%)	12,793 (51%)	

Table 1. Demographics

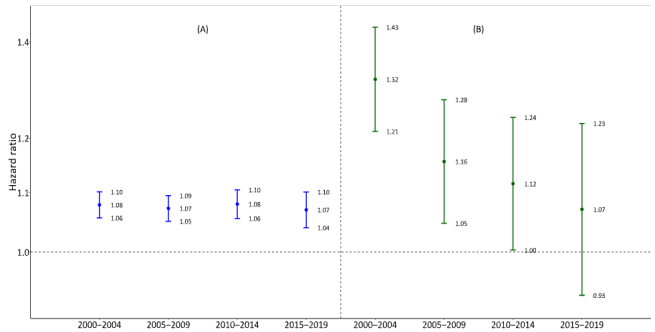

Figure 1. Hazard ratio for 3-year overall graft loss obtained from Cox regression analyses for (A) number of HLA-A+B+DR MM and (B) CDC PRA (>0% vs 0%) for the four periods 2000-2004, 2005-2009, 2010-2014 and 2015-2019.

PP_028 RECOVERY OF GLOBAL LIVING KIDNEY TRANSPLANTATION FOLLOWING THE COVID-19 PANDEMIC: A COMPARATIVE ANALYSIS

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Background: In 2020, there was a global decline in solid-organ transplantation through the Covid-19 pandemic. There were clear reasons for reducing or pausing transplant activity, including logistical challenges and medical uncertainty; combined with decreased numbers of both living and deceased donors. This study explores the impact of the COVID-19 pandemic and subsequent recovery in Global Living Kidney Donor (LKD) Transplant activity.

Methods: Using open access data obtained from the International Registry in Organ Donation and Transplantation, we compared rates of LKD from 2018 – 2023 (inclusive), in countries with a LKD transplant rate of more than 15 per million population (pmp) and/or a population size of >40 Million people and LKD rate of 5-15 pmp in the 2 years prior to the COVID-19 pandemic.

Results: Most countries reported reduced LKD activity during the pandemic. 8 countries had LKD activity >15 pmp before the pandemic (Turkey, UK, Netherlands, Iceland, Sweden, Norway, Israel and Denmark). By 2023 Turkey was back to pre-pandemic LKD rates, Denmark and Israel had exceeded pre-pandemic levels, the UK and the Netherlands were recovering but had not yet achieved pre-pandemic levels and Iceland, Sweden and Norway had sustained losses in LKD rates. Countries with LKD rates of 5-15 pmp and populations >40 million (Germany, France, Italy, Spain) showed recovery by 2023, with Italy and Spain exceeding pre-pandemic levels.

Conclusions: Global LKD rates vary widely. Those with larger LKD programmes have generally recovered following the COVID-19 pandemic, but not all have managed to achieve pre-pandemic rates. The factors influencing national LKD rates and their subsequent pandemic recovery are both diverse and unique to each county. These may include transplant specific issues, eg: the actions taken around organ donation activity during the pandemic, existing opinions on the relative place of living vs deceased kidney donation and the availability of deceased donor kidneys; in addition to unique healthcare and political influences.

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PP_029 ACCESS TO KIDNEY TRANSPLANTATION WAITLISTING FOR PEOPLE WITH MENTAL ILLNESS, AN AUSTRALIAN COHORT STUDY 2006-2020

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Background: In Australia, like many other countries, mental illness is not an absolute contraindication for kidney transplantation. However, other contraindications such as medical nonadherence and substance use are more prevalent among those with mental illness, which may limit access to waitlisting and transplantation. We aimed to determine whether people with mental illness experience delayed access to waitlisting or transplantation.

Methods: We analyzed data from the Australian and New Zealand Dialysis and Transplant Registry, linked to administrative health data from New South Wales (NSW, largest state in Australia with population over 8 million). We included all adult dialysis recipients in NSW 2006-2020. Pre-existing mental illness was classified as severe or persistent (SPMI), other, or none, based on hospitalizations and non-admitted mental health service contacts. The primary outcome was time to waitlisting (for deceased donor kidney transplant) or transplantation (from a living donor). Time to waitlisting/transplantation by mental illness was estimated using Cox regression, adjusted for age, sex, ethnicity, BMI, smoking, socioeconomic status, and remoteness. We truncated our analysis at 3 years since most patients would have been waitlisted or transplanted within this timeframe.

Results: Of 11459 patients analyzed, 546 (5%) had SPMI, and 813 (7%) had other mental illness. Those with other mental illness were waitlisted/transplanted at similar rates to those with no mental illness (HR 1.00, 95%CI 0.86-1.17, p=0.9), while those with SPMI had much lower rates of waitlisting/transplantation (HR 0.53, 95%CI 0.42-0.65, p<0.001).

Conclusions: People with severe mental illness are particularly disadvantaged when accessing kidney transplantation. Mitigating the burden of kidney failure experienced by this group would contribute to bridging the health gap that they experience.

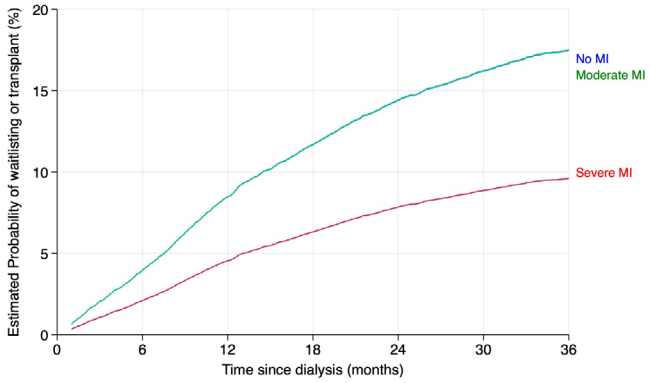

Figure 1: Modelled cumulative incidence of waitlisting or transplantation by mental illness

PP_030 TRANSITION OF CARE IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: STRETEGIES TO IMPROVE AUTONOMY AND TREATMENT ADHERENCE

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Background: The transition from adolescence to adulthood is a crucial phase for adolescent and young adult (AYA) patients with childhood-onset chronic kidney disease (CKD), including kidney transplant recipients. Suboptimal transitions are linked to poor treatment adherence and negative health outcomes. This study aims to assess the autonomy of adolescent kidney transplant recipients in managing their condition, adhering to therapy, and coordinating follow-up care. It also examines the role of education and family support in fostering independence.

Methods: This prospective study included 52 patients aged 16 to 20 years who had undergone kidney transplantation at our center. Informed consent was obtained from both patients and their families. Participants completed a structured questionnaire, developed with a multidisciplinary team. The "Transition Readiness" questionnaire contained 40 items covering five key areas: disease knowledge, use of healthcare services, communication with healthcare providers, lifestyle and activities of daily living (ADLs), and emotional management. The first phase involved administering the questionnaires, followed by data analysis in the second phase to identify areas for improvement.

Results: Preliminary findings indicate that many patients have limited autonomy, particularly in medication adherence, scheduling follow-up appointments, and recognizing health deterioration. Family involvement plays a key role in the transition process, although the level of engagement varies. Many patients also struggle with independent management of ADLs. Further analysis will explore the effectiveness of educational materials and the specific needs of these patients.

Conclusions: This study highlights the importance of promoting autonomy in young kidney transplant recipients during the transition from pediatric to adult care. Preliminary results suggest that education and active family involvement are vital for supporting this process. Further analysis will provide insights into improving education and self-management strategies to optimize long-term health outcomes.

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PP_031 ESTABLISHMENT OF A DELISTING STRATEGY FOR IMILFIDASE CANDIDATES, HIGHLY SENSITISED PATIENTS

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Background: Imlifidase has been recommended by NICE as a desensitisation treatment as a single dose treatment. Its use will facilitate transplantation of highly sensitised renal patients (HSPs), however, an incremental risk approach is recommended to reduce the risk of rejection post transplant.

Methods: A total of 22 HSPs were identified as potential candidates for Imlifidase therapy based on the NICE criteria. All candidates were screened for HLA antibodies using single antigen bead (SAB) testing (Neat and 1:16) and C3d HLA antibody assay. Any antibody that was MFI<5000 MFI by SAB, negative by C3d and where no specific immunising epitope could be identified, were considered for delisting. Flowcytometric crossmatching (FCXM) was carried out on 9/22 patients. Serum samples were incubated for 4 and 6 hours with 6µg/ml of Imlifidase prior to the FCXM. It should be noted that samples were treated with Imlifidase and not the patients themselves.

Results: The HLA antibody delisting strategy resulted in the average calculated reaction frequency (CRF) in this patient group reducing from 100% to 99.20% (range 91.62%-100.00%). This active delisting strategy has resulted in a total of 7/22 patients proceeding to transplant without the use of Imlifidase. On average, HLA antibodies with MFI > 5000 at 1:16 dilution did not reduce sufficiently post *in-vitro* Imlifidase treatment (MFI remained >2000) – Figure 1A. A total of 7/9 patients (P001, P002, P004, P005, P006, P007, P008), who had positive pre-Imlifidase FCXM results became negative following Imlifidase treatment (Figure 1B). In 1/9 patients (P003) the T-cell result remained weak positive, despite reduction of HLA DSA following Imlifidase treatment. In a further 1/9 patients, the FCXM and SAB results remained positive following treatment with Imlifidase. We did not observed a difference between 4 and 6hr incubation.

Conclusions: An active HLA antibody delisting strategy can lead to transplantation without the use of Imlifidase. However, by combining patient's SAB result with C3d antibody testing and dilution of serum to 1:16, it is possible to better stratify the transplant candidates who are more likely to respond to Imlifidase treatment and potentially, those who may not (P009).

MFI @ 1:16	MFI + 6ug/ml @ 4hrs
<=0	-59
0-2000	817
2000-5000	2163
5000-1000	3321
>10000	4978

Figure 1A - MFI @1:16 Dilution predicts Imlifidase MFI reduction

Patient ID	FCXM											
	T-Cell						B-Cell					
	Untreated		6ug/ml-4h		6ug/ml-6h		Untreated		6ug/ml-4h		6ug/ml-6h	
	Result	MCS	Result	MCS	Result	MCS	Result	MCS	Reault	MCS	Result	MCS
001	POS	90	NEG	-4	NEG	-8	POS	87	NEG	-3	NEG	-17
002	NEG	22	NEG	-6	NEG	-6	W. POS	55	NEG	-92	NEG	-96
003	POS	197	W. POS	69	W. POS	74	POS	119	NEG	-12	NEG	-60
004	POS	147	NEG	21	NEG	16	W. POS	62	NEG	-74	NEG	-124
005	POS	108	NEG	-12	NEG	-19	POS	122	NEG	-23	NEG	-40
006	POS	150	NEG	-3	NEG	-1	POS	128	NEG	-54	NEG	-59
007	W. POS	43	NEG	-5	NT	NT	W. POS	68	NEG	7	NT	NT
008	NEG	29	NEG	-4	NT	NT	POS	159	NEG	29	NT	NT
009	POS	170	POS	145	NT	NT	POS	169	POS	143	NT	NT

Figure 1B - FCXM results with (4 and 6hrs) and without Imlifidase in-vitro.

Figure 1 - 1:16 Antibodies predict Imlifidase reduction and flow cytometric crossmatch results

PP_032 HOW DOES MENTAL ILLNESS IMPACT ACCESS TO THE KIDNEY TRANSPLANT WAITING LIST IN AOTEAROA NEW ZEALAND?

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Background: Those with comorbid kidney failure and mental illness face barriers to accessing care, compounded by social determinants of health. Poorer outcomes have been demonstrated for these patients across several clinical measures, however, the impact of mental illness on transplant waitlisting has not been assessed. We aimed to determine the burden of pre-existing mental illness in kidney failure, including associations, and determine its impact on kidney transplant waitlisting.

Methods: We identified New Zealand adults starting dialysis July 2008 - December 2019 from the Australian and New Zealand Dialysis and Transplant Registry, and linked to pharmaceutical claims and mental health service use. Pre-existing mental illness was classified as severe (any inpatient service) or moderate (community/residential services only). Medication included antipsychotics and antidepressants. Predictors of mental illness were determined with logistic regression, while time to waitlisting was modelled with Cox regression adjusted for age, sex, ethnicity, BMI, socioeconomic deprivation, remoteness, kidney disease, dialysis modality, smoking, late referral, and comorbidities.

Results: Among 5643 patients, 655 (11%) had any mental illness, 45% severe, and 108 (16%) medicated. Mental illness was associated with younger age (p<0.001), European ethnicity (p<0.001), and increasing comorbidity burden (p<0.001). Medication was more common among females (aOR 1.64, 95%CI 1.33-2.03, p<0.001), and regional residents (aOR 1.90, 95%CI 1.15-3.14, p=0.01). Compared with no mental illness, those with unmedicated mental illness had lower rates of waitlisting (aHR 0.60, 95%CI 0.46-0.78, p<0.001), but those receiving medications were waitlisted more (aHR 2.32, 95%CI 1.71-3.15, p<0.001).

Conclusions: More than 1 in 10 dialysis patients have mental illness, and are generally younger, European, and more comorbid. Those unmedicated have reduced access to the kidney waitlist.

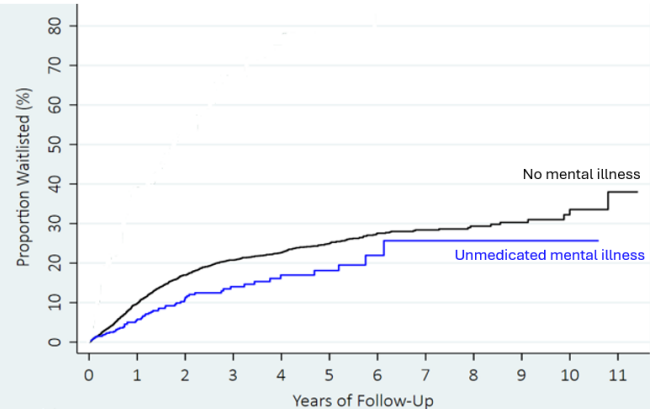

Figure 1: Cumulative incidence of waitlisting for those with unmedicated mental illness versus no mental illness.

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PP_033 EXPLORING TREATMENT BURDENS EXPERIENCED BY PATIENTS AIMING FOR LIVE DONOR KIDNEY TRANSPLANTATION: A QUALITATIVE STUDY

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Background: Pre-emptive live donor kidney transplantation (LDTx) offers the best clinical, quality-of-life and cost-effectiveness outcomes for people with advanced chronic kidney disease (CKD), yet only 6.6% of patients initiate kidney replacement therapy (KRT) with a transplant in the UK. Patients approaching the need to start KRT and under consideration for LDTx are asked to enact complex management plans. Treatment burden has been defined as the effects of healthcare workload, and the capacity a person has to manage that workload, on wellbeing. High treatment burden can reduce engagement with health services. The aim of this study is to explore the treatment burdens associated with pre-emptive LDTx and how they evolve over time.

Methods: Serial semi-structured interviews were conducted with 23 patients under consideration for pre-emptive LDTx over the initial 12 months of KRT. The patient population includes those that have undergone pre-emptive transplantation and those who have experienced some element of LDTx workup but started KRT by a different modality. Data were analysed qualitatively with a framework analysis informed by Normalization Process Theory, Theory of Patient Capacity and Burden of Treatment Theory.

Results: Treatment burden in LDTx includes both the general treatment burden of managing advanced CKD and the imminent transition onto KRT, and treatment burdens distinct to LDTx. Three distinct types of treatment burden pertaining to LDTx were identified: the emotional burden of accepting a living donation, the burden of managing uncertainty, and the organizational burden of navigating the healthcare system and advocating for their own care.

Conclusions: Patients describe significant treatment burdens distinctly associated with LDTx. Better understanding of these burdens could lead to the development of interventions that minimize treatment burden, improve patient experience and improve rates of pre-emptive live donor transplantation.

PP_035 UREMIC BURDEN AS A PREDICTOR OF PREEMPTIVE KIDNEY TRANSPLANTATION OUTCOME - A COHORT ANALYSIS IN FRANCE

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Background: Timing of preemptive kidney transplantation (PKT) and the role of eGFR change in outcome prediction remains a subject of debate. This study aimed to assess potential factors, with special attention to uremic burden, which may be associated with 5-year outcomes. In our retrospective observational cohort study, first PKT adults registered in CRISTAL between 2013-2019 were analyzed to elucidate the role of eGFR and other associating factors with death and graftloss.

Methods: Recipient, donor and transplantation related features were analyzed by using multivariable logistic regression analysis. Conditional inference tree was applied for risk stratification.

Results: 2327 first PKT (52.8 (IQR 43-64)years; 38% females) were included. Mean percentage of PKT over time was 14%. Primary kidney disease (congenital anomalies, glomerulonephritis and other causes versus ADPKD), donor age and number of DR mismatches associated with combined 5-year outcomes (OR 2.64 (CI95% 1.42-4.93); 1.94 (1.1-4.93); 1.76(1.06-2.92); 1.03(1.02-1.05); 1.67(1.1-2.53) p<0.05), whereas donor type was not associated with the outcomes. By supervised decision-tree analysis, more than 30% risk of failure in PKT was attributed to high recipient risk, higher donor age, uremic burden index (UBI)-a novel parameter defined by the product of eGFR change and the logarithmic time on waiting list-and 2 DR mismatches.

Conclusions: eGFR and donor type were not associated with death or graft failure in PKT. UBI can potentially be a novel parameter of uremic burden and contribute to predict 5-year risk of failure. Clinical decision based on objective risk estimations might be crucial to approach the “PKT in due course” concept.

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PP_036 COMPARING PHYSICAL OUTCOMES FOR HEART TRANSPLANT RECIPIENTS, WITH OR WITHOUT MECHANICAL CIRCULATORY SUPPORT

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Background: Rehabilitation with a long term (LT) or short term (ST) mechanical circulatory support device (MCSD) has been shown to be safe. However, a paucity of data exists comparing outcomes post heart transplant (HTx). The United Kingdom (UK) operates a three-tiered urgency wait list system, where super urgent listing is usually only accessible in the presence of ST MCSD. The number of individuals who require this as a bridge to transplant (BTT) is ever growing. Therefore, it is vital to understand how these patients' outcomes may differ due to MCSD pre HTx.

Methods: Data were collected on all HTx recipients between Dec 2022 and Nov 2024, at a single UK cardiothoracic transplantation unit. Comparison was made between candidates that required either LT or ST MCSD pre HTx and those that did not.

Results: There were 98 HTx recipients. Baseline characteristics (median (IQR) unless otherwise stated) per group were Group 1: MCSD pre HTx, males n=36 (85.7%), age 47.5 years (29-53.7); Group 2: No MCSD pre HTx, males n=39 (69.6%), age 49.5 years (41.5-58); the leading diagnoses were dilated cardiomyopathy, n=44 (45%) and ischemic cardiomyopathy, n=18 (18%). Further demographics and outcomes displayed in Table 1. Group 2 progressed quicker with rehabilitation; 37.5% achieving a higher score of walking with assistance of 1 person on the Intensive Care Unit (ICU) Mobility Scale, compared to 28.5% of Group 1 at ICU discharge, despite starting rehab at similar times. However, Group 1 had caught up with their physical ability by the time of hospital discharge, with 85.7% walking independently without an assistive device compared with 90.7% of Group 2. Most patients were discharged home without support (Group 1: 80.9% and Group 2: 87%) and mortality rates similar, at 7.1% and 3.5% respectively.

Conclusions: Despite MCSD patients having more complex ICU stays with longer admissions, increased tracheostomy insertions and being slower to progress with rehabilitation initially; ultimately their overall trajectory is comparable to those without MCSD support pre HTx. This is encouraging in the current climate of increasing rates of heart failure and the need for ST MCSD as a BTT. These results have been observed in a small sample, at one centre, therefore it would be interesting to see if they would be the same in a larger population.

Table 1 – Demographics of patient groups

	MCSD pre HTx (Group 1)	No MCSD pre HTx (Group 2)
Total number of individuals (n)	42	56
Age (years)	47.5 (29-53.7)	49.5 (41.5-58)
Gender (n) (male)	36 (85.7%)	39 (69.6%)
Waiting list status (n)		
Routine	6	8
Urgent	5	48
Super Urgent	31	0
Time intubated (days)	2 (1-6)	1 (1-4)
Number of tracheostomy insertions (n)	10	7
Need for post HTx MCSD support (n)	5	10
Intensive care length of stay post HTx (days)	8 (5-15.5)	5 (3.8-9)
Total length of stay post HTx (days)	39 (26.5-63)	23.5 (18.8-39.3)
Time to first mobilisation (days)	3 (2-6.7)	3 (1.5-5)
Type of MCSD present pre HTx (n)		
Short Term	31	0
Long term	11	0

Data presented as median (IQR) unless otherwise stated

PP_037 MAXIMIZING DECEASED ORGAN DONATION THROUGH TARGETED HOSPITAL DEVELOPMENT STRATEGIES IN THE UAE

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Background: Maximizing donation rates from deceased organ donors (DOD) is critical to improving access to life-saving transplants. Hospital development strategies play a key role in equipping staff with tools and knowledge to streamline DOD processes. In-hospital donor coordinators are pivotal in facilitating organ donation and retrieval while driving process improvements through innovative interventions.

Methods: In 2023, a comprehensive hospital development initiative was launched across selected UAE donor hospitals. Key interventions included:Establishing hospital-based donor committees led by executives to oversee donation processes. Monthly reviews of missed opportunities by hospital mortality committees. Designating ICU directors as organ donation focal points. Allocating ICU nurses as organ donor coordinators. Deploying Organ Procurement Organization (OPO) nurses in key donor hospitals to support activities. Conducting in-hospital seminars and awareness campaigns to educate and engage staff. Developing and disseminating organ donation policies and Standard Operating Procedures (SOPs).

Results: The initiative involved 18 donor hospitals and led to significant improvements in organ donation processes: 38% of donor referrals originated from participating hospitals. Increased brain death diagnoses and family interviews compared to non-participating hospitals. Reduced time between donor referral and family approach, from 10 days to 3 days. A rise in the national donation rate from 5.5 donors per million population (DPMP) in 2022 to 11.6 DPMP in 2024.

Conclusions: Organ donation requires a coordinated, multidisciplinary approach to address its complexities. The UAE's success demonstrates the effectiveness of tailored hospital development strategies. Key drivers included leadership within hospitals, improved donor identification, the role of donor coordinators, and stronger collaboration with OPOs. These interventions provide a robust model for optimizing DOD outcomes and meeting the growing demand for transplantation.

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PP_038 IMPACT OF IN VITRO IMILFIDASE ON FLOW CYTOMETRIC CROSSMATCH TESTING IN HIGHLY SENSITISED RENAL PATIENTS

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Background: Imlifidase cleaves the heavy chain of all human IgG sub-classes, creating a window of opportunity to find an acceptable matched kidney for highly sensitised patients (HSPs). Imlifidase also cleaves Rabbit IgG, therefore, caution should be exercised when selecting HLA detection antibodies for Imlifidase treated patients to avoid false negative results. To ensure our flow cytometric crossmatching (FCXM) fluorochromes were suitable for use, we simulated the *in-vivo* scenario in the laboratory.

Methods: First, 15µg/ml of Imlifidase (Hansa Biopharma, SE) was incubated for 2hrs with Rabbit-IgG FITC and Mouse-IgG CD3/19 (DAKO,DE) reagents. Post incubation reagents were then used to perform FCXM on negative, weak positive and strong positive controls using our standard FCXM protocol. Next, samples from nine HSPs were tested. Patient samples were incubated with 6µg/ml of Imlifidase (maximum serum concentration after one therapeutic dose administration of 0.25 mg/kg) for 4 and 6hrs. Post incubation samples were then tested by FCXM and Luminex Single Antigen Bead (SAB) (Werfen, ES) using our standard protocols. It should be noted that samples were treated with Imlifidase and not the patients themselves.

Results: The results of our controls only tests showed that the FCXM monoclonal antibody detection reagents in use in our protocol were not impacted following incubation with 15µg/ml Imlifidase (supratheraputic dose) for 2hrs. Both weak and strong positive controls remained positive with very little reduction in MCS values. In the patient samples tests, 7/9 FCXM sera (P001, P002, P004, P005, P006, P007, P008) became negative at 4 and 6hrs post Imlifidase treatment in both FCXM and SAB tests. One patient (P003), remained FCXM T cell weak positive, B cell negative, despite reduction of HLA DSA as detected by SAB. One patient (P009) saw no reduction in HLA antibodies as detected by SAB and remained FCXM positive (further testing is being carried out to explore the reasons).

Conclusions: *In-vitro* incubation of Imlifidase with serum from HSP did not affect the binding of FCXM detection antibodies, indicating that current flow crossmatch protocol is suitable for Imlifidase treated patient sera without false negative results.

	FCXM											
	T-Cell						B-Cell					
Control	Untreated		DAKO FITC-15ug/ml - 2hrs		DAKO CD3/CD19-15ug/ml - 2hrs		Untreated		DAKO FITC-15ug/ml - 2hrs		DAKO CD3/CD19-15ug/ml - 2hrs	
	Result	MCS	Result	MCS	Result	MCS	Result	MCS	Reault	MCS	Result	MCS
Negative	NEG	0	NEG	-2	NEG	-7	NEG	0	NEG	-85	NEG	-100
Strong Pos	POS	555	POS	478	POS	558	POS	452	POS	391	POS	462
Weak Pos	POS	165	POS	116	POS	151	POS	114	POS	71	POS	102

	FCXM											
	T-Cell						B-Cell					
Patient ID	Untreated		6ug/ml-4h		6ug/ml-6h		Untreated		6ug/ml-4h		6ug/ml-6h	
	Result	MCS	Result	MCS	Result	MCS	Result	MCS	Reault	MCS	Result	MCS
001	POS	90	NEG	-4	NEG	-8	POS	87	NEG	-3	NEG	-17
002	NEG	22	NEG	-6	NEG	-6	W. POS	55	NEG	-92	NEG	-96
003	POS	197	W. POS	69	W. POS	74	POS	119	NEG	-12	NEG	-60
004	POS	147	NEG	21	NEG	16	W. POS	62	NEG	-74	NEG	-124
005	POS	108	NEG	-12	NEG	-19	POS	122	NEG	-23	NEG	-40
006	POS	150	NEG	-3	NEG	-1	POS	128	NEG	-54	NEG	-59
007	W. POS	43	NEG	-5	NT	NT	W. POS	68	NEG	7	NT	NT
008	NEG	29	NEG	-4	NT	NT	POS	159	NEG	29	NT	NT
009	POS	170	POS	145	NT	NT	POS	169	POS	143	NT	NT

	Luminex Single Antigen Bead HLA Antibody Testing					
	DSA Cum-LSA		DSA Cum-LSA		DSA Cum-LSA	
Patient ID	Untreated		6ug/ml-4h		6ug/ml-6h	
	CI	CII	CI	CII	CI	CII
001	14700	0	576	0	627	0
002	4509	11819	213	492	80	161
003	23379	0	883		823	0
004	20577	658	6541	-77	2071	26
005	11945	6856	-1	48	218	142
006	7581	34070	211	1456	664	2453
007	6759	32510	1100	2580	NT	NT
008	3598	36522	-242	3081	NT	NT
009	46941	16094	33200	11299	NT	NT

Figure 1 - FCXM and Luminex SAB Testing following in vitro treatment with Imlifidase.

PP_039 IS THERE INEQUITY OF ACCESS AND EXPERIENCE FOR HEART AND LUNG TRANSPLANT PATIENTS IN THE UK?

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Background: To examine potential inequity of access and experience for patients who may benefit from a heart or lung transplant – research carried out as part of work to align UK heart and lung transplant rates with international best practice

Methods: Government, healthcare and heart and lung transplant patient and family representatives worked collaboratively to co-create an online survey using the Delphi method, seeking views about experience along the transplant care pathway. Quantitative analysis of the results was undertaken where responses were expressed in number form, Qualitative analysis was used for free text with categorisation of comments made.

Results: The study highlights several key findings about the experiences of heart and lung transplant patients across different demographic cohorts: • General Satisfaction: All cohorts expressed general satisfaction with the referral process but emphasized the need for improved communication, a more holistic approach to care, and better psycho-social support for both patients and their families.• Fertility Advice: 71% of male patients felt that fertility advice was unnecessary, compared to 56% of females. Among those who felt fertility advice was needed, 30% of males rated it as excellent, compared to 22% of females. • Concerns About Communication: Black and Asian patients reported more concerns regarding poor communication and a lack of understanding about care needs and availability. • Social Care Satisfaction: 40% of white patients, 38% of Asian patients, and 22% of black patients rated social care as excellent. However, 53% of black patients and 50% of mixed patients who required or utilized social care felt it was very poor. • Comfort Raising Concerns: 78% of males, 65% of females, 74% of white patients, and 57% of black patients felt comfortable raising concerns about their care. • Variability of Care Access: There was significant variability in access to routine care and innovative treatments across different transplant centres.

Conclusions: The study finds disparities in experiences between patient groups, with particular differences based on gender, race, and ethnicity. Further investigation is needed to determine the root causes of these disparities.

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PP_040 IMPACT OF AGE MISMATCH ON POST LIVER TRANSPLANT OUTCOME

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Background: It is imperative to consider utility in the allocation of livers to maximize graft survival. As the number of older recipients have increased, younger candidates could be disadvantaged from receiving the highest quality organs with our allocation system relying on a benefit score. The aim of this study is to analyse the impact of the age mismatch on liver transplantation outcome, and the potential impact of the introduction of National Liver Offering Scheme (NLOS) on 20 March 2018.

Methods: Data on first adult elective liver transplants performed in the UK between 2000 and 2022 were extracted from the UK Transplant Registry. The impact of age and the difference between donor and recipient age on patient, graft and transplant survival was analysed.

Results: 12270 liver transplants were reviewed. 21% of transplants involved donors and recipients in the same 10 year age group. 41% were age matched within +/- 10 years. Donor-recipient age differences were consistent pre and post NLOS. 5 year patient, graft and transplant survival was significantly lower for older donors and recipients. Donor and recipient age difference impacted graft and patient survival differently. An age difference of >20 years had a risk-adjusted 5-year graft failure HR of 1.32 (95% CI 1.09, 1.58) relative to an age difference of 0-9 years, the equivalent risk-adjusted 5-year mortality survival HR was 0.84 (0.79, 1.02). This equates to graft survival estimates being 4-5% lower at 5 and 10 years when the donor is at least 20 years older than the recipient.

Conclusions: Although the donor- recipient age differences were consistent pre and post NLOS, 5 year graft survival was statistically significantly lower when the donor was as least 20 years older than the recipient indicating that an element of age matching should occur when livers are offered.

PP_042 HEPATOCELLULAR CARCINOMA: DISPARITIES IN LIVER TRANSPLANT STRATEGIES AND OUTCOMES ACROSS REGIONS

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Background: Liver transplantation (LT) access and outcomes differ worldwide due to factors like donor availability, socioeconomic status, and organ allocation policies. This study evaluates LT strategies for HCC, examining disparities and outcomes in two regions with different healthcare systems and donor availability.

Methods: This retrospective study recruited two HCC cohorts who underwent LT between 2012 and 2022 at two different LT centers; Ain shams university hospital, Egypt (LDLT, group 1, n=94) and Paul Brousse hospital, France (DDLT, group 2, n=324).

Results: Both cohorts had comparable mean ages (54.3 ± 6.5 vs. 60.5 ± 8.4 years, p=0.078) but significantly different underlying liver diseases (p=0.032). Group 1 primarily had HCV cirrhosis (89.4% vs 24.4%), while group 2 had alcohol-associated cirrhosis (28.7% vs 0%). Group 1 experienced significantly shorter wait times for LT (4.7 ± 4.3 vs. 9.8 ± 16.0 months, p=0.021) and less downstaging/bridging therapy (64.9% vs. 84.9%, p=0.031). MELD scores at LT were similar (13.9 ± 4.5 vs. 14.3 ± 7.9, p=0.098) while the majority of patients in group 1 had Child-Pugh score B and C. Group 2 had a significantly higher proportion of tumors within Milan criteria (78.7% vs. 56.7%, p=0.032). The follow up duration was significantly shorter among group 1 (39.7 ± 37.7 vs 61.5 ± 39.3 months, p=0.041). The 1,3,5 survival rates among both groups were comparable (76.8%, 68.7% & 61.7% vs 90.7%, 79.5% & 69.4%, p= 0.11). HCC recurrence rate was higher among group 2 (19.4% vs 5.3%, p= 0.001). Group 1 had significantly shorter time to HCC recurrence compared to group 2 (10.6 ± 9.2 vs 19.2 ± 16.6 months, p= 0.009). Site of HCC recurrence was extrahepatic among both groups (80% vs 58.7%, p= 0.043). The 1,3,5 RFS rates were comparable (LDLT group: 75.6%, 66.2%, 60.9% vs DDLT group; 85.2%,72.6%, 67.8%, p = 0.21).

Conclusions: This study highlights significant disparities in HCC patients' characteristics and transplant strategies based on regional healthcare contexts, donor availability, recipient compliance and tumor biology. LDLT had shorter waiting times but shorter time to recurrence compared to DDLT. DDLT patients received more downstaging/bridging therapies leading to longer waiting times. Overall 5-years survival and RFS rates were comparable between LDLT and DDLT.

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PP_043 LITE DELISTING TO FACILITATE KIDNEY TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Background: Delisting less deleterious antigens from a recipient's unacceptable antigen profile offers an opportunity for transplantation for highly sensitised patients. This strategy is now being widely implemented. The aim of this study was to explore how adoption of this strategy has impacted waiting times and outcomes.

Methods: We analysed data for highly sensitised kidney transplant recipients from a prospectively maintained database between 1st January 2022 – 31st December 2024. This included all referrals approved for delisting within our antibody incompatible transplant (AIT) programme. Only recipients receiving deceased donor kidneys were included. The primary outcome of interest was impact of delisting on waiting time, graft survival and acute rejection. Supplementary data on donor-specific antibody (DSA) median fluorescence index (MFI) was retrieved.

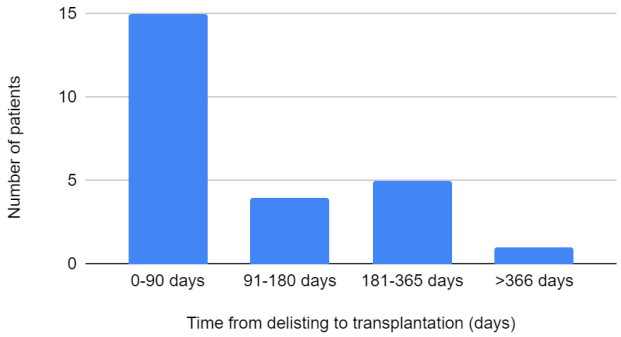
Results: A total of 25 patients were included. Patient characteristics are described in Table 1. All recipients were immunologically high risk, crossmatch negative and received Alemtuzumab induction. None underwent any desensitisation therapy. Mean calculated reaction frequency (CRF) pre-delisting was 99.5 ± 1.5%. Mean CRF post-delisting was 86.3% with a mean change of 13.2 ± 20.9%. Time spent on the waiting list pre-delisting was available for 23 recipients, with a mean of 3474 days. After delisting, the time to transplantation is shown in Figure 1. Biopsy-proven rejection occurred in 2 (11.1%) recipients (1 humoral, 1 cellular), both within 3 months of transplantation. One-year graft survival was 90% (using data for 10 patients who had reached this time-point at analysis).

Conclusions: Delisting strategies can enable transplantation for highly sensitised patients despite pre-formed DSA's. Heterogenous approaches to delisting and risk stratification of patients across the UK may have a significant impact on organ allocation. Long term data are needed with a view to creating a national delisting protocol to ensure equitable and timely access to transplantation opportunities.

Characteristics	All patients n=25
Recipient age	45 ± 11.9
Sex (female)	14 (56%)
Graft number	1 (n=7), 2 (n=14), 3 (n=3), 4 (n=0), 5 (n=1)
Graft CIT (hours)	15.3 ± 5.2
Donor age	48.5 ± 15.7
DSA MFI <5000	10
DSA MFI 5000-10000	9
DSA MFI >10000	6

Table 1: Patient Characteristics

Figure 1:Time from delisting to transplantation (days)



PP_044 ARES, ARTIFICIAL INTELLIGENCE FOR BETTER TRANSPLANT, IS BORN FROM DATA INTEGRATION ARCHITECTURE

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Background: Artificial intelligence is already a reality and offers many possibilities in the organ donation and transplantation. But it requires refined, and quality data that comes from multiple non-interconnected information systems. Our goal is to design an architecture for integrating and standardizing data from different information sources to be able to test and validate artificial intelligence models.

Methods: Development of an integrative data architecture in a federated system. The information systems: SAP Hana (hospital data), Nefrolink (nephrology, organ donation and transplant data), and Ariadna (immunology and histocompatibility data). Development phases: Integrate the data from the backend with the model, defining the architecture for real-time inference; Validate the viability of federated training that allows relaxing the restrictions on data sharing; Define the architecture with scalable, open source and economically sustainable tools and environments; and Define a standardized data model to allow shared retraining of the artificial intelligence algorithm and a reliable inference model. The Ethics Committee approved the study.

Results: Data from 5,600 transplant patients, identifying interoperability with data sources and clinical repositories and integrating real-time data from different sources in shared-use repositories, based on the APIfication of information repositories. From SAP Hana through the shared-use source DataMesh. From Ariadna, the API has been created, and a Tomcat has been obtained where the application has been deployed (Rest API). From Nefrolink, data has been obtained in table format for its integration into the designed architecture. An artificial intelligence algorithm for predicting graft survival has been developed with data at the time of transplantation, the algorithm code has been introduced into the architecture and, through a GPU, the algorithm has been trained by automatically collecting data from the system and with improvements in survival prediction.

Conclusions: The design of an architecture that integrates several information systems facilitates the training of artificial intelligence algorithms to validate the prediction model that provides us with information that predicts transplant survival at the time of donation.

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PP_045 LIVER TRANSPLANTATION FOR METALD IN ITALY: AN ITALIAN LIVER TRANSPLANT REGISTRY STUDY

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Background: An international consensus has recently introduced a new definition of metabolic and alcohol-associated liver disease (MetALD). We sought to analyse the epidemiological trends, clinical characteristics, and intention-to-treat (ITT) survival of patients with MetALD waiting for liver transplantation (LT) in Italy.

Methods: This is an ancillary analysis of a recent Italian Liver Transplant Registry study focused on metabolic-associated steatotic liver disease (MASLD). Between January 2012 and December 2022, adult patients listed for primary LT attributable to MetALD, MASLD, and non-metabolic ALD (nmALD) were included. The study compared the annual trends of waiting list inscriptions, clinical patient characteristics, and intention-to-treat survival outcomes of MetALD, MASLD, and nmALD patients.

Results: A sample of 13,142 listed patients, including 1,550 with MetALD, 1941 with MASLD, and 1,044 with nmALD, was considered. From 2012 to 2022, the prevalence of MetALD as an indication for LT significantly increased, from 7.9% to 15.2% (from 10.8% to 24.0% in non-HCC patients and from 3.1% to 8.9% in HCC patients). Projections suggest that during these years, MetALD has become the second most common indication for LT after MASLD in Italy. Compared to MASLD patients, MetALD were younger (58 vs 61 years, p<0.01), more frequently males (20.4% vs 12.6%, p<0,01), with higher MELD-sodium values (20 vs 15, p<0,01), and less frequently had associated HCC (22.6% vs 61.5%, p<0.01). While ITT survival was similar in non-HCC patients, it was significantly better in MetALD and MASLD than nmALD HCC patients after adjustment for recipient age, gender, and liver function.

Conclusions: MetALD is now the second indication for LT in Italy overall and the first among non-HCC patients. MetALD HCC patients have better ITT survival outcomes than nmALD.

PP_046 LIVER TRANSPLANTATION AS SALVAGE PROCEDURE IN PATIENTS WITH POSTHEPATECTOMY LIVER FAILURE

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Background: Some advantages have been reported for liver transplantation (LTx) in treatment of post-hepatectomy liver failure (PHLF) due to liver resection, liver trauma and iatrogenic injuries; although, the evidence in regards to systematically assessed these patients is scarce.

Methods: PubMed, Scopus Web of Science databases were searched from their inception until end of March 2024 for studies assessing outcomes of LTx in patients with PHLF, liver trauma, and iatrogenic injuries. A single-arm meta-analysis of studies reporting short- and long-term outcomes after LTx for these indications was carried out.

Results: 63 articles (452 patients) were included in the final analysis, which 13 articles assessed the outcome of LTx after PHLF, 26 articles assessed outcomes of LTx in liver trauma, and 25 articles evaluated outcomes of LTx in iatrogenic liver injuries. Re-transplantation rates after LTx for PHLF, liver trauma, and iatrogenic injury were reported as 0.3%, 2.4%, and 3.1%, respectively. Short-term (< 90 days) mortality rates following LTx for PHLF, liver trauma, and iatrogenic injury were 18.8%, 26.4%, and 24.9%, respectively. Additionally, the 1-year survival rates for patients undergoing LTx for PHLF, liver trauma, and iatrogenic injuries were 66.3%, 60.1%, and 69.2%, respectively. Five-year overall survival rates following LTx for patients with PHLF, liver trauma, and iatrogenic injuries were 29.7%, 44.3%, and 47.1%, respectively.

Conclusions: In treatment of PHLF after liver resection, iatrogenic injuries and liver trauma, LTx can be the salvage option to prevent life-threatening events. Optimal selection of patients should be considered for better outcomes.

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PP_048 IMPACT OF SOCIO-ECONOMIC DEPRIVATION ON DONOR OUTCOMES AFTER LIVE-KIDNEY DONATION

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Background: Socioeconomic Deprivation Status (SDS) is associated with worse access to transplantation, poorer graft outcomes and increased mortality in kidney recipients. The impact of socioeconomic status on Living Kidney Donor (LKD) selection and outcomes has not been reported in the UK. We examined the association between SDS, donor demographics, and post-operative outcomes in LKD transplant.

Methods: Demographics, patient co-morbidities, biochemistry, complications, length of stay and re-admission data were collected for 125 consecutive LKD patients at a UK regional transplant centre between 2021-2024. English Index of Multiple Deprivation (EIMD) rank (which combines several indicators of deprivation to stratify the population by relative SDS) was calculated (range 1 – 10, lower figures indicate higher levels of deprivation). Median EIMD score was used as a cut-off to create two groups: 'Most Deprived' (MD) and 'Least Deprived' (LD)). Categorical variables were analysed with Chi-Squared test and continuous variables by two-sample t-test (5% significance).

Results: Median follow up was 19 months (range 1 – 42 months). Median EIMD was 7 (IQR 4.75). There was no significant difference in age at donation between MD and LD groups (median age 49 (MD) vs 51 (LD), p = 0.127). Table 1 demonstrates the EIMD score for each component domain, and association between patient demographic/clinical factors and SDS. There was no LKD mortality in either group. LD patients had a significantly shorter length of stay (3.6 days vs 4.4 days, p = 0.0002).

Conclusions: Demographics and LKD nephrectomy outcomes in donors are not different in patients of varying SDS. Patients from less deprived areas are likely to have a shorter length of hospital stay. Analysis of EIMD score and association of socioeconomic status in proceeding versus non-proceeding donors (i.e. LKD selection) will be available at the time of presentation. Further work is required using national data to map deprivation factors that may affect likelihood of donation or donor outcomes, working towards reducing social inequalities in transplantation.

EIMD domain	Weighting (%)	Most Deprived (median decile)	Least Deprived (median decile)	
Overall EIMD score	-	4	9	
Income	22.5	4	9	
Employment	22.5	4	8	
Education	13.5	3	8	
Health	13.5	5	9	
Crime	9.3	4	8	
Housing	9.3	5	5.5	
Living Environment	9.3	5	8	
Demographic and Clinical factors		**Most Deprived (n)**	**Least Deprived (n)**	**Chi² (P value)**
Gender	Male	26	30	0.100 (0.751)
	Female	34	35	
Co-morbidity	Cardiovascular	4	8	1.14 (0.285)
	Respiratory	7	3	2.11 (0.147)
	GI	6	0	6.82 (0.009)
	Neurological	0	1	0.935 (0.335)
Re-admission		9	7	0.500 (0.479)
		Most Deprived	**Least Deprived**	**T-test P Value**
Length of stay (days)		4.4	3.6	P = 0.0002
Baseline GFR (ml/min/1.73 m²)		95	92	P = 0.144
Most recent GFR (ml/min/1.73 m²)		62	60	P = 0.297
Five-Year Kidney Failure Risk (%)		0.27	1.72	P = 0.360

Table 1

PP_049 ACTIVE DRINKERS WITHOUT ALCOHOL-RELATED HEPATITIS NEEDING URGENT LIVER TRANSPLANTATION: A PROOF OF CONCEPT STUDY

José Ursic Bedoya[1], **Alberto Ferrarese**[2], **Giovanni Perricone**[3], **Adelina Horhat**[4], **Line Ntandja Wandji**[5], **Christophe Duvoux**[6], **Giacomo Germani**[7], **Georges-Philippe Pageaux**[8], **Alexandre Louvet**[9], **Marina Berenguer**[10], **Luca Saverio Belli**[11]

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Background: Historically, patients with alcohol-related liver disease (ALD) required 6-month abstinence before being listed for liver transplantation (LT). A landmark study in 2011 demonstrated excellent outcomes early LT (eLT) for selected patients suffering from severe alcoholic hepatitis (sAH) not responding to steroids. However, active drinkers may develop a rapidly progressive impairment of liver function due to factors not directly related to alcohol abuse, such as bacterial infection or bleeding, usually in a context of alcohol-related cirrhosis without sAH. Should eLT be considered in this setting, despite active alcohol consumption?

Methods: We performed a retrospective multicentre cohort study across 6 European centres (3 in France, 2 in Italy, 1 in Spain). All adult patients admitted for decompensated ALD, and active alcohol consumption at index event, who were evaluated for LT between January 2018 and June 2024 were identified. Patients with histology consistent with sAH, or those being transplanted beyond 1 month after index event were excluded. Each potential case was centrally reviewed by a committee of four experts, and biopsy/explant histology was reviewed by local Pathologists.

Results: We identified 28 potential cases. 5 patients died on waiting-list without histology, 1 had no cirrhosis at explant histology and 8 had a too long time-frame between the index event and LT. 14 patients (males 71.4%, mean age 54±10 years, median MELD score at index event of 29). Bacterial infection was the commonest precipitating event (78.6%). The addiction profile was mostly favourable, with good social support and absence of prior failed rehabilitation. 3 patients died on the waiting list, whereas 11 (78%) patients underwent eLT (median time between index event and eLT 19 days, 78% with acute-on-chronic liver failure at time of eLT with median MELD of 35). Sepsis and pancreatitis were the cause of death in the two patients who died after eLT. Severe alcohol relapse occurred only in one patient (figure).

Conclusions: eLT for selected, sick cirrhotic patients, actively drinking at time of hospitalization, but without sAH was associated with optimal post-operative outcomes. Further prospective studies are needed to confirm these data.

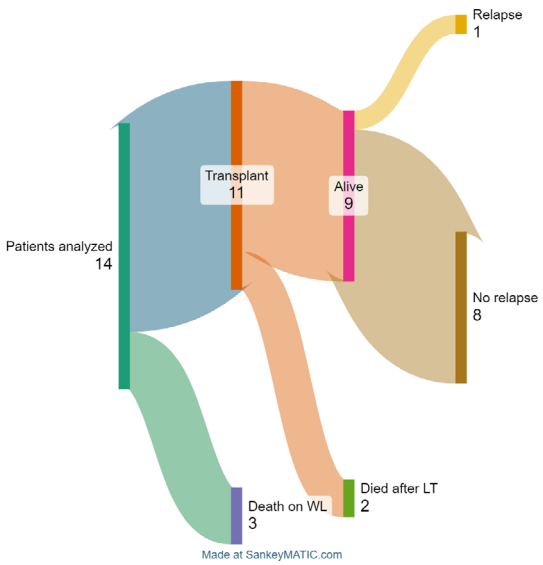

Figure: Sankey diagram of patients outcomes

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Current challenges in transplantation procedures

PP_050 SPEEDING UP TISSUE PROCESSING PROTOCOLS FOR TRANSPLANT PATHOLOGY

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Background: The histological evaluation of organs for transplant requires short response times, high accuracy for pre-implantation and incidental suspect neoplastic findings, preserving antigenicity for further predictive analysis. Routine processing protocols for formalin-fixed paraffin-embedded (FFPE) specimens in pathology laboratories are unsatisfactory in terms of time, and frozen sections can be prone to artefacts that can impair diagnostic reliability, leading to improper organ allocation. The introduction of microwaving-based fast processing protocols promises to reduce the turnaround times while remaining cost effective and ensuring diagnostic quality when compared to standard processing.

Methods: Here we test the time and quality performances of fast/ultrafast tissue processing protocols vs the “standard” routine FFPE approach on 35 ex vivo samples (biopsies -CNB- and surgical -SS-) from different organs (breast, lung, liver and kidney) as evaluated by three different Italian pathologists.

Results: Fast and ultrafast protocols were significantly faster for both CNB (55 and 44 min vs 480, -89% and -91%, respectively) and SS (447 and 402 min vs 960, -53% and -58%, respectively), as compared to the standard processing protocol. In terms of quality and time for the diagnosis, no differences were noted with the standard for both fast and ultrafast samples (p=0.828 and 0.275 for quality and p=0.737 and 0.905 for time, respectively). Good to optimal agreement in the diagnosis of lung and breast cancer was recorded (k = 0.84 and 0.76 for lung and k = 0.9 and 1 with fast and ultrafast methods, respectively). The Karpinski (≤3 and >3) and mHAI (<3 and ≥3) scores showed no statistically significant differences among processing methods (p=0.8 and p=0.6, respectively). Nuclear and membrane immunohistochemical stains (Figure) showed good to optimal agreement with the standard (e.g. k = 0.84 and 0.64 for ER in breast) and comparable results for HER2 and PD-L1 between the two rapid methods (k = 0.59 and k = 0.81).

Conclusions: Optimised fast/ultrafast processing methods are safe, allowing a reliable and rapid assessment by pathologists for both pre-implantation procurement biopsies and incidental nodules characterization, allowing antigenicity preservation for subsequent utilisation of these specimens.

PP_052 A RECYCLABLE SOLUTION TO ORGAN SHORTAGE IN LIVER TRANSPLANTATION: DOMINO LIVER TRANSPLANTATION

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Background: Domino liver transplantation (DLT) is the use of an explanted liver from patients with a limited number of liver diseases, as a graft for other suitable patients. DLT can be a important option for patients with low chances on the waiting list and who do not have a suitable donor to live a healthy life. In this study, we presented three DLT and their results.

Methods: Case-1: She was a 12-year-old with primary hyperoxaluria type-1 (PH1). We performed left lobe LT from her mother and we transplanted the liver, which was obtained from this girl with PH-1, to 55-year-old patient with hepatocellular carcinoma (HCC). Case-2: The patient was a 5-year-old boy and was diagnosed with propionic acidemia (PA). We performed left lobe LT from his mother. We transplanted the liver we obtained from the patient with PA to our 6-year-old girl, who ınderwent living donor LT for metabolic liver disease 2 years ago but is currently in the process of chronic rejection. Case-3: A 2-year-old patient with mapple syrup urine disease (MSUD) underwent left lateral lobe LT from his father. We transplanted the liver graft obtained from the patient to a 6-year-old boy with familial hypercholesterolemia.

Results: The patient with PH1 underwent kidney transplantation (KT) 1 month after LT. The total bilirubin (T.bil) level of the patient diagnosed with HCC decreased to 0.8 mg/dl in the first month after LT. T.bil level of the patient diagnosed with metabolic liver disease after LT decreased to 0.8 mg/dl in the 4th postoperative month. The total cholesterol value of the patient with familial hypercholesterolemia decreased to 263 mg/dl on POD 8. All patients were discharged without any problem.

Conclusions: DLT, if performed carefully by selecting the right patients with the right indications, can be an important graft source for patients who do not have a suitable donor and are on the waiting list for liver transplantation.

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Current challenges in transplantation procedures

PP_055 INCISIONAL HERNIA AFTER LIVER TRANSPLANTATION: INCIDENCE AND MANAGEMENT IN A HIGH-VOLUME TRANSPLANT CENTRE

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Background: Incisional hernia is an undesirable complication following liver transplantation (LT) that can negatively impact quality of life. This study aims to evaluate the incidence and management of incisional hernias in LT patients at a high-volume transplant centre.

Methods: The retrospective study analysed data from LTs performed at King's College Hospital between 2014 and 2023, with a focus on the management of incisional hernias.

Results: Over 10 years, 1949 adult liver transplants (LTs) were performed, with 1384 recipients included. Of these, 126 had regrafts. The Mercedes-Benz incision was most common (n=1143; 82.6%), followed by reverse L (n=153; 11.0%). Skin-only closure was used in 58 recipients (4.2%), 65.5% of whom underwent delayed muscle closure. During the study, 189 recipients (13.6%) developed incisional hernias, 31.2% (59) of which required surgery; 10% recurred after repair. Biological meshes were most used (50.8%), followed by non-composite meshes (35.6%), primary repair (11.9%), and composite meshes (1.7%). Patients with hernias had higher weight (82.2 vs. 78.4 kg; p<0.007), BMI (27.8 vs. 26.9 kg/m²; p=0.034), more regrafts (19.6% vs. 7.5%; p<0.001), renal support (10.0% vs. 6.4%; p=0.005), wound infections (11.6% vs. 5.0%; p<0.001), and longer hospital stays (23 vs. 19 days; p<0.001). Graft and patient survival were comparable between groups.

Conclusions: Incisional hernias affect 13.6% of liver transplant recipients, likely an underestimation, and are significantly associated with higher BMI, regrafts, and postoperative complications such as wound infections and prolonged hospital stays. Timely management, including mesh repair, leads to optimal outcomes without compromising patient or graft survival.

PP_056 SMART PACKAGING FOR STATIC COLD PRESERVATION AND TRANSPORT OF ORGANS AND TISSUES FOR TRANSPLANTATION

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Background: Structural abnormalities of the lower urinary tract present significant challenges in renal transplantation. due to their impact on perioperative and postoperative outcomes. This case report highlights only reported renal transplantation in a patient complex bulbar urethral stricture treated with perineal urethrostomy, underscoring the feasibility of transplantation in patients with such anatomical challenges.

Case Presentation: A 72-year-old male with end-stage renal disease (ESRD) on haemodialysis, and urine output of 200ml, presented for a deceased donor renal transplantation. His medical history included coronary artery bypass grafting (CABG) following myocardial infarction and aortic valve replacement on anticoagulation. Patient previously denied lower urinary tract symptoms (LUTS). Intraoperatively, difficulties with urethral catheterization prompted an urological consultation and flexible urethroscopy confirming a dense bulbar urethral stricture. A contracted bladder made suprapubic catheter (SPC) placement unfeasible and led to cancellation of procedure. Multidisciplinary discussions identified perineal urethrostomy as the optimal intervention, avoiding the high surgical risks of urethroplasty due to the patient's elevated cardiac risk. A year following perineal urethrostomy, the patient underwent renal transplantation. Post operative course was uneventful with primary graft function but with persistent and significant LUTS, attributed to overactive bladder syndrome. Symptoms improved markedly with antimuscarinic therapy. At six months post-transplantation, the patient exhibited stable graft function with good voiding control via the perineal urethrostomy and only mild residual LUTS and negative urine cultures.

Conclusions: Renal transplantation in patients with urinary diversion or structural lower urinary tract abnormalities poses complex challenges but is achievable with meticulous preoperative planning and multidisciplinary collaboration. This report represents the first documented instance of successful renal transplantation following perineal urethrostomy. Comprehensive postoperative monitoring and prompt management of complications, including infections and LUTS, are critical to optimizing patient outcomes.

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Current challenges in transplantation procedures

PP_057 SPK-TX IN MELAS: PIONEERING A PROMISING TREATMENT PATH AGAINST MITOCHONDRIAL DYSFUNCTION DISORDER

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Background: Mitochondrial encephalomyopathy with lactic acidosis, and stroke-like episodes (MELAS) is a rare mitochondrial DNA disorder that, in severe cases, can result in insulin-dependent diabetes and end-stage renal disease (ESRD). While organ transplantation is a potential treatment, documented cases remain scarce.

Methods: A 40-year-old man with dialysis-dependent ESRD and insulin-dependent diabetes secondary to MELAS underwent simultaneous pancreas-kidney (SPK) transplantation. The perioperative and postoperative periods were uncomplicated, requiring minimal deviations from standard protocols.

Results: During the 4-year follow-up, the patient maintained normal renal function, complete independence from dialysis, and no need for insulin therapy. These outcomes demonstrate both short- and long-term success, highlighting the efficacy of the SPK transplantation in addressing both renal and metabolic complications associated with MELAS.

Conclusions: SPK transplantation offers a promising treatment option for MELAS patients with ESRD and insulin-dependent diabetes. This case demonstrates that SPK can be performed safely, achieving excellent renal and metabolic outcomes over a 4-year period. To our knowledge, no previous publications have reported successful simultaneous pancreas-kidney (SPK) transplantation in MELAS patients. This was also the first such case at our transplant center, underscoring the evolving concept of addressing genetic mitochondrial disorders with organ transplantation as a viable and innovative therapeutic approach.

PP_058 HEMODYNAMIC PARAMETERS AND BOLUS FLUID REQUIREMENT IN LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Effective intraoperative fluid management during kidney transplantation (KT) is critical to prevent complications such as delayed graft function or acute renal failure. Fluid management during KT has done through various parameters. The aim of present study was to examine the predictive performance of each parameter on bolus fluid infusion during KT.

Methods: This prospective observational study included 60 adult recipients of living donor KT at Samsung Medical Center, Korea, from January 2023 to May 2024. Balanced crystalloid solution 2ml/kg was infused during anesthetic induction followed by 1ml/kg/hr continuous infusion. Target mean blood pressure were 60mmHg before reperfusion and 90mmHg after reperfusion. Bolus fluid (3ml/kg) was infused after optimization of anesthetic depth, contractility, and afterload. Recipients were divided into two groups: those requiring bolus fluid infusion (n=7) and those who did not (n=53). Central venous pressure (CVP), pulse pressure variation (PPV), corrected flow time (FTc), and pleth variability index (PVi) were recorded at 6 time points. Receiver operating characteristic (ROC) analysis was conducted to evaluate the ability of hemodynamic parameters immediately after anesthetic induction to predict bolus fluid requirements.

Results: CVP showed the highest discriminative ability for predicting the need for bolus fluid infusion (AUC = 0.830, 95% CI: 0.682–0.978, p = 0.005), followed by PPV with moderate ability (AUC = 0.756, 95% CI: 0.523–0.989, p = 0.029). PVi was not significantly associated with bolus fluid requirements (AUC = 0.675, 95% CI: 0.475–0.875, p = 0.134), and FTc showed lowest AUC values (AUC = 0.577, 95% CI: 0.346–0.808, p = 0.512).

Conclusions: CVP and PPV immediately after anesthetic induction are useful indicators for bolus fluid infusion in KT. Further studies are needed to validate the clinical significance of this results.

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Current challenges in transplantation procedures

PP_059 PERI-OPERATIVE ALBUMIN ADMINISTRATION IN ADULT LIVER TRANSPLANT RECIPIENT: A SYSTEMATIC REVIEW

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Background: Hypoalbuminemia is an independent risk factor for mortality in end-stage liver disease (ESLD) patients and can persist even after liver transplantation (LT) as a biomarker of post-operative delayed functional recovery of the graft. This literature review aims to identify the current evidence regarding albumin administration indication as a treatment for complications or for prevention of further hemodynamic decompensations

Methods: We conducted a systematic review, in accordance with the PRISMA 2020 guidelines, to define the role of albumin in the fluid management of patients undergoing LT, and trace initial steps for indicating perioperative albumin administration.

Results: Six studies were included in the review, encompassing a total of 592 patients. Among these, four randomized controlled trials were sought, whereas two studies were non-randomized studies of interventions. The overall quality of the studies was judged to have some concerns, with two ranked as with low risk of bias, and two studies judged as having some concerns, with main sources of bias being the selection of reported results due to the absence of a preexisting analysis plan and protocol.

Conclusions: This literature review identified three post-transplant clinical scenarios wherein the use of albumin could be advised both as a treatment for complications and for prevention of hemodynamic decompensations, even though strong recommendations cannot be drawn:1)patients with low serum albumin levels and unstable hemodynamics;2)patients with persistent ascites after LT with low serum albumin levels. In these patients non oncotic causes of ascites should be excluded;3)In the early postoperative period in patients with low intravascular volume and low cardiac output in order to prevent graft dysfunction. (Figure 1) Further research is needed to identify the optimal ascites replacement regimen and the target serum albumin level for hypoalbuminemia correction after LT.

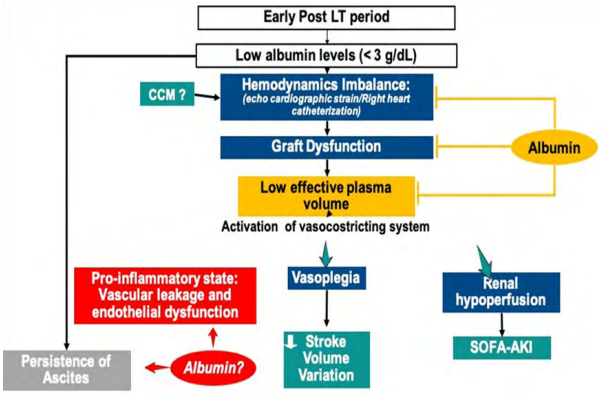

Figure 1. Rationale for the use of albumin after LT proposed by the permanent committee on LT of the Italian Society for the Study of Liver Diseases

PP_060 STATUS REPORT ON LIVING KIDNEY DONORS AND EVALUATION OF THEIR GLOMERULAR FILTRATION RATE IN ALGERIA

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Background: The evaluation of the potential kidney donor requires a rigorous evaluation based on several criteria, one of the main evaluations is that of GFR before the donation; it is provided either by measurement of GFR or by estimation using the creatinine-only equations or the cystatin C-alone equations or a combination of the two endogenous markers as the mixed CKD-EPI equation.

Objective: the aim of the determination of blood cystatin C in the candidate donor before the donation is to calculate their GFR using the mixed CKD-EPI and to evaluate it according to the authorized donation threshold (90 ml.mn.1.73m²).

Methods: a prospective, longitudinal, comparative and analytical multicenter study carried out between 2018 and 2021, it concerned a sample of 55 donors, they benefited from a serum cystatin C assay before the donation and the calculation of their GFR by the different equations (MDRD, CKDEPICr, CKDEPI cyst, CKDEPICr-cyst)

Results: We calculated the eGFR of the 55 donors by the 4 equations. We compared the means of the eGFR by these equations according to the authorized threshold of the donation (Cut-off: 90 ml.mn.1.73 m²). The MDRD classified the donors: 18 donors had an eGFR before the donation less than 90 ml.mn.1.73m² and 37 donors had more than 90 ml.mn.1.73m². The CKDEPI Cr-cyst reclassified the 18 donors according to the Cut-off: 90 ml.mn.1.73m² as follows: 8 donors out of 18 had an eGFR greater than 90 ml.mn.1.73m² and 10 donors out of 18 had an eGFR less than 90 ml .mn.1.73m².

Conclusions: CKDEPICr-cyst based on creatinine and cystatin C confirmed its ability to reassess eGFR before donation according to the authorized donation threshold: at 90 ml.mn.1.73m², and eGFR between 60 and 89 ml.mn .1.73m².

Keywords: Donor, Cystatin C, CKDEPI, donation threshold, eGFR, MDRD.

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Current challenges in transplantation procedures

PP_061 FAILURE-TO-RESCUE OF BRONCHIAL DEHISCENCE AND FISTULIZATION AFTER LUNG TRANSPLANTATION

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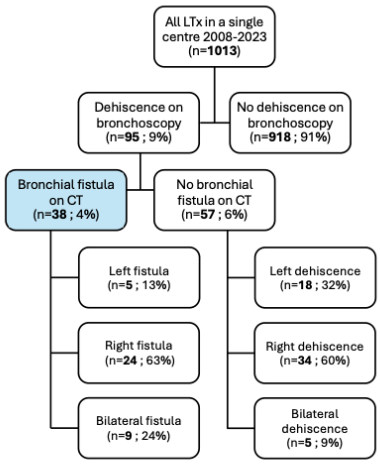
Background: Bronchial dehiscence (BD) is a common complication after lung transplantation (LTx) where the airway anastomosis loses its integrity. Progression to bronchial fistula (BF) where a connection with the pleural space or a blood vessel develops, is known to be associated with a high risk of mortality. The aim of our study is to analyze failure-to-rescue (FTR) after BF *vs.* BD.

Methods: Bronchoscopic diagnosis of BD was retrospectively reviewed for all LTx cases (2008-2023) performed at a single center. The presence of BF was subsequently confirmed by chest CT or intraoperatively during surgical revision. Failure-to-rescue was defined as the proportion of patients who died after diagnosis of BD or BF.

Results: In our cohort of 1013 LTx cases, BD was diagnosed in 95 patients (9%) and BF was present in 38 patients (4%) (Fig. 1A). The characteristics and outcomes of BD and BF cases are summarized in the Table. Time to diagnosis after LTx was 38 days for BD *vs.* 24 days for BF (p=0.16). Most BFs were diagnosed after double-LTx (95%) for COPD (45%) and interstitial lung disease (26%). BF was more common in donation after circulatory death (p=0.0310), male donor (65%) / recipient (79%), preoperative intensive care admission and intra- and postoperative extracorporeal membrane oxygenation. The majority of BFs were right-sided (63%). Watchful waiting was chosen in 50% of BF patients, and the other half underwent at least one surgical intervention. One- and three-year survival rates for BF were 60.5% and 57.6%, respectively, compared to 91.2% and 80.4% for BD without BF (p=0.0030). Overall and airway complication-related one-year FTR for BF was 39% and 34%, respectively, which was higher than for BD without fistula with 9% and 4% FTR, respectively (Fig. 1B). Median survival was 4.8y after BF and 11.3y after BD diagnosis.

Conclusions: Progression from BD to BF is associated with significant morbidity and mortality. Further characterization of cases in which we fail to rescue the patient is critical to better prevent and manage BF, and to improve post-LTx outcome.

A



B

Figure legend 1: (A) Flow chart of included lung transplant cases. **(B)** One-year failure to rescue (FTR) for cases with postoperative bronchial dehiscence (BD) or bronchial fistula (BF).

Lung transplant characteristics		Bronchial dehiscence without fistula (n = 57)	Bronchial fistula (n = 38)	p value	statistic
Donor characteristics					
Donor type					
Donation after circulatory death	n/N (%)	10/57 (18%)	15/38 (39%)	**0.0310**	Fisher's exact
Donation after brain death		47/57 (82%)	23/38 (61%)		
Age (years)	Median (IQR)	51 (35-60)	50 (41-59)	0.9774	Mann Whitney
Male	n/N (%)	37/57 (65%)	31/38 (82%)	0.2600	Fisher's exact
Warm ischemia time (minutes)	Median (IQR)	9 (9-12)	9 (8-11)	0.5411	Mann Whitney
Total ischemia time (minutes)					
Right lung	Median (IQR)	322 (272-382)	349 (287-433)	0.2843	Mann Whitney
Left lung		443 (382-523)	479 (393-562)	0.1375	Mann Whitney
Mechanical ventilation time (hours)	Median (IQR)	59 (36-123)	73 (45-116)	0.4170	Mann Whitney
Implantation time (minutes)					
Right lung	Median (IQR)	74 (63-78)	67 (61-79)	0.4058	Mann Whitney
Left lung		64 (60-73)	67 (62-80)	0.3425	Mann Whitney
Last PaO2/FiO2 ratio	Median (IQR)	434 (371-484)	435 (395-506)	0.5597	Mann Whitney
Recipient characteristics					
Age (years)	Median (IQR)	60 (53-63)	58 (52-63)	0.8873	Mann Whitney
Male	n/N (%)	36/57 (63%)	30/38 (79%)	0.1167	Fisher's exact
Body mass index (kg/m^2)	Median (IQR)	23 (20-25)	22 (19-26)	0.7437	Mann Whitney
Indication					
COPD/Emphysema		28/57 (49%)	17/38 (45%)		
Interstitial lung disease		14/57 (25%)	10/38 (26%)		
Cystic fibrosis/Bronchiectasis	n/N (%)	10/57 (18%)	4/38 (11%)	0.2949	Fisher's exact
Re-transplant/CLAD		4/57 (7%)	4/38 (11%)		
Vascular		0/57 (0%)	3/38 (8%)		
ARDS		1/57 (2%)	0/38 (0%)		
Preoperative intensive care unit	n/N (%)	5/57 (9%)	9/38 (24%)	0.0737	Fisher's exact
Preoperative extracorporeal membrane oxygenation	n/N (%)	2/57 (4%)	4/38 (11%)	0.2262	Fisher's exact
High-urgency listing	n/N (%)	3/57 (5%)	5/38 (13%)	0.2596	Fisher's exact
Surgical variables					
Era of transplant					
2008-2011		7/57 (12%)	7/38 (18%)		
2012-2015		22/57 (39%)	8/38 (21%)	0.0647	Fisher's exact
2016-2019		15/57 (26%)	6/38 (16%)		
2020-2023		13/57 (23%)	17/38 (45%)		
Intraoperative extracorporeal membrane oxygenation	n/N (%)	8/57 (14%)	14/38 (37%)	**0.0133**	Fisher's exact
Type of lung transplant					
Double		53/57 (93%)	36/38 (95%)	>0.9999	Fisher's exact
Single	n/N (%)	2/57 (4%)	1/38 (3%)		
Lobar		2/57 (4%)	1/38 (3%)		
Multi-organ					
Combined with liver transplant	n/N (%)	1/57 (2%)	1/38 (3%)	0.4000	Fisher's exact
Combined with kidney transplant		3/57 (5%)	0/38 (0%)		
Re-transplant	n/N (%)	4/57 (7%)	4/38 (11%)	0.7094	Fisher's exact
Transfusion packed red blood cells during surgery	Median (IQR)	1 (0-3)	3 (0-6)	0.0459	Mann Whitney
Postoperative ECMO	n/N (%)	1/57 (2%)	7/38 (18%)	**0.0063**	Fisher's exact
Revision thoracotomy for hemothorax	n/N (%)	6/57 (11%)	7/38 (18%)	0.3692	Fisher's exact
Intensive care unit stay (days)	Median (IQR)	15 (9-35)	32 (14-49)	**0.0250**	Mann Whitney
Hospital stay (days)	Median (IQR)	34 (25-61)	49 (34-76)	**0.0107**	Mann Whitney
Follow-up (months)	Median (IQR)	60 (25-117)	26 (4-91)	**0.0084**	Mann Whitney
Diagnostic and treatment characteristics					
Interval lung tranplant to diagnosis (days)	Median (IQR)	38 (20-91)	26 (16-38)	0.1600	Mann Whitney
Location					
Only right	n/N(%)	34/57 (60%)	24/38 (63%)	**0.0376**	Fisher's exact
Only left		18/57 (32%)	5/38 (13%)		
Bilateral		5/57 (9%)	9/38 (24%)		
Treatment					
Watchful waiting		55/57 (96%)	19/38 (50%)		
Intercostal muscle flap		0/57 (0%)	13/38 (34%)		
Pericardial flap		1/57 (2%)	5/38 (13%)	<0.0001	Fisher's exact
Pleural flap		1/57 (2%)	3/38 (8%)		
Omentoplasty		0/57 (0%)	4/38 (11%)		
(Sleeve) lobectomy		1/57 (2%)	2/38 (5%)		
Pneumonectomy		0/57 (0%)	1/38 (3%)		
Stenosis bronchial anastomosis	n/N (%)	19/57 (33%)	15/38 (39%)	0.6627	Fisher's exact
Follow-up (months)	Median (IQR)	60 (25-117)	26 (4-91)	**0.0084**	Mann Whitney
1-year survival		91%	61%		
3-year survival	Kaplan Meier	*80.4%*	*57.6%*	**0.0030**	Log-rank
median survival (years)		11.3	4.8		
Airway complication related mortality		5/57 (9%)	15/38 (39%)	**0.0006**	Fisher's exact
1-year failure-to-rescue					
Overall	n/N (%)	5/57 (9%)	15/38 (39%)	.	.
Airway complication related		2/57 (4%)	13/38 (34%)		

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Current challenges in transplantation procedures

PP_062 REEVALUATING HEPATORENAL TRANSPLANT CRITERIA: OUTCOMES IN SINGLE RENAL TRASPLANT IN CIRRHOTIC PATIENTS

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Background: In patients with liver cirrhosis (LC) and chronic kidney disease (CKD), simultaneous hepatorenal transplantation is standard. However, patients with CKD and compensated LC (Child A, HVPG <10 mmHg) do not meet combined transplantation criteria, making isolated kidney transplantation (KT) the preferred option. The aim of our study is to analyse the outcomes of isolated KT in cirrhotic patients, focusing on graft survival and hepatic decompensation.

Methods: A retrospective study was conducted on 13 compensated LC patients who underwent isolated KT at Hospital Clínic of Barcelona (2015–2023), with a median follow-up of 49.1 [32.8–67.1] months.

Results: 84.6% were male, median age was 67.8 [61–77] years, 54% were diabetic, and 76.9% were hypertensive. The most common cirrhosis etiologies were HCV (53.8%) and alcohol (38.5%). Median MELD score was 20.5 [19.75–21.25]. Median CHILD score was 5 [5–6.5] (A 69%, B 15.2%, C 7.7%, unknown for the rest). Pre-transplant, 61.5% had ascitic-edematous decompensations, 84.6% splenomegaly and 36.4% esophageal varices. 76.9% received hemodialysis, 15.4% peritoneal dialysis and 7.7% underwent preemptive KT, with a median dialysis duration of 20 [9–92.75] months. The type of KT were Maastricht type III (46.3%), brain death donation (30.8%), and living donation (23%). Induction therapy was performed with basiliximab (46.2%) and thymoglobulin (53.8%). Maintenance immunosuppression was achieved with mycophenolic acid (69.2%) and mTOR inhibitors (30.8%). Median creatinine level one week after KT was 2.24 [1.7–2.95] mg/dl and 1.98 [1.64–2.03] mg/dl at one year, with a median urinary protein-to-creatinine ratio at one year of 503 mg/g. No hepatic decompensations occurred during the first year. KT complications were graft rejection within one year (23.1%), delayed graft function (15.4%) and graft lost (23.1%) with a median time to loss of 9.3 [5.5–10.6] months.

Conclusions: In our series of patients with Child A liver cirrhosis or without signs of hepatic decompensation and chronic kidney disease who underwent isolated kidney transplantation, no worse outcomes were observed in terms of renal graft survival or hepatic decompensation. Controlled studies with a larger number of cases are needed to confirm these findings.

PP_063 VASCULAR COMPLICATIONS IN CHILDREN RECEIVING A SIZE-MATCH WHOLE LIVER TRANSPLANT

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Background: Liver transplant is gold standard for end-stage chronic liver disease and some acute liver failures. Whole liver transplant (WLT) offers some advantages (logistically, technically and possibly functionally) compared to reduced/split/living donor. Evidence regarding complications in children WLT is still inconclusive.

Methods: retrospective, cross-sectional study on patients <19 years old who received a WLT between 2000-2024. Exclusion criteria: redo. N=64, classified according to the donor's weight in: A (≤15 kg) and B (>15 kg). Studied variables: recipient and donor gender, age and weight, *donor-ratio-weight-ratio* (DRWR), indication, elective/super-urgent, ischemia times, surgical technique, early hepatic artery thrombosis (HAT), portal vein thrombosis (PVT) and need for super-urgent re-transplantation (30 days post-surgery). Qualitative variables were described as absolute frequency and percentage cross-sectional test was used. Quantitative variables were described as mean and standard deviation and U-Mann-Whitney test was used. Statistical significance: $p<0.05$.

Results: group A (N=12, 18.75%) had lower age (1.78 ± 1.40 vs 12.29 ± 4.21; $p<0.05$) and weight (10.23 ± 3.62 vs 46.35 ± 19.35; $p<0.05$), as did their donors [(age: 2.03 ± 0.93 vs 23.56 ± 16.00; $p<0.05$. Weight (12.04 ± 3.05 vs 54.47 ± 23.39; $p<0.05$)]. However, both groups were comparable in terms of gender, elective/super-urgent, DRWR, cold and warm ischemia times and surgical technique (piggy-back/classical technique, end-end /graft in portal vein and hepatic artery, and roux-loop/end-end biliary anastomosis). Biliary atresia was the most frequent indication in group A (41.7%), while group B was more diverse. Regarding complications, there was higher incidence of HAT (N=3, 25% vs N=3, 6.12%; p=0.039), PVT (N=2, 16.67% vs N=1, 1.92%; p=0.0029)) and re-transplantation (N=2, 16.67% vs N=0, 0%; p=0.03) in patients receiving WLT from donors ≤15 kg.

Conclusions: children transplanted with a WLT have a higher risk of developing early vascular complications and necessity for super-urgent re-transplantation. Therefore, the acceptance of thse grafts should be carefully considered at the time of the offer.

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Current challenges in transplantation procedures

PP_064 LAPAROSCOPIC APPROACH FOR THE SURGICAL MANAGEMENT OF DUODENAL STUMP LEAK AFTER PANCREAS TRANSPLANTATION

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Background: Duodenal stump leak (DSL) remains as an important complication associated with graft loss and mortality during pancreas transplantation. Open surgical repair and image guided interventions are used with various results and dismal long-term prognosis. Few records of surgical management through a laparoscopic approach exist. We aim to present a case of surgical laparoscopic repair of DSL.

Methods: 37-year-old male with a clinical history of type 1 diabetes and end stage renal disease subjected to pancreas-kidney transplantation in May 2024. Systemic venous drainage to the vena cava and exocrine drainage to a Roux-en-Y limb of jejunum was implemented. The duodenal-jejunal anastomosis was performed in a 2-layer hand-sewn fashion. DSL was confirmed postoperatively by drain amylase and CT scan. Failure of conservative management and sepsis rendered a surgical intervention. We chose a laparoscopic approach to minimize surgical dissection, systemic inflammatory response, and prevent graft loss. A diffuse peritonitis was found, due to a 180º dehiscence of the duodenal-jejunal anastomosis. It was repaired with a continuous monofilament absorbable suture. The postoperative outcome was favorable, with a slow but steady decline in the anastomotic leak. To date the patient has a normal functioning pancreatic graft.

Results: The management of DSL depends on its size, location and general conditions of the patient. Although graft pancreatectomy provides a definitive treatment, it involves loss of quality of life for the recipient and the need for re-transplantation. In the absence of graft damage, a cautious approach is desirable. Surgical repair of DSL has proven useful in recent studies, while the laparoscopic approach remains poorly explored.

Conclusions: Laparoscopic repair of DSL in pancreas transplantation is to be considered in selected cases. It could minimize the inflammatory response associated with graft pancreatitis and thus help salvage the pancreatic graft.

PP_066 DEVELOPMENT AND IMPROVEMENT OF REJECTION MOLECULAR CLASSIFIERS USING GENERATIVE SYNTHETIC DATA

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Background: Molecular classifiers are promising tools for precision diagnostics of kidney allograft rejection, but their development is hampered by the need for large and well phenotyped cohorts. Here, we aimed to develop and validate molecular classifiers for antibody-mediated (AMR) and T cell-mediated rejection (TCMR) and improve their performances with generative synthetic transcriptomic data.

Methods: This international multicenter study included a derivation cohort of 639 kidney allograft biopsies performed between November 2004 and May 2021 across 8 European centers, enhanced through generative adversarial networks (GAN). An external validation cohort of 343 biopsies was sourced from 2 North American centers. All biopsies were sequenced using the Banff Human Organ Transplant panel on the NanoString nCounter® platform. AMR and TCMR were defined according to the international Banff 2019 classification.

Results: The original data-based AMR molecular classifiers showed a ROCAUC of 0.829 (0.778 – 0.872), PRAUC of 0.711 (95% CI 0.618 – 0.797), and a Brier Score of 0.165 (0.146 – 0.186) in the external validation cohort. The original data-based TCMR molecular classifier showed a ROCAUC of 0.864 (0.813 – 0.906), a PRAUC of 0.701 (0.597 – 0.785), and a Brier Score of 0.122 (0.107 – 0.138) in the external validation cohort. With synthetic data augmentation, the 50% augmented set based molecular classifier performed the best with enhanced and comparable ROCAUCs of 0.861 (0.816 – 0.903) and 0.860 (0.807 – 0.904), PRAUCs of 0.801 (0.731 – 0.859) and 0.704 (0.597 – 0.788) and, for AMR and TCMR, respectively (**Figure**). Genes linked to B cell, T cell, macrophage activation, and endothelial cell activation were captured more important in augmented sets for predicting AMR. Likewise, genes associated with immune cell recruitment and interaction, chemotaxis, inflammatory and immune response, and cell adhesion and migration emerged as more significant in augmented sets for predicting TCMR.

Conclusions: The performances of the original data-based molecular classifiers for detecting antibody-mediated and T cell-mediated rejection were enhanced with generative synthetic transcriptomic data.

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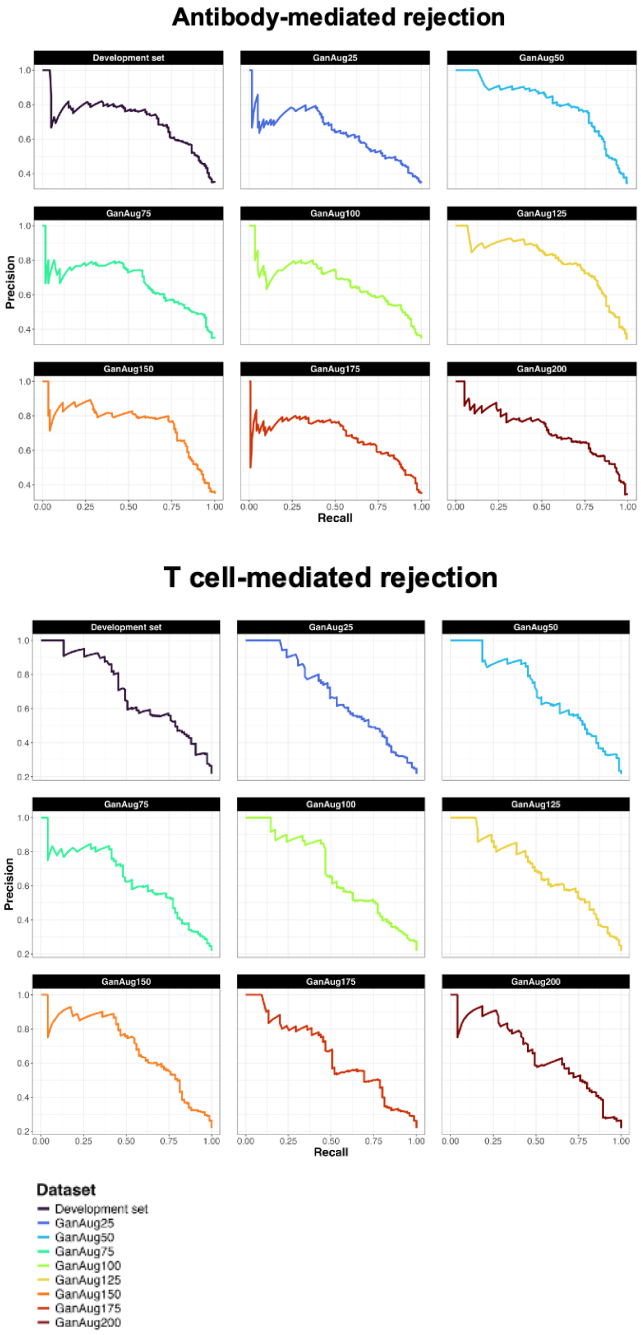

Figure. Predictive performances of the original and augmented data-based molecular classifiers (precision-recall curves).

PP_069 FACTORS ASSOCIATED WITH RENAL FUNCTIONAL RESERVE IN LIVING KIDNEY DONORS

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Background: Factors associated with renal functional reserve (RFR) – presence or absence – are not completely clear and remain under-investigated.

Methods: In this observational study, we evaluated the characteristics associated with the presence or absence of RFR in healthy subjects – living kidney donors – before donation. Renal function was assessed with measured glomerular filtration rate (GFR) – the clearance of iohexol – and RFR with the infusion of amino acids. An increase in GFR >10% after amino acid infusion indicated the presence of RFR. We defined *a priori* three groups of donors: without, with, and using RFR. Subject using RFR had baseline GFR >100 ml/min but without an increase in GFR after stimulation.

Results: Subjects without RFR were predominantly women (81%) with the lowest body surface area (BSA) (1.71 ± 0.17 m^2), and basal GFR (85 ± 9 ml/min). Subjects with RFR were also mostly women (85%), with a higher BSA (1.83 ± 0.18 m^2; p 0.039) and basal GFR (93 ± 15 ml/min). Subjects using RFR were mostly males (56%) and had the highest BSA (1.94 ± 0.18 m^2; p <0.0001 vs *without RFR*; p ns vs *with* RFR), basal GFR (123 ± 20 ml/min; p <0.0001 vs subjects *without* RFR; p <0.0001 vs *with* RFR), and weight (82.1 ± 13.2 Kg; p <0.0001 vs *without RFR*; p ns vs *with* RFR).

Conclusions: The presence or absence of RFR was associated to differences in gender, weight, BMI, BSA, and basal GFR. Women with small BSA may have lower GFR and no RFR, indicating possibly a lower renal endowment even in the normal range of renal function. The use of RFR may indicate a response to a higher metabolic demand in subjects with higher renal endowment. The clinical consequences of the presence or absence of RFR after living kidney donation, both in donors and recipients, shall be prospectively evaluated.

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Current challenges in transplantation procedures

PP_070 1500 LUNG TRANSPLANTATIONS IN THE LEUVEN LUNG TRANSPLANT PROGRAM: A RETROSPECTIVE ANALYSIS

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Background: Lung transplantation (LuTx) as a lifesaving and -prolonging treatment option for patients with advanced pulmonary diseases, has significantly progressed over the years. In 2024, our center successfully performed 1,500 lung transplants. We conducted an outcome analysis of these 1,500 lung transplant recipients at our center, with emphasis on the changes within this population over the past three decades.

Methods: All 1,500 patients who received a LuTx at our center between 1991-2024 were included in this retrospective, observational study. Patients were categorized based on transplant era: 1991–2000, 2001–2010, 2011–2020, and 2021–2024. Graft survival was analyzed using log-rank analysis and visualised by Kaplan-Meier survival curves. Demographic parameters were assessed with Kruskal-Wallis, Fisher's and Chi-square test.

Results: Median graft survival improved across the eras: from 3.5 years for 1991 - 2000, 9.9 years for 2001 - 2010, to 11.2 years for 2011 – 2020 ($p < 0.0001$). Significant differences across the eras were observed in type of procedures, type and age of donors, recipients' age at transplantation, and indications for lung transplantation (all $p < 0.0001$).

Conclusions: Improved posttransplant survival rates, along with changes in type of transplant procedures and indications, and demographic changes in donors and recipients profiles, have occurred over the past eras. To further enhance both outcomes and quality of life for LuTx recipients, it is essential to address key areas, such as frailty assessment, management of comorbidities, and prevention of chronic lung allograft dysfunction, in an aging lung transplant population. Continuous outcome assessment and state-of-the-art patient management, with implementation of evidence-based treatment policies, are crucial for improving and sustaining long-term, high-quality lung transplant care.

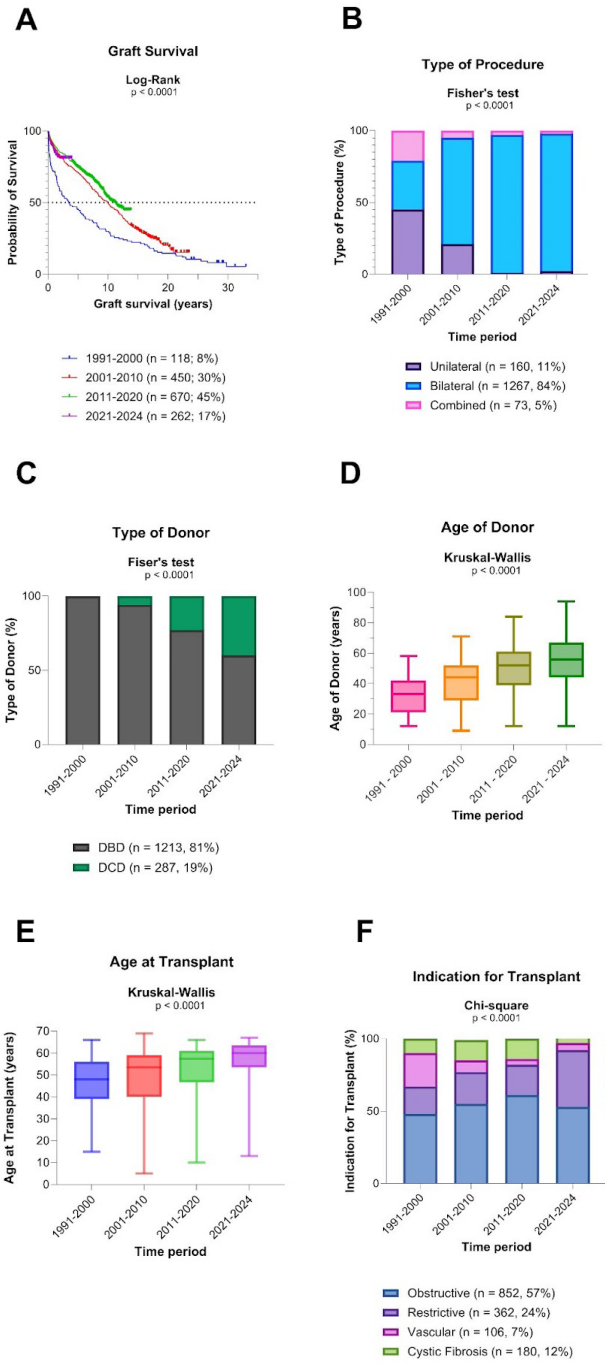

Figure: Graft survival and demographics of 1,500 lung transplant recipients

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Current challenges in transplantation procedures

PP_071 DONOR-SPECIFIC BLOOD TRANSFUSION TO LIVER TRANSPLANT RECIPIENTS; PRELIMINARY OUTCOMES A RCT

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Background: Liver transplantation (LT) is crucial for patients with end-stage liver disease or acute liver failure and often requires substantial blood transfusions. Blood bank shortages pose a challenge, and transfusions are linked to increased mortality and morbidity. Donor-specific blood transfusion (DST), where blood from brain-dead organ donors is transfused into recipients, shows promise, especially as DST may improve immune responses and graft survival. This study investigates DST's impact on LT outcomes.

Methods: A single-center, double-blind, randomized controlled trial (RCT) at the Abu Ali Sina Organ Transplant Center (January-December 2023) assessed the impact of using whole blood from brain-dead liver donors on recipient outcomes. The trial involved 61 LT recipients, divided into DST (intervention) and standard transfusion (control) groups, with data collected during surgery and postoperatively.

Results: The RCT included 61 LT recipients divided into two groups: one receiving DST and the other receiving standard transfusions. Intraoperative outcomes showed significantly lower mean blood loss in the DST group (1289 mL) compared to the control group (2074 mL). Postoperative liver function tests and complication rates were similar. However, the DST group had a significantly lower incidence of positive postoperative blood cultures (3.3% vs. 29%). Mortality rates and causes were not significantly different between groups. DST appeared to be a safe and potentially beneficial strategy during LT.

Conclusions: DST during LT is safe and potentially beneficial, reducing intraoperative blood loss and positive postoperative bacteremia. These findings highlight DST's feasibility and advantages in LT, offering a promising strategy to address blood product shortages and improve transplantation outcomes.

PP_074 SYSTEMATIC REVIEW & META-ANALYSIS: PRE-LUNG TRANSPLANT BODY COMPOSITION AND POST-LUNG TRANSPLANT OUTCOMES

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Background: Lung transplantation (LTx) is a life-saving intervention for end-stage pulmonary disease, requiring a thorough evaluation of medical and physical suitability. Pre-LTx body composition significantly impacts post-LTx outcomes, yet specific guidance on its assessment is lacking. Studies have indicated that not just the quantity, but also body fat distribution and proportion of lean muscle mass can influence short and long-term outcomes in different solid organ transplantation. Therefore, this study aimed to systematically assess the relationships of various body composition parameters before LTx with outcomes post-LT.

Methods: A systematic literature search was performed in six databases for articles until the 22nd of April 2024. We included studies on LTx recipients (age > 18 years) providing an association between pre-transplant body composition parameters and post-transplant outcomes. A meta-analysis was performed on the articles assessing the relationship between BMI classification and all-cause mortality.

Results: 41 articles met the inclusion criteria, of which five articles were included in the meta-analyses. In the multivariate analysis, being underweight was significantly associated with increased all-cause mortality (pooled HR of 1.35 (95% CI, 1.10-1.66, I2=0%, p-value < 0.001). Overweight and obesity were not significantly associated with mortality (pooled HR of 1.06 (95% CI, 0.94-1.19, I2=0.01%, 1.15 (95% CI, 0.69-1.89, I2=70%), respectively). Other studies reported that a favorable change in BMI was more predictive of mortality than baseline BMI. Furthermore, low albumin was associated with post-operative parameters. Multiple studies showed that quality and quantity of muscle measured by CT scans were associated with short-term post-transplant outcomes and survival.

Conclusions: Various body composition parameters are associated with post-transplant outcomes. Due to the considerable heterogeneity among the studies and the absence of comparative analyses across different body composition metrics, no conclusions can be drawn regarding which measures provide the best yield. For future studies, we recommend focusing on mutual comparison between body composition parameters and outcomes to support clinical recommendations in future guideline development.

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Current challenges in transplantation procedures

PP_076 TRANSPLANT PHYSICIANS AND PATIENTS' BELIEFS AND ATTITUDES REGARDING TELEMEDICINE FOR POST-KIDNEY TRANSPLANT MONITORING

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Background: The Ap'Tx study (NCT03750331) is a randomized controlled trial that aims at evaluating tele-monitoring of stable kidney transplant recipients (KTR) using Ap'Telecare? as compare to a conventional monitoring. A total of 700 KTR have been enrolled and are being followed for 2 years. Herein, we sought to investigate healthcare professionals and patients/users' beliefs and attitudes regarding the use of telemedicine for post-kidney transplantation monitoring.

Methods: Semi-structured interviews were conducted with transplant physicians and patients applying the methodology framework proposed by Paillé and Mucchielini to conduct the thematic analysis using the Nvivo software. Themes were generated according to the CFIR codebook. Transcripts, and themes, were not returned to participants for comment and/or correction. The participants did not provide any feedback on the results.

Results: Thirty semi-structured interviews were conducted with healthcare providers (n=5), patients who discontinued telemonitoring prematurely (n=5) and patients who remained adherent (n=20). Three main themes emerged: (1) An overall good level of acceptability and satisfaction, with a central and facilitating role played by the coordinator-nurse; (2) An innovation that complements the medical monitoring and provides the opportunity for enhanced therapeutic education and (3) The difficulty to generalize implementation to every patient.

Conclusions: Both caregivers and users, irrespective of their initial belief on telemedicine, acknowledge the added value of Ap'Telecare for post-transplant telemonitoring. They however emphasize the necessity of co-constructing the software interface in order to facilitate implementation. Patients' perception was that Ap'Telecare? does not substitute to but complements conventional medical follow-up.

PP_078 ANTICOAGULATION THERAPY IN PERI-OPERATIVE SURGERY OF A KIDNEY TRANSPLANT: A CAUTIONARY TALE

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Background: Although evidence of acenocoumarin (ACO) benefit in preventing stroke in atrial fibrillation or thrombosis in hypercoagulability conditions in dialysis is weak and data about safety on anticoagulant reversion before surgery and/or its impact on haemorrhagic risk or other outcomes are few.

Methods: This is a retrospective observational study analysing including patients that received a kidney transplant at our institution in period 2018-2023. We identified 69 patients were taking ACO before the transplant. Through a propensity matching analysis score with ratio 1:1, we paired them with other 69 patients not taking ACO and with same clinical characteristics.

Results: Basal cohort characteristics showed a median age of 70 years old [62-76], a prevalence of diabetes of 38 % and a time on dialysis of 39 months (SD 36). Reverse therapy for ACO group was phytometadione (75 %), phytometadione + human prothrombin complex (HPC-14 %) or no therapy (10 %). Need of blood transfusion was more common in ACO group vs not (39 % vs 29 %). ACO group experienced more complications such us need of a second surgery - including allograft nephrectomy - (12 % vs 3 % p. 0.048). Other relevant outcomes such as death and graft loss at 12 months were more frequent in ACO group (10 % vs 2.9 % and 8.7 vs 1.4 %). Cox Regression logistic analysis showed ACO use and acute rejection were predictive of a composite outcome of reoperation, graft loss and death(see Figure 1). Finally, patients having an INR before surgery > a 1.5 that were treated just with vitamin K agonist had a 30 % incidence of reoperation while no one patient treated adding HPC needed a second intervention.

Conclusions: In this elderly population receiving a kidney transplant, presence of ACO and a not optimal management of its reversion before surgery was associated with worst outcomes indicating a need for alternatives strategies to anticoagulation while on waiting list.

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Current challenges in transplantation procedures

PP_080 THE OUTCOMES OF THE DECEASED DONOR KIDNEY TRANSPLANTATION USING EXTEDED CRITERIA DONOR

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Background: Deceased donor kidney transplantation (DDKT) using grafts from extended criteria donors (ECD) presents a useful option for resolving the critical shortage of organs for transplantation. While ECD graft offers benefit s such as shorter wait time and improved quality of life for recipients, the long-term outcome of ECD graft is not well understood. The aim of this study is to identify the long term-outcomes of the deceased donor kidney transplantation using extended criteria donor.

Methods: Between March 2011 and Feb. 2024, 99 patients underwent DDKT at department of surgery at Konyang university hospital, Daejeon, Korea. We compared two groups according to using ECD graft: no ECD group (n=81), ECD group (n=18). The following characteristics were evaluated retrospectively through the medical records.

Results: The 5-year patient survival in the ECD group was 84.4% compared to 92.5% of the no ECD group (P = 0.537). The 5-year graft survival were 100.0% and 94.8% in the ECD group and no ECD group (P = 0.325) retrospectively. Also, hospital stay, operation time and complication rates were not significant differentiated between the two groups. However, the eGFR level by period of recipients was significantly more increased in no ECD group (12months: 75.9±21.8 ml/min vs. 54.2±17.5 ml/min, P<0.001, 60th months; 81.5±22.4 ml/min vs. 60.3±22.2 ml/min, P=0.033).

Conclusions: According to this study, the outcomes of DDKT using ECD graft suggest a long-term decline in renal function. However, it tis consider a safe and useful method for resolving the shortage of organs for transplantation.

PP_081 REVOLUTIONIZING ORGAN TRANSPORT: THE ADVENT OF DRONE DELIVERY SYSTEMS FOR ORGANS

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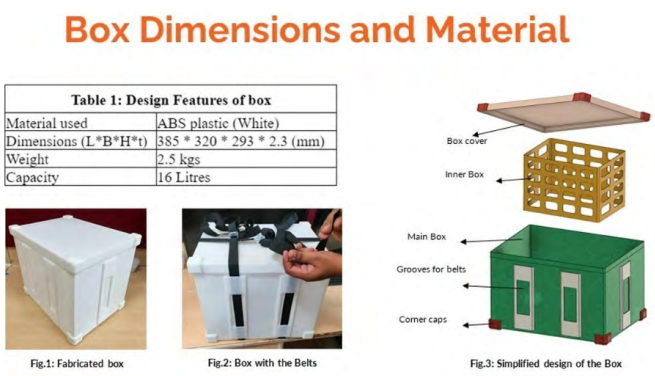
[1]Mohan Foundation; Nil, [2]Mohan Foundation; Managing Trustee, [3]Iit Madras, [4]Mohan Foundation

Background: In India's cities, organ transport during peak traffic relies on 'green corridors' established by traffic police, which halt traffic for organ-carrying vehicles. While effective, this approach causes significant public inconvenience and demands additional police resources. Drones offer a promising alternative to bypass urban congestion, providing a seamless, efficient method for transporting organs. This paper introduces a temperature-regulated, lightweight, and crash-resistant container designed for drone delivery of organs, addressing the critical need to maintain cold chain for sensitive items.

Methods: The primary goal was to design a resilient, lightweight container to mitigate impact damage. Additionally, a cost-effective drone capable of carrying 8–10-kilogram payload for up to 45 minutes over 30 kms was identified. The container, designed to weigh 3-4 kg, accommodates the organ, preservation fluid, ice packs, sensors and tracking devices, maintaining a total payload of 8 kg.

Results: Constructed from carbon fiber and aluminium, the container achieved an optimal strength-to-weight ratio (Table 1 & Fig 1, 2 & 3). It features sensors for temperature monitoring and emergency tracking, including an accelerometer, gyroscope, GPS, and temperature sensors, managed by an Arduino Uno microcontroller and powered by lithium-ion batteries. Insulation and impact protection are enhanced by a thermocol casing, with phase change material (PCM) ensuring stable temperatures. Extensive testing for durability and temperature regulation, and three flight tests using a goat heart demonstrated the system's ability to maintain temperatures between 1-2 °C. The project was funded by SBI Foundation.

Conclusions: The drone delivery system offers an innovative, eco-friendly, and cost-effective solution for organ transport, enhancing delivery efficiency and reliability. It addresses the urgent needs in transplantation medicine, presenting a viable alternative to conventional methods.



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Current challenges in transplantation procedures

PP_082 RETROPERITONEAL ACCESS ROBOTIC VERSUS HAND-ASSISTED APPROACH

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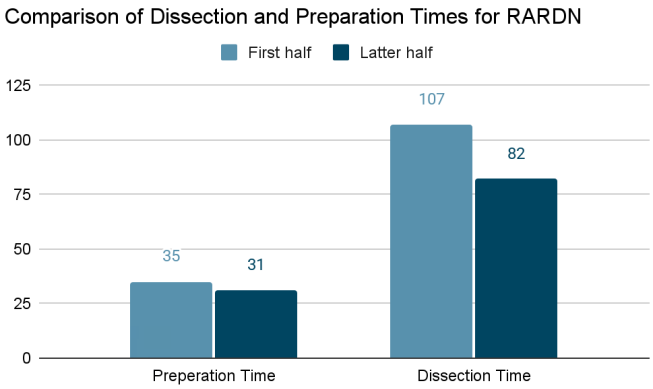
Background: After adopting hand-assisted retroperitoneoscopic donor nephrectomy (HARPDN) in our clinic (over 1300 cases), we introduced Robot-Assisted Retroperitoneoscopic Donor Nephrectomy (RARDN) as an alternative surgical technique after having experience with laparoscopic robotic approach (12 cases). This study compares two retroperitoneal approaches in regards to surgical and donor outcomes.

Methods: This retrospective analysis included 533 patients (467 HARPDN, 66 RARDN) from March 2018 to November 2024. We performed a hybrid technique for RARDN in which hand assistance is used for retroperitoneal space creation and trocar insertion. Vessel stapling and kidney removal was performed with hand assistance in selected cases (n=25). Robotic instruments included hook cautery, bipolar forceps, and graspers, with ligasure and vascular stapler introduced via the Alexis port.

Results: The mean follow-up was 7.3 months in HARPDN and 7.2 months in RARDN. The mean age was similar (47 vs. 48), while RARDN group had more females (63.6% vs. 52.4%) and donors with lower BMI (26.4 vs. 28.4). Right nephrectomy rates were higher in HARPDN (29.1% vs. 25.6%). Multiple artery rates were higher in HARPDN (20.7% vs. 18.1%). Dissection times were comparable for both (left 112 vs. 105 min, right 95 vs. 78 min). In RARDN, both preparation and dissection time decreased (35 vs. 31 and 107 vs. 82 min respectively) in the latter half. The peritoneal opening was more frequent in HARPDN (15.8% vs. 12.1%). No major bleeding and blood transfusion was required in both groups. There was 4 major artery injury in HARPDN but none in RARDN. Postoperative mean creatinine levels were similar. Graft survival rate was 96.6% in HARPDN and 98.5% in RARDN. Three cases in HARPDN had postoperative hernias versus none in RARDN. Robotic donors' satisfaction and procedure recommendation were high.

Conclusions: RARDN enabled successful outcomes and high donor satisfaction, with significantly fewer wound complications. It avoids intraabdominal complications and reduces postoperative hernia formation compared to HARPDN.



PP_085 EFFICACY AND SAFETY OF PTC AND BILIARY STENT PLACEMENT IN CHILDREN WITH BILIARY STRICTURES

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Background: Percutaneous transhepatic cholangiography (PTC) is a well-established treatment for the management of biliary strictures (BS) in adults, however its application in children remains limited, particularly regarding the employment of biodegradable biliary stents (BBS). This study aimed to assess the efficacy and safety of PTC and BBS placement in a cohort of pediatric patients.

Methods: We retrospectively reviewed data from children treated with PTC for BS at the University Hospital of Padova between 2014 and 2024. Collected data included demographics, BS type, PTC procedure characteristics and complications. A PTC cycle consisted of the series of procedures required to address a single BS episode. PTC success was defined as the successful placement of the biliary drainage tube, while PTC efficacy as the absence of stricture recurrence at tube removal. The recurrence of significant BS impairing bile flow was assessed throughout the follow-up period.

Results: Eighteen patients (55% males; median age 6 years; range 0.75-18 years) were included. The median follow-up time was 21 months (range 3-75). BS were categorized as anastomotic (10/18), intrahepatic (1/18), anastomotic and intrahepatic (1/18), complex (4/18), other (2/18). 86 procedures were performed and 19 cycles completed. Success and efficacy rates were 90.9% and 100%, respectively. BS recurrence occurred after 5 completed cycles (26.3%), with recurrence rates of 25% after the first cycle and 33.3% after the second. Cholangitis occurred after 24% of procedures. Life-threatening complications were rare, with sepsis and bleeding registered in 4.6% and 3% of patients, respectively.

Conclusions: PTC is an effective treatment for biliary strictures in children, with a success rates of 90-100%. Compared to recurrence rates of 50-60% with standard PTC, BBS reduce the risk of restenosis to approximately 25%. Prospective studies with larger pediatric cohorts are required to confirm these findings.

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Current challenges in transplantation procedures

PP_087 REDUCING AIRWAY COMPLICATIONS AFTER LUNG TRANSPLANTATION: A SINGLE-CENTER SUCCESS STORY

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Background: Airway complications (ACs) following lung-transplantation (LTx), which occur in 2% to 33% of all cases (Crespo, 2021), are associated with significant morbidity and mortality. In this study, we examine the incidence and outcomes of airway complications (ACs) in patients at our transplant center.

Methods: This single center, retrospective exploratory study, conducted from January 2012 to January 2024 examined all LTx recipients that experienced ACs requiring intervention within the first year post-LTx. ACs were classified according to the 2018 ISHT guidelines into four categories: Ischemia and Necrosis, Dehiscence, Stenosis, and Malacia. All surgeons performed a running end-to-end bronchial anastomosis using a 4-0 polydiaxanone suture, ensuring the preservation of the native peri-bronchial blood supply.

Results: During the study period, 3.6% of LTx recipients (26/723) and 2.09% of all bronchial anastomoses (29/1335) developed ACs. Among the 26 affected recipients, hypertension and gastroesophageal reflux were prevalent comorbidities, observed in 61.5% and 50% of patients, respectively. The most common type of airway complication was stenosis (84.6%), followed by dehiscence (7.7%), ischemia/necrosis (3.8%) and malacia (3.8%). Of the 29 affected anastomoses, 21 were right-sided and 8 were left-sided with a median time of 5.5 (1.8 - 11) months from LTx to intervention. All 26 patients initially underwent balloon dilation. Six patients required additional stent placement, and one patient necessitated further surgical and laser interventions. Survival at 90 days and 1-year post-LTx was 100%, and 3-year survival was 78.9%. In comparison, the historical 3-year survival rate for the program ranges between 88% to 90%.

Conclusions: The single running suture technique, employing a monofilament absorbable suture while preserving peri-bronchial blood supply, resulted in a low incidence of ACs following LTx and contributed to excellent short and mid-term survival. Future studies will further investigate the risk factors associated with ACs, with the goal of refining patient management strategies and improving long-term outcomes.

References: Crespo M. M. (2021). Airway complications in lung transplantation. Journal of thoracic disease, 13(11), 6717–6724.

PP_089 OUTCOMES OF INTESTINAL TRANSPLANTATION (ITX) AT A SINGLE LARGE ADULT CENTRE OVER A 17-YEAR PERIOD

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Background: ITx is now an established procedure for treating patients with intestinal failure and its associated complications. Indications have expanded, with increasing numbers performed for portomesenteric vein thrombosis (PMVT), extensive tumours (desmoids) & failure of medical management of Crohn's. Outcomes have improved by recipient/donor selection, perioperative care, modifying surgical techniques, immunosuppression, & infection management.

Methods: A retrospective analysis of a prospectively maintained database from Dec 2007 to May 2024 was undertaken. We have analysed demographics, complications and outcomes in various types of grafts.

Results: A total of 159 ITx were performed in 151 patients (8 re-transplants). The median age at transplant was 45 years (16-65 years) including 51% males, 49% females. Median length of stay was 71.5 days. Indications for ITx are shown in Figure 1. Table 1 shows the different type of grafts. Surgical Innovations: Elective intra-operative filtration allows for metabolic stability during the explant & reperfusion. For recipients with PMVT, pre-operative embolisation of the native SMA +/- coeliac axis has led to a reduction in blood loss & use of products. Avoiding MVT & increasing LSB implants has boosted 5-year survival from 28% to 60% for liver-containing (LC) grafts. Medical improvements: 62/151 patients experienced at least 1 episode of rejection. 39.5% LC grafts, 43% non-liver containing (NLC) grafts. Treated with steroids, and varying combinations of ATG, plasma exchange and alemtuzumab. Prior to 2014 recipients were not matched for CMV & 40% of patients had CMV disease. Since then, we have matched for CMV and our rate is now down to 22.2%. 27/151 (17.8 %) recipients developed PTLD. 22/27 (81.5%) had EBV viraemia. All patients were treated with rituximab, in addition R-CHOP chemotherapy(n=2) & cell-based therapies(n=3). 8/151(5.3%) patients had biopsy proven GVHD (LC grafts only). Since 2018 we have actively monitored for chimerism & reduced immunosuppression. We have only had one patient with GVHD after that. One-year patient survival for LC grafts is 76.9%, NLC grafts 88.4% & 5 yrs survival is 59.9% and 82.1% respectively.

Conclusions: This is an adult only single centre study over a 16-year period describing the patient outcomes and complication rates.

ID	LTx Type	Age	Sex	Hypertension	GERD	Primary AC	Laterality	Balloon Dilation	Stent Placement	Surgical Intervention	Laser Intervention	Time from LTx to Intervention (Months)	90d Survival	1yr Survival	3yr Survival
1	Double	54	F	No	Yes	Stenosis	Right	Yes	No	No	No	6.5	Yes	Yes	Yes
2	Double	33	F	No	Yes	Dehisence	Right	Yes	Yes	No	No	4.7	Yes	Yes	Yes
3	Double	62	M	No	Yes	Stenosis	Right	Yes	No	No	No	1.81	Yes	Yes	Yes
4	Double	58	M	Yes	Yes	Stenosis	Right	Yes	No	No	No	4.11	Yes	Yes	Yes
5	Double	49	M	Yes	Yes	Dehisence	Both	Yes	Yes	No	No	2	Yes	Yes	Yes
6	Double	48	F	Yes	No	Ischemia and Necrosis	Both	Yes	Yes	Yes	Yes	5.19	Yes	Yes	No
7	Single	68	M	Yes	No	Stenosis	Right	Yes	No	No	No	5.65	Yes	Yes	Yes
8	Single	66	M	Yes	No	Malacia	Right	Yes	Yes	No	No	5.91	Yes	Yes	Yes
9	Double	67	M	No	Yes	Stenosis	Right	Yes	No	No	No	4.53	Yes	Yes	Yes
10	Double	68	M	Yes	No	Stenosis	Left	Yes	No	No	No	6.57	Yes	Yes	Yes
11	Double	36	M	Yes	Yes	Stenosis	Right	Yes	No	No	No	2.33	Yes	Yes	Yes
12	Double	57	F	Yes	Yes	Stenosis	Left	Yes	No	No	No	6.41	Yes	Yes	Yes
13	Double	61	M	Yes	Yes	Stenosis	Left	Yes	No	No	No	6.5	Yes	Yes	Yes
14	Double	59	F	No	Yes	Stenosis	Right	Yes	No	No	No	6.57	Yes	Yes	No
15	Double	51	M	No	No	Stenosis	Right	Yes	No	No	No	10.97	Yes	Yes	No
16	Single	65	F	Yes	Yes	Stenosis	Left	Yes	No	No	No	7.23	Yes	Yes	No
17	Double	34	F	No	Yes	Stenosis	Left	Yes	No	No	No	2.53	Yes	Yes	Yes
18	Double	65	F	Yes	No	Stenosis	Right	Yes	No	No	No	10.97	Yes	Yes	Yes
19	Double	58	F	No	No	Stenosis	Right	Yes	No	No	No	6.44	Yes	Yes	Yes
20	Double	43	M	Yes	No	Stenosis	Right	Yes	Yes	No	No	4.99	Yes	Yes	N/A
21	Double	60	M	Yes	No	Stenosis	Right	Yes	No	No	No	3.25	Yes	Yes	N/A
22	Double	74	M	Yes	No	Stenosis	Right	Yes	No	No	No	4.57	Yes	Yes	N/A
23	Double	67	M	Yes	No	Stenosis	Right	Yes	No	No	No	4.08	Yes	Yes	N/A
24	Double	61	M	No	No	Stenosis	Right	Yes	No	No	No	5.88	Yes	Yes	N/A
25	Double	57	M	Yes	No	Stenosis	Right	Yes	Yes	No	No	8.31	Yes	Yes	N/A
26	Double	59	M	No	Yes	Stenosis	Both	Yes	No	No	No	5.26	Yes	Yes	N/A

LTx - Lung Transplant, GERD - Gastroesophageal Reflux Disease, ECMO - Extracorporeal Membrane Oxygenation, AC - Airway Complication

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Current challenges in transplantation procedures

PP_090 PROSPECTIVE ASSESSMENT OF INTRAOPERATIVE RENAL PERFUSION WITH TRANSIT TIME FLOW MEASUREMENTS IN KIDNEY TRANSPLANTATION

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Background: Optimal graft perfusion is key to achieving satisfactory post-transplant function. The possibility of evaluating vascular flows can lead to the early identification of vascular complications and reflect graft quality and outcome.

Methods: From 1-2022 to 8-2024 transit time flow measurements (TTFM) were prospectively recorded in 103 consecutive kidney transplants (KTx) and analyzed alongside donor, recipient, transplant and outcome data.

Results: Correct measurements were obtained in all cases. Patients receiving living-donor transplants showed higher arterial TTFM (385 (248-537) vs 294 (168-384) ml/min, p=0.010) but similar venous TTFM (p=0.506). Arterial TTFM presented an inverse correlation with donor BMI (r=-0.241, 95%CI: -0.449--0.008, p=0.036). Two patients (1.3%) with severely reduced TTFM (<50 ml/min) developed intraoperative vascular complications and underwent immediate treatment. Patients experiencing delayed graft function (DGF) presented lower arterial and venous TTFM (190 (117-306) vs 338 (271-446) ml/min, p<0.001 and 218 (170-391) vs 369 (272-456) ml/min, p=0.015), respectively. In patients with higher arterial TTFM the serum creatinine levels showed a faster decrease (r=-0.493, 95%CI: -0.652--0.293, p<0.001). Arterial TTFM (OR: 0.993 (0.989-0.998), p=0.004) and donor arterial hypertension (OR: 9.292 (2.337-36.935), p=0.002) resulted independent risk factors for DGF development at the multivariable logistic regression analysis. The identified arterial cutoff for better outcomes was 310 ml/min (AUROC 0.765).

Conclusions: The intraoperative TTFM evaluation in KTx was safe and effective in the early recognition of vascular complications. Arterial TTFM reflect graft quality, with lower flows (<310 ml/min) correlating with slower post-transplant serum creatinine decrement and representing an independent risk factor for DGF development.

PP_091 STUDY THE OUTCOMES OF SPLIT PEDIATRIC KIDNEY TRANSPLANT IN ADULT RECIPIENTS: RETROSPECTIVE COHORT STUDY

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Background: As demand has outpaced the supply of organs. Paediatric split kidney donors are now looked as a potential source of good quality organs at par with adult diseased donors and living kidney donors and en-bloc paediatric kidney donors.

Methods: A single-centre retrospective cohort study was done from August 2017 to August 2022, Total number of transplants done were 922 and out of which deceased donor were 233, during the study period. Fourteen split kidneys from seven paediatric donors weighing less than 18 kg were transplanted into recipients which were free from any comorbidities. Patients' data were retrieved from an electronic database, case file, and Outpatient department follow-up in the department of renal transplant surgery Post graduate institute of medical education and research, Chandigarh, INDIA.

Results: The male and female recipients were (11:3). The mean (standard deviation [SD]) age of donors was 3.4 (1.1) years and recipients 27.7 (9.9) years. The mean (SD) estimated glomerular filtration rate increased steadily from 58 (31.8) mL/min/1.73m^2 at the time of discharge to 116 (24.8) mL/min/1.73m^2 at end of 12 months. The mean (SD) eGFR remained stable at 24– and 36 months post-transplant with the decrease in mean (SD) eGFR to 104 (17) mL/min/1.73m^2 at mean follows up of 31 (23.5) months. Rejection was noticed in 1/14 transplant recipients and 1/14 had Delayed graft function, no vascular and urinary complications were seen in any of the patients. 6/14 patients (42.8%) had covid infection post-transplant, 3/14 patients (21.4) had Urinary tract infection, and 2/14 patients (14.2) had surgical site infection.

Conclusions: Split paediatric kidneys can contribute to the organ donor pool with good outcomes and robust graft function in long term but are associated with manageable adverse outcomes in short term and the technical difficulties can be dealt with good surgical skills of the operating transplant surgeon.

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PP_093 NOVEL APPROACH TO VIABILITY ASSESSMENT OF SPLIT LIVER GRAFTS USING HYPOTHERMIC OXYGENATED PERFUSION

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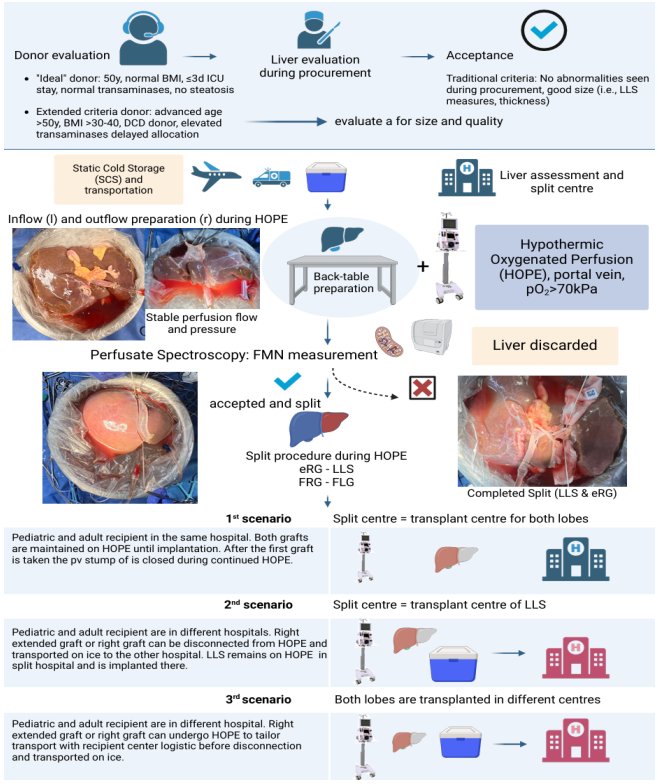
Background: Hypothermic oxygenated perfusion (HOPE) has shown success in whole-graft liver transplantation, reducing graft injury, complications, and improving survival. However, evidence for its use in split grafts for pediatric transplants is limited to a few European case series. Spectroscopic analysis of mitochondrial injury during HOPE reliably predicts graft function and survival, potentially enabling more livers to be split. Here, we present a novel donor-liver evaluation pathway and a split series of human livers during HOPE.

Methods: Human deceased donor livers are evaluated for split and undergo HOPE (Vitasmart) with subsequent flavin mononucleotide (FMN) analysis in perfusate. Following initial HOPE-treatment through the portal vein different types of splits were successfully performed during HOPE. Perfusates and tissues were analyzed for mitochondrial injury and function and signs of inflammation, senescence and regeneration.

Results: Ten extended criteria human donor livers were allocated to this new split pathway between May and November 2024. Following standard procurement with cold flush, and transport on ice, 5 whole DBD and 5 DCD livers underwent HOPE with perfusate spectroscopy for FMN. Donors were between 40 – 69y of age with a BMI of 23.4-40.1kg/m^2 and 4-22hrs cold storage prior to HOPE. Despite such extended risk, three grafts met perfusate FMN-acceptance criteria for transplantation (FMN£0.02mg/mL within 60min HOPE). One was a DCD liver with short donor warm but long cold ischemia time (22hrs) before HOPE. Six livers underwent “classic” split (left lateral segment and extended right lobe), three received a full left- and right split and one liver was reduced (S6-7). Livers with acceptable FMN release showed less complex I and II activation, higher regenerative capacity and less inflammation during HOPE.

Conclusions: By adding FMN-based viability assessment and split during HOPE, this novel liver-evaluation pathway may help to safely increase the number of available liver grafts for the pediatric recipient population. The use of HOPE during and after splits further reduces ischemia times, improves graft quality and helps with the various logistic challenges associated with this type of liver transplantation.



PP_094 IMPACT OF THE HIGH BASELINE ANTI-A/B ANTIBODY TITER IN ABO-INCOMPATIBLE LDLT

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Background: Recently, advances in desensitization protocol have made ABO-incompatible (ABOi) living donor liver transplantation (LDLT) feasible option in the era of organ shortage. Although, multiple sessions of plasmapheresis can successfully reduce preformed anti-A/B titer prior to transplantation, the clinical significance of baseline anti-A/B antibody titers remains uncertain. The aim of this study is to investigate the clinical outcomes of ABOi LDLT in patients with a high baseline anti-A/B antibody titer.

Methods: A total of 50 patients who received ABOi LDLT from 2010 to 2020 at two tertiary hospitals were evaluated retrospectively. Two centers used a protocol composed of rituximab, plasmapheresis, and/or splenectomy. The patients were classified according to baseline anti-A/B titer (<1:256, n=88 or ≥1:256, n=62) and compared the clinical outcomes among these groups. Graft survival rates were calculated using the Kaplan-Meier methods according to the groups.

Results: In the high baseline titer group, the number of plasmapheresis required to reach the target titer (1:16) was significantly higher (4.4±2.2 sessions) than in the low baseline titer group (1.9±1.2 sessions, P<0.001). 14 (16.4%) patients in high baseline titer group and 7 (9.2%) patients in low baseline titer group experienced postoperative titer rebound to ≥1:32, (P=0.014). The occurrence of both cellular rejection and antibody-mediated rejection did not show a significant difference (P=0.251 and P=0.147, respectively). The 1-,3-, and 5-year graft survival was not different among groups (high titer vs. low titer;94.2%, 83.3%, and 59.0% vs. 92.1%, 86.3%, and 79.5%, P=0.326). In multivariate analysis showed that high baseline anti-A/B titer and postoperative rebound titer did not adversely affect clinical outcomes after ABOi LDLT.

Conclusions: Although, the patients with high baseline anti-A/B titer showed the higher tendency of postoperative antibody rebound, the baseline and rebound anti-A/B titer may not be as important factors for clinical outcomes of ABOi LDLT if appropriate desensitization is performed.

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PP_095 PROTECTION OF ENDOTHELIUM BY ALBUMIN AND SULODEXIDE IN PORCINE MODEL OF KIDNEY TRANSPLANTATION

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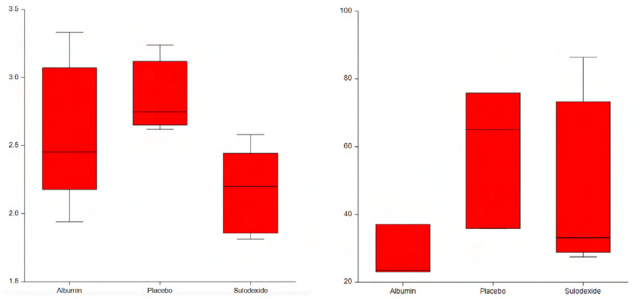
Background: Kidney transplantation (KT) relies heavily on maintaining the integrity of the endothelial glycocalyx (EG), which is susceptible to ischemia-reperfusion injury (IRI). This study explores the protective effects of albumin and sulodexide on the EG in a porcine KT model.

Methods: Fourteen piglets were divided into three groups: control, albumin-treated, and sulodexide-treated. Serum syndecan-1 levels and urinary glycosaminoglycan concentrations were measured at multiple time points post-reperfusion to assess EG integrity. Histological analysis of the renal cortex was also performed.

Results: Sulodexide treatment resulted in significantly lower serum syndecan-1 levels at 5 minutes post-reperfusion (p=0.046), while albumin-treated piglets showed reduced urinary glycosaminoglycans at the same time (p=0.041). Histological changes were minor across all groups, and no significant differences were observed at later time points.

Conclusions: Both albumin and sulodexide showed potential in protecting the EG during KT. These findings suggest a need for further studies to explore their potential to improve graft outcomes.



Boxplots of syndecan-1 levels in ng/ml (left) and urinary glycosaminoglycans in ng/ml (right) at 5 minutes post-reperfusion

PP_096 A NEW DRUG FOR PREVENTING ISCHEMIA REPERFUSION INJURY: PIRACETAM. AN EXPERIMENTAL STUDY

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Background: Ischemia-reperfusion injury (IRI); cause hepatic dysfunction and biliary tract complications in major liver surgeries and liver transplantation. During the reperfusion phase, the production of free oxygen radicals causes damage to the liver tissue. Piracetam improves cognitive functions by acting on the cell membrane and plays an important role in cell damage repair by increasing microcirculation and cell membrane stability. It prevents the formation of free oxygen radicals.

Methods: We used 21 rats were used in 3 groups. The groups were named Control group (CG), ischemia reperfusion group (IG), Piracetam group (PG). After laparotomy in CG, blood samples and liver tissue samples were taken without any additional procedure. In IG, the hepatic artery and portal vein were clamped for 45 minutes, causing ischemia in the liver, and then the clamps were opened and reperfusion was achieved, and it was waited for 60 minutes. Tissue samples were then taken from blood and liver. In PG, 200 mg/kg piracetam was injected intraperitoneally 60 minutes before the operation, and the same procedures were applied at the end of the 60th minute as in the IG group. Biochemical and histopathological examinations were performed on blood and tissue samples taken from rats.

Results: Total bilirubin, direct bilirubin, AST, ALT, ALP were significantly lower in the PG group. Tissue Caspase 3, malonaldehyde levels were found to be significantly lower in the PG group, and reduced glutathione levels were higher in the PG group. In the pathological examination, while the necroinflammatory focus was found to be significantly less in the PG group. Although not statistically significant in other pathological parameters, piracetam was shown to reduce IRI.

Conclusions: Regards to piracetam administered intravenously before liver surgery, the damage to the liver in ischemia-reperfusion situations can be reduced. Thus, liver dysfunction and biliary tract complications can also be reduced.

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PP_097 CHARACTERIZATION AND EFFICACY OF A C2-BLOCKING ANTIBODY IN A RAT KIDNEY TRANSPLANT MODEL

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Background: Delayed graft function (DGF) following kidney transplantation is associated with inferior short- and long-term transplant outcomes and is not preventable by current therapies. The complement pathway has been proposed as a target for DGF prevention, as it majorly contributes to ischemia-reperfusion injury (IRI) underlying DGF. We addressed the impact of blocking the classical (CP) and lectin (LP) complement pathways at the level of complement factor C2, thereby leaving the alternative (AP) complement pathway intact, in a rat model of kidney transplantation.

Methods: Recipient rats received a kidney exposed to a long cold ischemia time and were treated intravenously with anti-C2 monoclonal antibody (mAb) or placebo control in the peri-transplantation period. Serum creatinine levels and blood urea were analyzed at Day 3 post transplant. Transplanted kidneys from surviving animals were histologically examined at Day 14. As the involvement of the three distinct complement pathways in IRI is species dependent, we further assessed the relative importance of the CP/LP in IRI-induced complement activation on different human endothelial cells *in vitro* using a hypoxic chamber.

Results: Blocking C2 activity significantly improved serum creatinine and blood urea nitrogen levels 3 days post transplant compared with those kidneys treated with placebo. Furthermore, kidney health at 2 weeks post transplant improved, as indicated by a reduced incidence and/or severity of IRI-related histopathological findings, including tubular regeneration, kidney enlargement, and discoloration, which were associated with reduced kidney weight. In several human endothelial cell types, C3 fixation was consistently dependent on C2 presence and could be prevented by anti-C2 mAb treatment in a dose-dependent manner.

Conclusions: We confirmed in preclinical models that C2 is a suitable target to prevent complement-induced IRI and subsequent DGF after kidney transplant.

PP_098 UNVEILING PROTEINURIA IN POTENTIAL KIDNEY DONORS: KEY BIOPSY INSIGHTS FOR RENAL DONOR SELECTION

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Background: Proteinuria remains a controversial marker in kidney donor evaluation, often resulting in the exclusion of candidates without further diagnostic exploration. While low levels of proteinuria may not necessarily indicate significant kidney pathology, its presence raises concerns about long-term donor health and graft outcomes. Understanding proteinuria's histopathological (HP) and ultrastructural (US) correlations is crucial to refining donor selection criteria and ensuring donor safety and transplant success.

Methods: HP and US findings were evaluated in 70 renal donor candidates with proteinuria. Donors with insignificant biopsy findings were divided into two groups: Group 1 (<300 mg/day) and Group 2 (≥300 mg/day). Renal allograft survival data for recipients and post-transplant renal health of donors were also assessed.

Results: Biopsy results revealed 35 donors with glomerulonephritis (GN) and 2 with tubulointerstitial nephritis (TIN), while 33 had insignificant findings. Proteinuria levels were higher in donors with GN and TIN (557±363 mg/day) compared to those with insignificant biopsy findings (304±105 mg/day, $p<0.001$). HP and US scores were highest in Group 2 ($p<0.01$), with significant differences between both groups ($p<0.001$). Of the 33 donors, 21 donated kidneys. The 5- and 10-year graft survival for kidney transplant recipients was 90% and 80%, respectively. Donor renal function remained normal post-transplant.

Conclusions: Our study highlights the critical role of proteinuria as a marker of glomerular pathology and renal disease. While kidneys from donors with low HP and US scores are generally considered suitable for donation, caution is recommended for those with proteinuria exceeding 300 mg/day. We suggest incorporating renal biopsy into the assessment process for all proteinuric donors to ensure a thorough evaluation of potential risks, ultimately improving the outcomes of kidney transplantation.

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PP_099 USE OF ORGAN FROM MARGINAL DONOR DURING THE WAR: EXTENDED DONOR CRITERIA IN HEART TRANSPLANTATION

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Background: Heart transplantation is a life-saving procedure for patients with end-stage heart failure. The critical shortage of donor organs, martial law in Ukraine, the inability to deliver donor heart safely and promptly due to check-points on the roads and closed airspace have compelled us to change logistical approaches to transplant organization. This led to expand the criteria for selecting donor hearts using the so-called “marginal donors.” Due to the use of marginal donor heart can increase the donor organ pool by 40%.

Methods: We analyzed the outcomes of patients who underwent orthotopic heart transplantation during the period of martial law from February 2022 to September 2024. All donor hearts were obtained from donors with brain death. The results of transplantation of 48 patients who were transplanted with marginal donor hearts were evaluated (total number 106). Marginal donor heart included: donor hearts with coronary artery stenosis, with mitral valve insufficiency, with congenital heart disease, use normothermic regional perfusion in donor, prolonged cold ischemia time, inconsistency of the mass- height index.

Results: During the period of martial law, 106 orthotopic heart transplantations were performed. In the marginal donor group, the average cold heart ischemic time was ±5 min (63-386) min, CPB time was ±107 min (95-124), lung ventilation time was ±5 hs and ICU length of stay - ±5 days. Hospital survival was 85%, while 1-year survival was 81% and comparable in the marginal vs. non-marginal groups. The most common postoperative complication was primary graft dysfunction, while infectious complications predominated in the long-term period.

Conclusions: The results of our study demonstrated the feasibility of successful heart transplantations during wartime – even with marginal donor hearts. The use of marginal donor hearts can be successful in cases of timely and effective correction. Our results are encouraging, follow – up is ongoing.

PP_101 PREDICTORS OF GRAFT OUTCOMES OF KIDNEY TRANSPLANT FROM DONORS FROM ACUTE KIDNEY INJURY. A NHSBT REGISTRY DATA ANALYSIS

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Objectives: To identify risk factors associated with one-year graft failure in recipients of deceased donor kidneys with acute kidney injury (AKI) through multivariate analysis.

Design: A retrospective cohort study utilizing time-to-event analysis and hierarchical modeling.

Setting: Analysis of comprehensive data from the UK National Transplant Database, incorporating longitudinal outcomes.

Participants: A cohort of 856 adult recipients (≥18 years) of deceased donor kidneys with AKI, transplanted between January 2000 and December 2019, with complete follow-up data (loss to follow-up <3%).

Main outcome measures: Primary outcome was graft failure at 1 year post-transplant, defined by a composite endpoint of dialysis requirement, re-transplantation, or death with functioning graft. Time-to-event analysis was performed with competing risk assessment.

Methods: Multivariate Cox proportional hazards regression with robust variance estimation was employed, incorporating interaction terms and spline functions for continuous variables. Model discrimination was assessed using Harrell's C-statistic (0.82, 95% CI 0.79-0.85). Propensity score matching was utilized to minimize selection bias.

Results: Using stepwise regression and bootstrap validation (1000 iterations), significant predictors of graft failure emerged. AKI severity demonstrated a dose-dependent relationship with failure risk: Stage 2 (aHR=1.21, 95% CI 1.02-1.44, p=0.028) and Stage 3 (aHR=1.41, 95% CI 1.12-1.78, p=0.003) versus Stage 1. Additional independent predictors included prolonged cold ischemia time >550 minutes (aHR=1.04 per minute, 95% CI 1.03-1.05, p<0.001), elevated donor terminal creatinine >221 µmol/L (aOR=1.24, 95% CI 1.08-1.43, p=0.002), donor-recipient age disparity >10 years in recipients >50 years (aHR=1.28, 95% CI 1.06-1.53, p=0.009) and donor comorbidities (joint $\chi 2=15.3$, p<0.01).

Conclusions: This robust statistical analysis identifies key predictors of one-year graft failure in AKI kidney transplantation, providing an evidence-based framework for organ allocation and risk stratification.

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PP_102 EFFECT OF A MITOCHONDRIAL ANTIOXIDANT THERAPY, UBIQUINONE, IN PORCINE PRECISION CUT-KIDNEY SLICES

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Background: During the process of ischemia-reperfusion injury (IRI), the transient shortage of oxygen and nutrients leads to formation of reactive oxygen species (ROS) that are primarily produced in the mitochondria. Oxidative stress, or the disbalance between large amounts of ROS and reduced quantities of antioxidants, is associated with inferior graft and patient outcomes. Therefore, scavenging ROS with a mitochondrial antioxidant therapy, like ubiquinone, prior to transplantation could be an interesting strategy to improve preservation and ultimately graft function. The aim of this study was to find the optimal dosing range for kidney tissue in a pre-clinical animal precision-cut kidney slices (PCKS) model.

Methods: Porcine kidneys endured 30 min of warm ischemia and thereafter were preserved on oxygenated hypothermic machine perfusion. PCKS were created from cortex biopsies and incubated with ubiquinone (MitoQ), in various concentrations (0.1, 0.5, 1.0, 5.0 and 10.0 µmol/L) during the first 24 hours of incubation, either an oxygenated hypothermic or normothermic set-up. This was followed by 24 hours of normothermic incubation. Primary endpoint was real-time mitochondrial respiration, measured by high-resolution respirometry. Secondary endpoints were tissue ATP, TBARS, and incubation medium injury markers (LDH and ASAT). Statistical analyses were performed using a two-way ANOVA or Kruskal Wallis test.

Results: Mitochondrial maximum respiration and maximal respiratory capacity was significantly higher in 0.1 µmol/L MitoQ treated PCKS after 24 hours of normothermic incubation compared to control and PCKS treated with >0.5 µmol/L. Treatments groups of <1 µmol/L had comparable levels of tissue ATP, TBARS and incubation medium LDH and ASAT levels (P>0.05). PCKS treated with 5 and 10 µmol/L had significant inferior function in all endpoints (P<0.05).

Conclusions: Treatment with 0.1 umol/L MitoQ in normothermic conditions shows superior mitochondrial functioning of in the PCKS compared to control. However, MitoQ administration of >5umol/L showed tissue toxicity and emphasizes the importance of this dose-finding study in a pre-clinical animal model. Future studies using pre-clinical machine perfusion studies are needed, to include kidney functions like filtration and reabsorption.

PP_103 DONATION AFTER CIRCULATORY DEATH: THE SWISS PERSPECTIVE ON A POTENTIAL WITH CHALLENGES

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[1]Swisstransplant

Background: Since September 1st 2011 donation after circulatory death (DCD) has resumed in Switzerland after the DCD program had been halted for a four-year period due to jurisdictional and medico-ethical discrepancies. This form of organ donation has gained in relevance due to the scarcity of donated organs and now accounts for nearly half of all donations in the Swiss transplant setting. This study assesses the data of Swiss controlled DCD (cDCD) donors from 1.09.2011 to 31.08.2024 and compares the procurement techniques rapid procurement (RP) and normothermic regional perfusion (NRP) as well as the organ preservation techniques static cold storage (SCS) and hypothermic machine perfusion (HMP). Functional warm (fWIT) and cold ischemia time (CIT), organ utilization rates (OUR) and early outcome are analyzed as endpoints.

Methods: 664 cDCD donors were included within the time frame mentioned. Donor characteristics and recipient data were exported from the Swiss Organ Allocation System (SOAS). Subgroup analysis was performed for procurement and preservation technique and tested for statistical significance using Chi-Square-, Fisher- and Prop-Test.

Results: Of 499 utilized cDCD organ donors, 416 (83.4%) donors were procured using RP and 82 (16.4%) using NRP. 68.9% were male. The median cDCD donor was male, 60.0 years old, 174.0 cm tall, weighted 80.0 kg and had a BMI of 25.8 kg/m^2. Median FWIT was 26.0 minutes, without any differences in the subgroups RP and NRP. In kidney transplants delayed graft function (DGF) occurred significantly more often in RP versus NRP (54.7% versus 19.8%). Primary nonfunction (PNF) was more common in liver transplants procured using RP than NRP (4.7% versus 1.6%). The OUR of liver transplants was significantly lower in RP versus NRP (0.62 versus 0.76, inclusion of effective donors).

Conclusions: Patient characteristics in the subgroups RP and NRP were comparable. NRP had a positive effect on early outcome and OUR in kidney and especially liver transplants. While HMP impacted early kidney transplant outcomes slightly positively, the same effect could not be proven for liver transplants.

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PP_104 HYPEROXYGENATION OF PRESERVATION SOLUTION IN DCD DONORS UNDERGOING NORMOTHERMIC REGIONAL PERFUSION

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Background: The organs of donors undergoing circulatory determination of death (DCDDs) and abdominal normothermic regional perfusion (A-NRP) are exposed to a period of static cold storage (SCS) before ex-vivo machine perfusion and/or transplantation. Intravascular cooling is ussually induced through the administration of a high volume of cold preservation solution (CPS) by gravity. The NRP circuit may be employed to infuse and oxygenate CPS, ensuring a controlled flow and increasing dissolved oxygen (O_2) in a hemoglobin-free perfusate. Providing O_2 to the tissues may have a synergistic effect with CPS in limiting the damages which grafts may sustain due to ischemia and hypothermia.

Methods: We aimed to assess feasibility and effectiveness of increasing CPS partial pressure of O_2 ($P_{CPS}O_2$) in controlled DCDDs undergoing A-NRP. Immediately after interrupting NRP, CPS was actively administered through the circuit, accompanied by a flow of O_2 to the membrane lung (ML). The CPS flow was set at 0.4 LPM if body surface area ≤1.7, or 0.5 if >1.7, with 1:1 CPS to gas flow ratio. We measured $P_{CPS}O_2$ at the beginning and at the and of CPS administration.

Results: We implemented this approach in 11 DCDDs (table). A median $P_{CPS}O_2$ of 646 mmHg (IQR 90.75), was achieved in all samples. Mean and median $P_{CPS}O_2$ were consistently above 600 mmHg for Celsior® and IGL-1® samples. Mean $P_{CPS}O_2$ was 500 mmHg with Belzer UW® solution, administered in one donor; this is still compliant with hyperoxygenation definition. Mean/median $P_{CPS}O_2$ were consistently above 600 mmHg for all circuits, independently from these integrating polypropylene (PP) or polymethylpentene (PMP) MLs. Hyperoxygenation was stable throughout CPS administration (5-8 L). $P_{CPS}O_2$ in samples from bags before administration was below 100 mmHg. Median $P_{CPS}O_2$ in controls samples infused through the circuit across ML fibers, but without O_2 flow, was 187 mmHg (IQR 45).

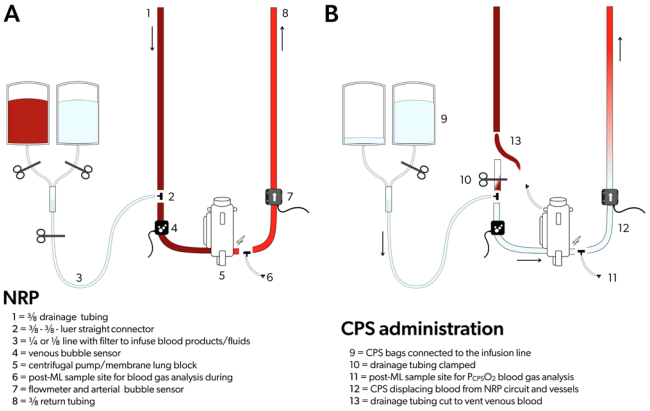
Conclusions: The infusion of an oxygenated CPS through the extracorporeal circuit empoyed for NRP could be feasible and effective in ensuring a consistent CPS flow, and in enhancing the amount of dissolved oxygen. The oxygenation of a cold perfusate devoid of red blood cells may still provide organs with a metabolic substrate before SCS. This approach requires same equipment used for NRP, with no increase in procedure related costs.

CPS administration through NRP circuit

Circuit Type	ML	CPS type	$P_{CPS}O_2$ mm Hg Initial	$P_{CPS}O_2$ mm Hg Final	volume (L)	flow (LPM)	SGF (LPM)	FsO_2	Mechanical Complications	Portal Vein infusion (by gravity) volume (L)	Organs considered for Procurement/ Transplantation Liver	Kidney
BE-MECC	PP	Celsior®	479	649	6	0,4	0.4	1	NO	2	P/T	P/T
BE-MECC	PP	IGL-1®	747	583	7	0.5	0.5	1	NO	-	P/T	P/T
BE-MECC	PP	IGL-1®	648	658	7	0.4	0.4	1	NO	2	P/T	-
BE-MECC	PP	IGL-1®	714	671	7	0.5	0.5	1	NO	1	P/T	P/-
BE-MECC	PP	Celsior®	765	723	8	0.5	0.5	1	NO	-	-	P/T
HLS 7050	PMP	IGL-1®	587	644	6	0.5	0.5	1	minor air entrance	2	P/T	P/T
BE-MECC	PP	Celsior®	618	641	7	0.5	0.5	1	NO	2	P/T	P/T
HLS 7050	PMP	IGL-1®	547	619	6	0.5	0.5	1	NO	2	P/T	P/-
Euroset AMG PP1	PP	Belzer UW ®	454	547	7	0.5	0.5	1	NO	2	P/T	P/T
HLS 7050	PMP	IGL-1®	602	660	5	0.5	0.5	1	NO	2	P/T	P/T
HLS 7050	PMP	Celsior®	683	681	7	0.5	0.5	1	NO	2	P/T	P/-

	Overall n = 22	Initial n = 11	Final n = 11	Celsior® n = 4	IGL-1® n = 6	Belzer® n = 1	PP ML n = 7	PMP ML n = 4
$P_{CPS}O_2$ mm Hg mean (SD)	632.7 (±78.6)	622.2 (±102.4)	643.3 (±47.5)	654.9 (±85.2)	640.0 (±56.6)	500.5*	635.5 (±93.4)	631.5 (±48)
$P_{CPS}O_2$ mm Hg median (IQR)	646 (90.75)	618 (131.5)	649 (38.25)	665 (57.75)	646 (64.5)	-	648.5 (111.5)	648.5 (67)

CPS, cold preservation solution; IQR, interquartile range; LPM, later per minute; ML, membrane lung; NRP, normothermic regional perfusion; $P_{CPS}O_2$, partial pressure of oxygen in the CPS; P, procured; PP, polypropylene; SD, standard deviation; T, transplanted. * Only administered once during the study period.



NRP

1 = ⅜ drainage tubing
2 = ⅜ - ⅜ - luer straight connector
3 = ¼ or ⅛ line with filter to infuse blood products/fluids
4 = venous bubble sensor
5 = centrifugal pump/membrane lung block
6 = post-ML sample site for blood gas analysis during
7 = flowmeter and arterial bubble sensor
8 = ⅜ return tubing

CPS administration

9 = CPS bags connected to the infusion line
10 = drainage tubing clamped
11 = post-ML sample site for $P_{CPS}O_2$ blood gas analysis
12 = CPS displacing blood from NRP circuit and vessels
13 = drainage tubing cut to vent venous blood

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PP_105 VASOREACTIVITY AS A MEASURE OF KIDNEY VIABILITY DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) could serve as a platform to assess deceased-donor kidney viability before transplantation, yet it remains unclear which parameters indicate renal viability. As vascular integrity is important for adequate renal function after transplantation, this study aimed to investigate the influence of warm ischemic injury on vascular smooth muscle cell (VSMC) responsiveness to vasoactive drugs during NMP.

Methods: Fourteen porcine kidneys (n=7 per group) were exposed to either 30 or 60 minutes of warm ischemia (WI), followed by 3.5 hours of cold machine perfusion. After cold perfusion, kidneys underwent 4 hours of NMP (37°C). During NMP, vasoactive drugs were sequentially infused into the renal artery at 30-minute intervals, starting with epoprostenol (10 µg), followed by dopamine (1 mg), sodium nitroprusside (2 mg), acetylcholine (1 mg), norepinephrine (10 µg), and finally verapamil (2.5 mg).

Results: Renal blood flow during NMP changed significantly in both groups after administration of dopamine, acetylcholine, norepinephrine, and verapamil, but not following epoprostenol and sodium nitroprusside infusion (Figure 1). In kidneys subjected to 30 minutes of WI, the response to dopamine and norepinephrine was more pronounced, and oxygen consumption and blood pH were higher compared to kidneys that sustained 60 minutes of WI.

Conclusions: This study indicates that prolonged warm ischemic damage diminishes the contractility of VSMCs through the α-adrenergic receptors. Our findings suggest that the renal vascular response to dopamine and norepinephrine, as well as decreased oxygen consumption and blood pH, could serve as objective indicators to quantify warm ischemic injury during renal NMP.

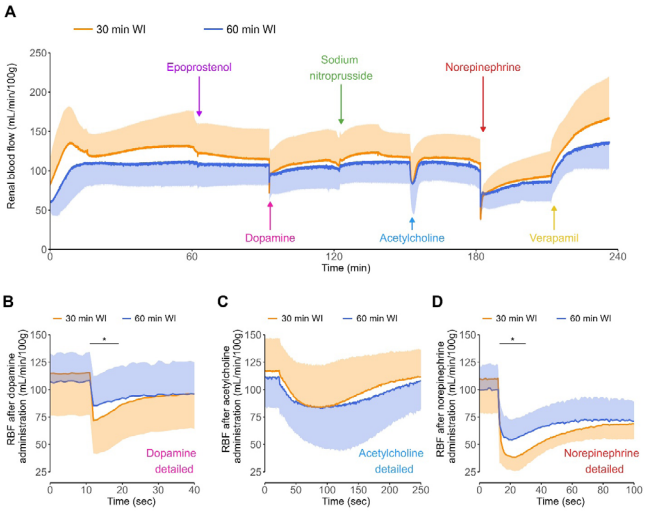

Figure 1. Renal blood flow (A), and changes in RBF after dopamine (B), acetylcholine (C) and norepinephrine (D) administration, during normothermic machine perfusion. Means and standard deviations are shown. RBF, renal blood flow; WI, warm ischemia. *P<0.05.

PP_106 POST-TRANSPLANT HEALTH-ECONOMIC IMPACT OF NMP (BACK-TO-BASE MODEL) IN DCD LIVER TRANSPLANTATION

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Background: The widespread use of normothermic machine perfusion (NMP) has enabled greater utilization of donation after circulatory death (DCD) liver grafts for transplantation. Use of NMP can cost an additional $40,000 – $100,000 USD. The aim of our study was to see if the use of NMP would lower post-operative costs after DCD liver transplantation (LT).

Methods: Retrospective data of all DCD LTs performed at our center between 08/19/2022 and 05/31/2024 were analyzed. The OrganOx Metra device, back-to-base, was used for NMP at our center. UNOS data were used to present national DCD LT volumes and waitlist outcomes.

Results: Sixty-seven NMP and 44 static cold storage (SCS) transplants were performed. In the NMP group, donors were older (50 vs 45 years, p=0.0260), were of increased risk (US donor risk index 2.43 vs 2.12, p=0.006), incidence of early allograft dysfunction (42% vs 75%, p=0.0008) and post-reperfusion syndrome (25% vs 48%, p=0.0239) was lower, and recipients had better native kidney function at 3 months (estimated glomerular filtration rate 73 vs 62, mL/min/1.73 m^2, p=0.0205). Use of NMP did not decrease post-operative costs. On multivariate analysis, an additional 56 min of cold ischemic time increased post-operative costs by $14,300 USD (p=0.01) (figure1).

Conclusions: Use of NMP does not decrease post operative direct costs after DCD LT. But with the use of NMP, greater number of DCD liver grafts can be used, from a broader range of donors, wait time to transplant can be reduced and waitlist survival can be improved, while improving relevant clinical outcomes.

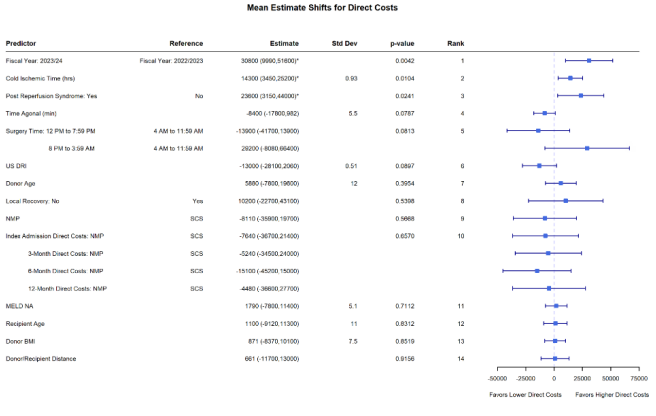

Figure 1: Forest plot of multivariate analysis depicting mean shift in cumulative postoperative direct costs

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PP_107 BENEFITS OF PROLONGED HYPOTHERMIC MACHINE PERFUSION IN KIDNEY TRANSPLANTS

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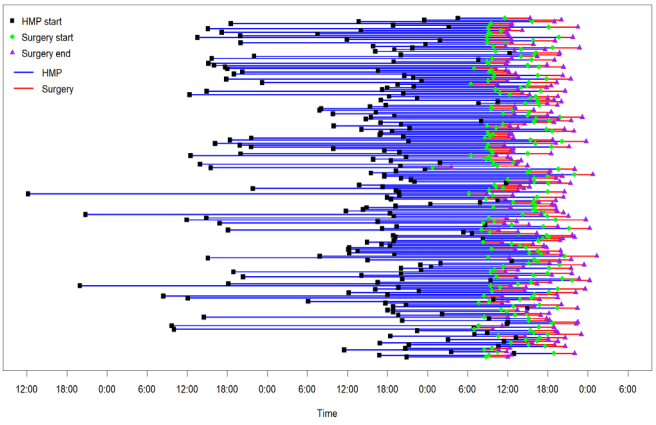
Background: Kidney transplant (KT) timing is affected by factors like organ transport, biopsy analysis, and recipient preparation, complicating scheduling. Hypothermic machine perfusion (HMP) offers a solution to logistical constraints by enabling prolonged kidney preservation and facilitating KTs during elective surgery hours. This study aims to evaluate the impact of prolonged HMP on transplant outcomes.

Methods: We retrospectively analyzed KTs preserved with HMP at our center from April 2017 to December 2023. The Youden Index identified the optimal HMP duration threshold. Univariable and multivariable logistic regression assessed associations between HMP duration, delayed graft function (DGF), and 1-year graft survival.

Results: A total of 197 KTs were analyzed. No adverse events attributable to HMP use were observed. The median duration of static cold storage was 10h, while the median duration of HMP was 20h. Notably, 83% of the KTs were performed during daytime surgery hours (8:00 AM – 8:00 PM), without affecting the schedule for the next day (**Figure**). DGF occurred in 24.9% of cases, and 1-year graft survival was 85%. The optimal threshold for HMP duration was identified as 9h 53min, beyond which kidneys showed a 70.3% reduction in the incidence of DGF (p=0.006). Multivariable logistic regression, adjusted for potential donor and recipient confounders, confirmed that extended HMP duration was independently associated with a significant reduction in DGF (p=0.002).

Conclusions: Our findings indicate that prolonged HMP for KTs is feasible and safe. Extending cold preservation by maintaining kidneys in HMP resolves logistical challenges without adversely affecting transplant outcomes. Furthermore, prolonged HMP seems associated to a reduction in the risk of DGF.



PP_108 MONITORING LIVER VIABILITY: FLUORESCENCE SPECTROSCOPY OF CELLULAR METABOLITES IN ISCHEMIA-REPERFUSION

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Background: The assessment of liver graft viability is crucial for improving transplantation outcomes. Mitochondrial function, a key determinant of graft quality, can be evaluated through the fluorescence of metabolites such as Flavin Adenine Dinucleotide (FAD) and Nicotinamide adenine dinucleotide (NADH). This study investigates the use of fluorescence spectroscopy to monitor mitochondrial function in a porcine ischemia-reperfusion model, aiming to establish a non-invasive tool for graft evaluation and graft monitoring on perfusion machine.

Methods: Fluorescence measurements were acquired using a homebuilt experimental setup. This study includes 11 pigs with an ischemia-reperfusion protocol separated in 2 groups. One group of 7 pigs underwent the protocol described in Figure 1. A control group composed of 4 pigs underwent this protocol without the one hour warm ischemia. Fluorescence acquisitions were done during all the steps of this protocol in tissue and in perfusate during hypothermia perfusion.

Results: Fluorescence spectroscopy provided dynamic measurements of FAD and NADH concentration during ischemia and reperfusion in porcine livers. The observed fluorescence changes were consistent with expected mitochondrial metabolic shifts. The optical redox ratio, defined as [FAD]/ [FAD]+[NADH], increased during ischemia and decreased during reperfusion, indicating an NADH accumulation during ischemia and consumption during reperfusion. Livers with one hour warm ischemia showed a significative different fluorescence signal compared to the control group, indicating the ability of the method to track oxidative stress in real-time. Perfusate fluorescence showed an inverse correlation with tissue fluorescence indicating that the origin of FAD and NADH is a leakage from liver cells. This validates that perfusate fluorescence could be a biomarker of liver injury.

Conclusions: This study demonstrates the potential of fluorescence spectroscopy for non-invasive monitoring of mitochondrial function in liver grafts. The method aligns with known mitochondrial behavior during ischemia-reperfusion and could enhance graft viability assessment, contributing to better transplantation outcomes.

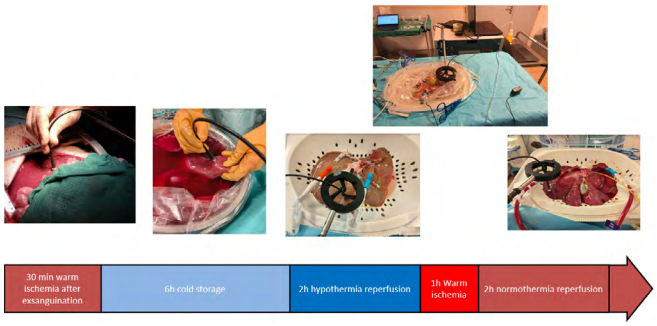

Figure 1. Ischemia reperfusion protocol with fluorescence measurement performed at each step

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PP_110 OUTCOMES OF KIDNEY DONORS WITH THIN BASEMENT MEMBRANE NEPHROPATHY

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Background: Thin basement membrane nephropathy (TBMN) in potential kidney donors, is sometimes a reason for exclusion from kidney donation. This study aimed to assess the outcomes of kidney donors diagnosed with TBMN.

Methods: Kidney donors who underwent biopsy for hematuria and subsequently donated kidneys between January 2016 and May 2024 were included. Donors were categorized into “Normal Biopsy” group and “TBMN” group. We evaluated pre- and post-donation (at the last clinic visit) clinical parameters.

Results: A total of 271 potential donors underwent kidney biopsy for microscopic hematuria. A total of 93 kidney donors who eventually donated the kidneys were included. Among these 65% were male and the mean age was 37y. The mean follow-up was 817 days (6 months to 8.5 years). Pre- and post-donation systolic blood pressure (SBP) remained similar (p = 0.24), as did diastolic blood pressure (DBP) (p = 0.10). Pre-donation serum creatinine increased from75µmol/L to 104µmol/L post-donation (p < 0.001). Among the 93 donors, 54 had normal biopsies, and 39 were diagnosed with TBMN. There were no significant differences between the two groups in terms of BP, serum creatinine levels, or changes in these measures before and after donation (Table). Post-donation urine albumin creatinine ratio was comparable between the two groups (0.81 ± 0.78 vs. 1.6 ± 2.9, p = 0.19).

Conclusions: Short-term outcomes between TBMN group were similar to the normal biopsy group. Further research is necessary to evaluate the long-term outcomes for donors with TBMN.

Variables	All	Normal Biopsy	TBMN	P value
Total	93	54	39	
Mean Systolic Blood Pressure mmHg (SD)				
Pre-donation	119.3 (8.8)	119.3 (8.3)	119.2 (9.6)	0.96
*Post-donation	121.2 (13.2)	120.4 (14.1)	122.3 (11.9)	0.50
BP Change *Post-donation	3.3 (17.8)	1.1 (14.3)	3.3 (11)	0.43
Mean Diastolic Blood Pressure mmHg (SD)				
Pre-donation	75.1 (7.8)	74.9 (8.1)	75.3 (7.5)	0.83
*Post-donation	77.0 (8.2)	76.4 (8.8)	77.9 (7.8)	0.42
BP Change *Post-donation	2.9 (12.7)	1.5 (9.2)	2.7 (10.8)	0.56
Mean Creatinine µmol/l (SD)				
Pre-donation	74.7 (15.1)	77.3 (14.7)	71.1 (15.1)	0.05
*Post-donation	104.1 (22.9)	106.3 (23.3)	101.0 (22.2)	0.27

*At last follow-up

PP_111 DCD LIVER TRANSPLANTATION WITHOUT MACHINE PERFUSION IN THE SETTING OF 20 MINUTES NO TOUCH PERIOD

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Background: In Italy, a 20-minute flat-line electrocardiogram is required for death declaration, raising the risks of liver transplantation (LT) after circulatory death (DCD). To mitigate warm ischemia time, normothermic regional perfusion (NRP) combined with end-ischemic machine perfusion (MP) has shown promising results, but data on DCD donation without end-ischemic MP are limited.

Methods: This study reports on controlled DCD (cDCD) LT using NRP followed by static cold storage (SCS) alone, comparing results with a control group using NRP plus dual hypothermic machine perfusion (D-HOPE MP).

Results: The analysis included 23 cDCD LTs performed from November 2021 to October 2024. Fourteen LTs were done with NRP alone, and nine with NRP + D-HOPE MP. Donor and recipient characteristics were comparable, although the control group had a higher MELD-Na score (23 vs. 17, p=0.64). Functional warm ischemia times were similar between the groups (36 vs. 39 minutes, p=0.18). All donors showed lactate clearance during NRP, with a larger drop in the NRP-alone group (5 mmol/L vs. 2.2 mmol/L, p=0.2). NRP duration was longer in the NRP-alone group (209 vs. 169 minutes, p<0.05), while total preservation time was shorter (188 vs. 277 minutes, p<0.05). There were no primary non-function cases in either group. Early allograft dysfunction was more frequent in the NRP-alone group (28.6% vs. 11.1%, p=0.33). One patient in the NRP-alone group died due to infection despite a functional graft. The biliary stricture rate was similar between the groups (22% vs. 21%, p=0.7), with median follow-ups of 11 months (5–17) and 30 months (3–42), respectively.

Conclusions: Our initial experience suggests that cDCD LT with NRP and SCS is not inferior to NRP plus end-ischemic D-HOPE MP, even in Italy’s 20-minute no-touch period. With careful management of NRP and coordination between procurement and transplant teams, this strategy may be an effective preservation approach in cDCD liver transplantation.

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PP_112 LEUKOCYTE REMOVAL REDUCES INFLAMMATORY GENE EXPRESSION IN LIVERS UNDERGOING NORMOTHERMIC PERFUSIONS

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Background: Ex situ normothermic perfusion (ESNP) is a method to evaluate and potentially recondition organs before transplantation. However, increased expression of inflammatory molecules, including by tissue-resident immune cells, may occur during the perfusion process, potentially negating the beneficial effects of perfusion.

Methods: We used RNA sequencing to assess gene expression in 31 livers undergoing ESNP, including 23 donated after circulatory death (DCD) and 8 donated after brain death. In 7 DCD livers, a leucocyte filter was added to the circuit during perfusion. Biopsies were available for transcriptomic assessment in all cases at the start of perfusion and at varying time points postperfusion.

Results: During ESNP in DCD livers, we observed an increase in proinflammatory, profibrinolytic, and prorepair pathway genes. *SERPINE1*, encoding plasminogen activator inhibitor-1, was among the genes most significantly upregulated during perfusion in DCD livers, potentially promoting fibrin clot persistence in vasculature. We also found increased expression of monocyte and neutrophil recruiting chemokine and proinflammatory cytokine transcripts during ESNP, but several prorepair molecules, including thymic stromal lymphopoietin, were also upregulated. In both DCD and donation after brain death livers, interferon-gamma response genes were enriched, whereas oxidative phosphorylation genes decreased in organs with high perfusate alanine transaminase, a biomarker associated with adverse clinical outcomes. The inclusion of a leukocyte filter in the perfusion circuit mitigated the induction of inflammation/immune pathway genes during perfusion and was associated with enrichment in oxidative phosphorylation genes.

Conclusions: Leukocyte removal during ESNP abrogates transcriptional changes that are associated with unfavorable clinical outcomes, potentially benefiting human livers undergoing ESNP.

PP_113 NATIONAL IMPLEMENTATION OF HMP INCREASES LOCAL KIDNEY UTILISATION RATE AND IS HIGHLY COST-EFFECTIVENESS

Tom Darius[1], **Ina Jochmans**[2], **Maxime Foguenne**[3], **Eric Hoste**[4], **Caren Randon**[5], **Geert Roeyen**[6], **Bart Bracke**[7], **Olivier Detry**[8], **Laurent Weekers**[9], **Daniel Jacob's-Tulleneers-Thevissen**[10], **Tineke Bogaerts**[11], **Dimitri Mikhalski**[12], **Jean-Philippe De Wilde**[13], **Jacques Pirenne**[14]

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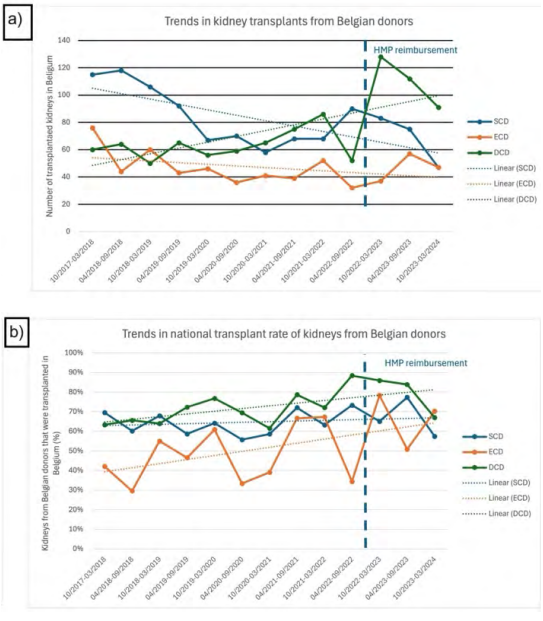
Background: Given the improved outcomes for higher-risk kidneys that are preserved by hypothermic machine perfusion (HMP), Belgium introduced reimbursement for this technique for expanded criteria donors (ECD) and kidneys donated after circulatory death (DCD) since 10/2022. The underlying hypothesis for reimbursement was to increase the national utilization rate of higher-risk kidneys from Belgian donors. This study presents the observed trends in national kidney transplantation rates of these kidneys before and after the reimbursement of HMP. We also present a cost-effectiveness analysis.

Methods: Data were retrospectively collected from Belgian donors transplanted between 10/2017 and 03/2024. Before 10/2022, the vast majority of these kidneys was preserved by cold storage.

Results: The national implementation of HMP resulted in 1) an increase of the total number of KT Belgian DCD and ECD donors regardless of donor age (Figure 1a), 2) an important increase in national transplantation rate (Figure 1b). The observed increase was more pronounced in the donor age groups between 50 and 65 years old and above 65 years, but not for DCD kidneys with donor age below the age of 50. 3) The cost-effectiveness was 4.365.651€ saved 1 year after its implementation (based on costs of HMP (3500€/procedure) and dialysis (44.932€/year/patient) but excluding hospitalization and immunosuppressive treatment costs during the first year).

Conclusions: The reimbursement and nationwide implementation of HMP for kidneys procured in Belgium resulted in an important increase of the national transplantation rate of ECD and DCD kidneys and was highly cost-effectiveness.



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PP_114 GLOBAL OUTCOMES WITH EXTENDED CRITERIA DONORS: AN UPDATED ANALYSIS OF THE INTERNATIONAL GUARDIAN HEART REGISTRY

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Background: The number of patients with advanced heart failure needing a heart transplant is increasing globally, while the number of donor hearts remains limited. Expansion of the donor pool is an increasingly important option in cardiac transplantation. Use of a static controlled hypothermic transport system (SCTS) has previously shown significant benefits in analyses of US data in the GUARDIAN-heart registry. With the recent publication of the EXPAND OCS trial results, we seek to further analyze the impact of the SCTS system on recipient outcomes who receive these extended criteria organs in the global data in the GUARDIAN registry, as the use of extended criteria donors is greater in the EU population.

Methods: A total adults 568 adults from 25 centers in the US and Europe SCTS (N=357) or historic ice storage (ICE, N=211) enrolled in the GUARDIAN-heart registry were found to meet the modified EXPAND OCS Trial criteria as extended criteria donors (see Table).

Results: There were a few baseline differences among recipients in the 2 cohorts, most notably both distance traveled and total ischemic time was significantly greater in SCTS, and significantly more donor hearts in the SCTS cohort were bridged with ECMO, although durable VADs were more frequent in the ICE cohort (see Table). Post-transplant MCS utilization, PGD, severe PGD and severe RVD were all significantly reduced in hearts preserved using CTS. Propensity matching using the extended donor criteria resulted in similar baseline characteristics, including durable VADs and ECMO, yet the post-transplant significant benefits remained.

Conclusions: This global subgroup analysis of the GUARDIAN registry demonstrates that SCTS at 4-8°C can be used to optimize post-transplant outcomes when using extended criteria donors, with low post-transplant adverse events despite significantly longer ischemic times.

Table:

	Overall			Propensity Matched#		
	ICE	SCTS		ICE	SCTS	
	n = 211	n = 357	*p-value*	n = 185	n = 185	*p-value*
Donor Inclusion Criteria						
>4h Total Ischemic Time	**106 / 211 (50.2%)**	**253 / 357 (70.9%)**	**<0.001**	106 / 185 (57.3%)	107 / 185 (57.8%)	>0.99
>2h Total Ischemic Time AND						
Age > 55 years	18 / 211 (8.5%)	26 / 357 (7.3%)	0.63	14 / 185 (7.6%)	14 / 185 (7.6%)	>0.99
Downtime > 20 mins	37 / 211 (17.5%)	56 / 357 (15.7%)	0.56	29 / 185 (15.7%)	29 / 185 (15.7%)	>0.99
LVEF 40-50%	44 / 211 (20.9%)	61 / 357 (17.1%)	0.27	38 / 185 (20.5%)	37 / 185 (20.0%)	>0.90
LVPW 12-16 mm	**30 / 211 (14.2%)**	**31 / 357 (8.7%)**	**0.049**	21 / 185 (11.4%)	21 / 185 (11.4%)	>0.99
Luminal Irregularities	5 / 211 (2.4%)	13 / 357 (3.6%)	0.47	3 / 185 (1.6%)	3 / 185 (1.6%)	>0.99
Donor Characteristics						
Donor Age (years)	35.4 ± 12.2	35.2 ± 11.1	0.83	34.8 ± 12.2	35.0 ± 11.5	0.90
Donor BMI (kg/m²)	28.4 ± 6.7	28.2 ± 6.9	0.71	27.8 ± 6.3	28.4 ± 7.4	0.39
Recipient Characteristics						
Recipient Age (years)	53.7 ± 11.7	55.6 ± 12.6	0.069	53.5 ± 11.9	55.6 ± 12.6	0.096
Recipient BMI (kg/m²)	27.7 ± 4.6	27.7 ± 4.8	0.93	27.5 ± 4.6	27.9 ± 4.8	0.44
Implantable VAD	**87 / 211 (41.2%)**	**97 / 357 (27.2%)**	**<0.001**	65 / 185 (35.1%)	66 / 185 (35.7%)	>0.99
Temporary IABP	36 / 211 (17.1%)	75 / 357 (21.0%)	0.27	34 / 185 (18.4%)	36 / 185 (19.5%)	0.89
Temporary ECMO/VAD	**15 / 211 (7.1%)**	**59 / 357 (16.5%)**	**0.001**	15 / 185 (8.1%)	18 / 185 (9.7%)	0.72
Waitlist Days	**178.0 ± 302.5**	**122.1 ± 324.5**	**0.039**	163.6 ± 298.7	136.8 ± 323.3	0.41
Match Characteristics						
F/M Mismatch	29 / 211 (13.7%)	45 / 357 (12.6%)	0.70	23 / 185 (12.4%)	28 / 185 (15.1%)	0.55
Distance to Organ (miles*)	**355 ± 301**	**561 ± 395**	**<0.001**	**385 ± 306**	**534 ± 375**	**<0.001**
Total Ischemic Time (hours)	**3.7 ± 0.9**	**4.3 ± 0.9**	**<0.001**	3.9 ± 0.9	4.0 ± 0.9	0.070
Average Temperature	**NA (<0°C)**	**5.5 ± 2.4°C**	--	NA (<0°C)	5.6 ± 2.9	--
Post-transplant Outcomes						
All Post Tx MCS	**61 / 211 (28.9%)**	**68 / 357 (19.0%)**	**0.009**	**56 / 185 (30.3%)**	**38 / 185 (20.5%)**	**0.042**
Cardioversion	36 / 211 (17.1%)	46 / 357 (12.9%)	0.18	34 / 185 (18.4%)	20 / 185 (10.8%)	0.055
PGD	**57 / 211 (27.0%)**	**60 / 357 (16.8%)**	**0.005**	**49 / 185 (26.5%)**	**29 / 185 (15.7%)**	**0.015**
PGD Severe	**29 / 211 (13.7%)**	**26 / 357 (7.3%)**	**0.018**	**26 / 185 (14.1%)**	**12 / 185 (6.5%)**	**0.025**
RV-PGD	9 / 211 (4.3%)	7 / 354 (2.0%)	0.12	8 / 185 (4.3%)	2 / 185 (1.1%)	0.10
RV Normal at 24 hours	**77 / 191 (40.3%)**	**168 / 306 (54.9%)**	**0.002**	**65 / 168 (38.7%)**	**94 / 165 (57.0%)**	**<0.001**
RV Severely diminished	**27 / 191 (14.1%)**	**16 / 306 (5.2%)**	**<0.001**	**26 / 168 (15.5%)**	**7 / 165 (4.2%)**	**<0.001**
ICU LOS	12.7 ± 18.5	11.2 ± 16.0	0.31	12.1 ± 16.4	11.7 ± 15.2	0.84
Median (min, max)	6.0 (1.0, 128.0)	6.0 (0.0, 137.0)	0.19	6.0 (1.0, 110.0)	6.0 (1.0, 92.0)	0.73
Total Hospital LOS	29.4 ± 30.9	26.8 ± 28.1	0.31	27.9 ± 28.0	28.3 ± 30.1	0.88
Median (min, max)	20.0 (7.0, 268.0)	18.0 (6.0, 294.0)	0.061	19.0 (7.0, 268.0)	19.0 (7.0, 294.0)	0.72
In-hospital Survival	201 / 211 (95.3%)	350 / 357 (98.0%)	0.075	176 / 185 (95.1%)	180 / 185 (97.3%)	0.41
1-year Survival	194 / 211 (91.9%)	309 / 334 (92.5%)	0.87	171 / 185 (92.4%)	173 / 184 (94.0%)	0.68
2-year Survival	181 / 208 (87.0%)	261 / 294 (88.8%)	0.58	160 / 182 (87.9%)	161 / 180 (89.4%)	0.74

Abbreviations: BMI = body mass index; SCTS = (Paragonix) SherpaPak cardiac transport system; ECMO = extracorporeal membrane oxygenation; F/M mismatch = female to male mismatch; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; LVPW = left ventricular posterior wall; LOS = length of stay; MCS = mechanical circulatory support; PGD = primary graft dysfunction; PHM = predicted heart mass; Tx = transplant; VAD = ventricular assist device.
Continuous data presented as average ± standard deviation.
Cohorts were propensity matched using the extended criteria variables.
* miles are in nautical miles.

PP_115 LACTATE'S ROLE AS A POST-TRANSPLANT OUTCOME PREDICTOR DURING NORMOTHERMIC MACHINE PERFUSION

***Rebecca Panconesi*[1], Sangheeta Satish[2], Chase Wehrle[3], Keyue Sun[2], Mingyi Zhang[2], Chunbao Jiao[2], Omer Karakaya[2], Tobias Diwan[2], Geofia Crasta[2], Selin Fatma Yildirim[2], Khaled Ali[4], Beatrice Cazzaniga[3], Yuki Miyazaki[2], Liu Qiang[5], Charles Miller[5], Koji Hashimoto[5], Andrea Schlegel[6]**

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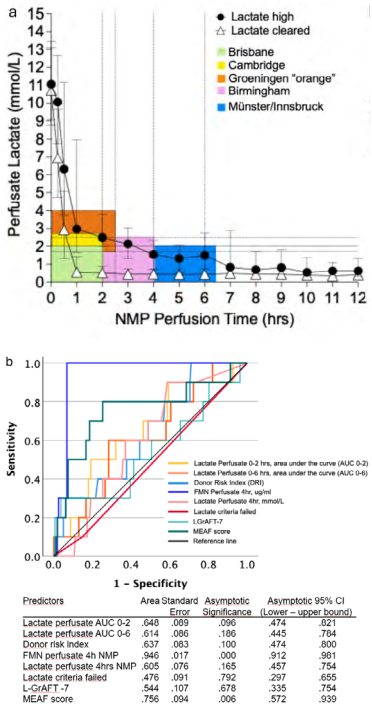
Background: The scarcity of donor organs has led to the increased use of extended criteria donors, which are associated with more complications and impaired survivals after liver transplantation. Machine perfusion techniques are increasingly used to improve and assess graft viability. Perfusate lactate clearance, albeit considered by many as important viability marker, lacks consensus on its predictive value.

Methods: Adult liver transplantations with prior normothermic machine perfusion (NMP) at our center between October 2022 and January 2024 were included. Perfusate lactate was quantified during NMP (EPOC-reader). Five proposed Lactate-viability criteria were assessed and their role predicting outcomes after liver transplantation (i.e., Groningen-, Birmingham-, Brisbane-, Cambridge-. Muenster)[1-5]

Results: Overall, 213 NMP livers were included in the study. The initially high perfusate Lactate (median: 10.76mmol/L; IQR:8.856 –13.09) was cleared by most grafts with median values of 0.51mmol/L (IQR:0.30 – 0.895) at 6h NMP. Only 33 livers did not meet any of the proposed lactate criteria (at 2, 2.5, 4 or 6hrs NMP). While only 13 of 213 livers were discarded at our center (6.1%), this percentage would have been significantly higher when following lactate criteria proposed by teams from Groningen (14.6%) or Brisbane (11.2%). Recipients of livers that did not fully clear lactate ("lactate high" group) had comparable outcomes to those with cleared lactate during NMP. Lactate levels played also no role predicting clinically relevant outcomes after liver transplantation (i.e., hospital stay, Clavien-Dindo-complications, CCI, biliary complications). Survival analysis showed no impact of Lactate clearance on death censored and overall graft survival and recipient survival. The AUC for lactate criteria was poor in ROC curve analyses (AUC:0.480). In contrast, the MEAF-score achieved a higher AUC (0.728) and perfusate Flavin-mononucleotide (FMN) at 4hours NMP had the highest AUC (0.948) with excellent prediction of graft survival (**Figure 1**).

Conclusions: The study underscores the limitations of lactate clearance as a solitary viability marker during NMP. Further research into more reliable biomarkers, including FMN, is needed to enhance graft selection and improve transplantation outcomes.



Predictors	Area	Standard Error	Asymptotic Significance	Asymptotic 95% CI (Lower – upper bound)	
Lactate perfusate AUC 0-2	.648	.089	.096	.474	.821
Lactate perfusate AUC 0-6	.614	.086	.186	.445	.784
Donor risk index	.637	.083	.100	.474	.800
FMN perfusate 4h NMP	.946	.017	.000	.912	.981
Lactate perfusate 4hrs NMP	.605	.076	.165	.457	.754
Lactate criteria failed	.476	.091	.792	.297	.655
L-GrAFT -7	.544	.107	.678	.335	.754
MEAF score	.756	.094	.006	.572	.939

Figure 1: Lactate Clearance and related Viability Criteria proposed by different Groups

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PP_117 HEPATICAN, A CRYOPRESERVABLE CELL THERAPY AND MEDICAL DEVICE TO RESCUE PATIENTS WITH LIVER FAILURE

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Background: Liver disease, is increasing worldwide. Transplantation is curative, but donor organ shortages are well-known, so best use of available organs is vital. As liver can regenerate, given time, solutions that "buy" that time are needed. HepatiCan™ , a cryopreservable bioartificial liver, provides temporarily, normal liver functions to patients in liver failure, so their own liver has time to regenerate.

Methods: We combine device design and testing with the cell therapy at human clinical scale (~70billion human cells as organoids). We developed a device for bedside use in an intensive care setting (ICU), tested for Electrical & Mechanical safety (IEC 60601). All patient-facing components were designed single use. The cell therapy biomass was prepared as described [1,2] and tested in the device for ~72h. Plasma samples were measured in Chem-Path; per-cell performance by fluorescence imaging of metabolic viability and cell number with nucleocounter.

Results: The cell therapy recovered to pre-freeze (PF) viable cell yields. PF yield, 63.3billion; Post cryorecovery (PC) 84.8 billion. Single use consumables comprised: chamber holding clinical scale biomass; safety & functional filters, a 3-circuit tubing set. The full system device, primed with human plasma, treated plasma at ~350ml/min, returning treated plasma at ~35ml/min, a rate used in patients for plasma exchange. Cell viability was maintained. Synthetic function indicated constant production, Glucose & Oxygen consumption exemplified metabolic function.

Conclusions: HepatiCan delivers a cell therapy (ATMP) at clinical scale for several days, maintaining cell function, interfaces with apheresis machines as secondary process device, meets electrical & mechanical safety requirements for use in an ICU. HepatiCan can temporarily provide liver function to patients in liver failure whilst their own liver repairs itself. HepatiCan will offer patients, especially those with acute or decompensated liver failure, an alternative to whole organ transplantation, allowing better use of donor organs. With new therapies in development for reducing cirrhosis/fibrosis, and targeted therapy for liver tumors, HepatiCan will offer the time for these new treatments to be effective. It can also prevent patient deterioration whilst awaiting transplant.

PP_119 LUNG TRANSPLANT (LTX) OUTCOMES UTILIZING VOLUNTARY ASSISTED DYING (VAD) DONORS: LESSONS LEARNT

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Background: Lung transplantation (LTx) is limited by a lack of suitable donors. DCD Category 5 (Cat 5) lung donors have been successfully utilized in 4 countries with promising results. Recently introduced Voluntary Assisted Dying (VAD) legislation in Australia created an opportunity for our LTx program to utilize this new lung donor pool.

Methods: Since 2019, VAD has been permitted in our home state for competent adults with an advanced illness and end-of-life prognosis of <12 months. Organ donation can only be discussed after a VAD permit is granted. With first-person consent for donation, specific assessments for lung donation are coordinated by the donation service, and approval given from LTx physicians that lungs are medically suitable for LTx. On a set date, the VAD patient is admitted to ICU (family is present) self-administers prescribed oral (IV only used if can't self-administer) medication. Following asystole a standard DCD Cat 3 donor retrieval process follows. This audit reports our program's early VAD LTx results.

Results: Since our first VAD donor in early 2023, there have been 9 VAD donor referrals with 4 actual lung donors [80% residing at home, 80% female, mean age 58 yrs (49-66), 80% Motor Neuron Disease, mean 9.8 (6-13) minutes medication-asystole] yielding 5 LTx [4 single & 1 bilateral LTx; 60% female, mean age 58 yrs (50-68); 80% ILD, 20% COPD]. 4 LTx had straight forward outcomes [mean 6 dys (4-7) ICU stay, 10 dys (8-13) ward stay and are alive with excellent graft function at median 290 dys (84-660). 1 single LTx (59yrs, male) remains in ICU at 84 dys after perioperative haemorrhage, sepsis, renal failure. Over the same time frame, there were 121 LTx from non-VAD donors. Specific VAD lung donor challenges included obtaining donor assessments (CT scans, cultures, arterial gases, blood work) on terminally ill potential donors in the community, limiting donor/DonateLife expectations that not all lungs will be suitable, and accessing credentialled VAD Physicians and elective ICU beds.

Conclusions: DCD Cat 5 lung donation is a practical, feasible way to increase LTx numbers in Australia, fitting within existing laws that enables high utilization of DCD Cat 3 lung donors. Flexibility in donor lung testing requirements and clear communication to meet the VAD donor and DonateLife expectations are vital for success.

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PP_120 EXTRACORPOREAL PERFUSION AND CIRCUIT RELATED COMPLICATIONS IN DCD DONORS UNDERGOING NRP

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Background: Normothermic regional perfusion (NRP) in increasingly implemented in donors undergoing circulatory determination of death (DCDDs). Complications occurring during NRP may negatively impact on its effectiveness, so on the results of procurement procedure, and potentially on feasibility and outcome of transplantation. Nevertheless, few data are available to characterize this peculiar aspect of NRP.

Methods: We performed an observational retrospective study aimed to assess the incidence of NRP related complications from January 2022 to December 2024. NRP procedures were performed by a mobile, experienced team serving a healthcare system including five centers enrolling controlled DCDDs. Complications occurring after NRP initiation, and involving circuit, cannulae, regionalization strategy, and NRP physiology (drainage insufficiency/return obstruction) were meticulously analyzed.

Results: 74 NRP procedures were analyzed: 70 abdominal (A), 4 thoraco-abdominal (TA). The occurrence of at least one severe complication was observed in 31%; complication rate was higher for TA vs. A-NRP (75% vs. 29%). However, the limited number of TA procedures precluded the feasibility of assessing the statistical significance of this data. A-NRP donors were older, and underwent longer procedures. Anyway, complications and their severity did not appear to raise with increased age or perfusion duration. No clear trend was observed over the years. Detailed analysis in the table. No procedure was discontinued due to the occurrence of complications, even in the setting of extreme events as accidental decannulation or massive air entrance. Perfusion was restarted and/or maintained perfusion until required after troubleshooting.

Conclusions: Perfusion related complications may frequently occur during NRP, particularly in the setting of complex procedures as TA configuration, A-NRP associated with lung procurement, or with marginal donors. Careful donor and circuit monitoring throughout reperfusion, enhanced coordination between team members, and focused simulation training may improve their prevention, early detection and successful management. Consistent NRP complications definitions may aide in data collection and reporting, and support the development of standardized educational pathways.

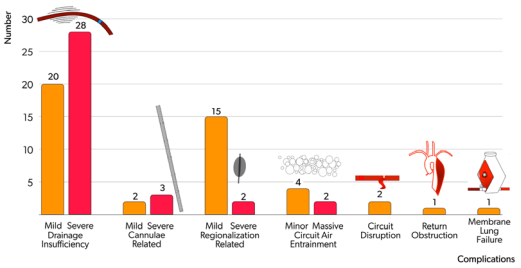
Circuit and Perfusion related Complications During NRP

Donors	Overall n = 74	A-NRP n = 70	TA-NRP* n = 4	2022 n = 4	2023 n = 6	2024 n = 1
Age, years mean (SD)	68.6 (±13)	70.1 (±11.6)	47.5 (±17.5)	69.5 (±10.3)	69 (±10.3)	68.3 (±13.4)
Age, years median (IQR)	71 (15.5)	72.5 (15.8)	51.5 (14)	71 (9.8)	75.5 (16.8)	68.5 (1.8)
NRP Duration, minutes mean (SD)	166 (±46.5)	167.9 (±46.3)	132.5 (±39.7)	191.2 (±28.6)	173.1 (±54.8)	138.9 (±37.8)
NRP Duration, minutes median (IQR)	170.5 (63.8)	172 (63.5)	129.5 (38)	190 (36.8)	164.5 (77.8)	130 (71.8)

Complication Type		Overall n = 74 n (%)	Configuration A (n = 70) n (%)	Configuration TA (n = 4) n %	Procedure, year 2022 n = 24	2023 n = 22	2024 n = 28	Donor Age, years < 50 n = 7	≥ 50-69 n = 24	≥ 70-79 n = 27	> 80 n = 16
Drainage Insufficiency	Overall	48 (64.9)	45 (64.3)	3 (75)	18 (75)	11 (50)	19 (67.9)	7 (71,4)	14 (58.3)	17 (63.0)	10 (62.5)
	Severe	20 (27)	17 (24.3)	3 (75)	12 (50)	2 (9,1)	6 (21.4)	2 (28.6)	5 (20.8)	10 (37.0)	3 (18.8)
Cannulae Related*	Mild	2 (2.7)	2 (2.9)	0	0	1 (4.5)	1 (3.6)	0	1 (4.2)	1 (3.7)	0
	Severe	3 (4.1)	1 (1.4)	2* (50)	1 (4.2)	0	2 (7,1)	0	1 (4.2)	1 (3.7)	1 (6.3)
EBOA Related*	Mild	15 (20.3)	15 (21.4)	-	1 (4.2)	7 (31.8)	7 (25)	2 (28.6)	7 (29.2)	3 (11.1)	3 (18.8)
	Severe	2 (2.7)	2 (2.9)	-	0	0	2 (7,1)	0	0	1 (3.7)	1 (6.3)
Air Entrainment	Minor	4 (6.8)	4 (5.7)	0	0	1 (4.5)	3 (10.7)	1 (14.3)	1 (4.2)	1 (3.7)	1 (6.3)
	Massive	2 (2.7)	1 (1.4)	1 (25)	0	0	2 (7,1)	0	1 (4.2)	0	1 (6.3)
Return Obstruction		2 (2.7)	1 (1.4)	1 (25)	0	0	2 (7,1)	0	1 (4.2)	0	1 (6.3)
Circuit Disruption		1 (1.4)	1 (1.4)	0	1 (4.2)	0	0	0	0	1 (4.2)	0
ML Failure		1 (1.4)	1	0	0	0	1 (3.6)	0	1 (4.2)	0	0
Gas Supply Interruption		0	0	0	0	0	0	0	0	0	0
Pump Failure		0	0	0	0	0	0	0	0	0	0
At least 1 Severe Complication		23 (31.1)	20 (28.6)	3 (75)	12 (50.0)	2 (9.1)	9 (32.1)	2 (28.6)	5 (20.8)	11 (40.7)	5 (31.3)

	A-NRP only n = 70 n (%)	2022 n = 24	2023 n = 21	2024 n = 25	< 50 n = 5	≥ 50-69 n = 22	≥ 70-79 n = 27	> 80 n = 16
At least 1 Severe Complication	20 (28.6)	12 (50)	2 (9,5)	6 (24.0)	1 (20)	3 (13.6)	11 (15.71)	5 (7.14)

Drainage insufficiency was defined as inability to maintain target blood flow not-related to organs/great vessels manipulation during surgery. It was considered as severe if refractory to blood/fluids administration. Severe cannula related complications where defined as complications requiring surgical repair/complete repositioning, while mild where defined as complications only requiring minor repositioning. Severe EBOA related complications where defined as complications requiring surgical repair, while mild where defined as complications only requiring minor repositioning/supplementary balloon inflation or switching to aortic cross clamping for A. *No complication related with ligation of arch vessels was reported for TA-NRP. Air entrainment into the circuit was defined minor if no interruption of blood flow was required for air removal, massive in blood flow had to be interrupted for de-airing. A, abdominal; BSA, body surface area; EBOA, endovascular balloon occlusion of the aorta; IQR, interquartile range; NRP, normothermic regional perfusion; SD, standard deviation; TA, thoraco-abdominal.



PP_121 MODELLING ISCHEMIC CHOLANGIOPATHY USING HUMAN CHOLANGIOCYTE ORGANOIDS FOR TRANSLATIONAL RESEARCH

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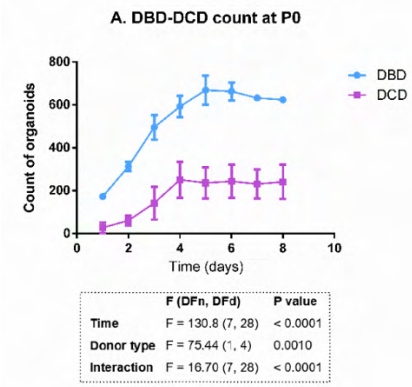
Background: One-third of liver transplant recipients will develop ischemic cholangiopathy (IC) within the 1st year post-transplant, with 50% requiring re-transplantation. Donation after circulatory death (DCD) increases the risk of IC by 11-fold, but our limited understanding of cholangiocyte ischemia-reperfusion injury impedes IC prevention and treatment. We aimed to explore human cholangiocyte organoids (CO) as a preclinical model to investigate the pathophysiology of cholangiocyte ischemia-reperfusion injury, by comparing COs derived from donation after brain death (DBD) and DCD livers.

Methods: The gallbladder epithelium from DBD (n=2) and DCD (n=2) livers was mechanically dissociated. Primary cholangiocytes were cultured in matrigel with R-spondin, Epithelial Growth Factor, Dickkopf-related protein 1, and Y-27632. The development of organoids was then followed daily for a month by live-cell imaging. RT-qPCR was used to confirm the expression of cholangiocellular markers cytokeratin 7 (KRT7) and 19 (KRT19), gamma-glutamyl transferase 1 (GGT1), and the SRY-Box Transcription Factor 9 (SOX9).

Results: CO were visible in bright field imaging as hollow spheres with cells lining a clear lumen from the first culturing day. In the following days, COs expanded, divided, propagated, and reached confluence within **6 (±1) days.** RT-qPCR confirmed the expression of cholangiocyte-specific marker genes KRT7, KRT19, GGT1, and SOX9 in COs, regardless of donor type. Live-cell imaging showed significantly fewer COs from DCD than DBD donors (**p=0.001**) at passage 0 **(see Fig 1A; Table 1B).** While organoid numbers increased significantly in both groups over time (**p<0.0001**), DCD-derived COs exhibited slower growth rates (**p<0.0001**). This difference was not visible at passages 1 and 3. COs size was similar.

Conclusions: We successfully generated COs with both stemness and mature cholangiocyte profiles. Importantly, our preliminary results suggest that this COs retain donation-induced injury traits. Further expansion of the sample size, thorough characterization, and functional testing necessary to further validate this model are in progress.

Figure 1



B.

Culturing day P0	Average CO number (SD) - DBD	Average CO number (SD) - DCD
1	173 (11.79)	27.333 (24.826)
2	313 (21.071)	60.667 (22.502)
3	495.667 (57.274)	142.333 (76.957)
4	592 (49.689)	251 (84.285)
5	669 (67.55)	236 (72.187)
6	663.333 (42.36)	243.667 (77.054)
7	632 (7.81)	230.667 (67.278)
8	624 (7.55)	240.667 (79.431)

Figure 1: Graph (1A) and table (1B) represent the averaged organoid count of DBD and DCD organoid culture replicates (n=3) at P0.

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PP_122 HEMOLYSIS DURING NORMOTHERMIC HUMAN KIDNEY PRESERVATION DRIVES IRON ACCUMULATION AND FERROPTOSIS

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Background: Ex vivo normothermic machine perfusion has been proposed to protect deceased donor organs, promoting metabolic recovery and allowing quality assessment. However, its benefits for preserving deceased donor kidneys remain ambiguous. We postulate that the use of red blood cells (RBCs) as oxygen carriers and associated secondary hemolysis may in fact cause renal injury, offsetting potential advantages.

Methods: Seven human kidneys were perfused at 37°C up to 48 hours using a RBC-based perfusate in a clinical grade perfusion platform. Next, in twelve additional multi-day human kidney perfusions, we evaluated the effects of either dialysis-based free hemoglobin removal at 37°C or cell-free perfusion at 25°C. Bulk transcriptomics, untargeted lipidomics (LC-MS/MS) and targeted oxidized phosphatidylcholine lipidomics (LC-MS/MS) were performed on tissue biopsies. Oxilipidomics (LC-MS/MS) was used to analyse the perfusate.

Results: During 48-hour normothermic perfusion of seven human deceased donor kidneys, we observed progressive hemolysis, leading to iron accumulation in perfusate, tissue, and urine. Untargeted lipidomic analysis revealed profound increases in oxidized phospholipid species in perfused kidneys, pointing towards iron-dependent cell death known as ferroptosis. Further experiments showed that removing free hemoglobin or using a cell-free perfusate reduced hemolysis, iron accumulation, phospholipid peroxidation, and acute kidney injury.

Conclusions: Our findings highlight the pathological role of hemolysis and iron on the kidney, urging restraint in the clinical application of RBC-based kidney perfusion.

PP_123 ONSET OF HYPERTENSION IN LIVING KIDNEY DONORS AFTER NEPHRECTOMY

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Background: Hypertension represents a deviation from the ideal living donor kidney evaluation study protocol. It has been considered to be a contraindication for live kidney donation because it is associated with or can promote the onset of cardiovascular and renal diseases. To date, few articles have been published regarding the long-term follow-up of these donors.

Methods: Between January 2011 and June 2023, 200 living donor kidney transplants were performed at this Kidney Transplant Unit. Demographic characteristics (age, BMI, sex, renal function, presence or absence of hypertension) of the potential donors were collected. Of these, 39 (19,5%) had pre-donation hypertension (≥140/90 mmHg) under medical therapy with 1 (85%) or 2 drugs (15%). The 200 donors were divided into two groups (hypertensive and normotensive donors) before the donation

Results: Results at 1, 2 and 3 years after donation were analyzed. The hypertensive and normotensive donors did not differ in BMI (p=n.s.), nor in renal function (p=n.s.) but did differ in age (p=0.00) since the hypertensives were older than the normotensives. In addition, 18 (11%) pre-donation normotensive donors developed hypertension and 8 (20,5%) pre-donation hypertensive donors had increased antihypertensive medications. After the donation, the creatinine and filtrate values (eGFR) of the hypertensive donors were comparable to those of the normotensive donors at 1, 2 and 3 years (p=n.s.). These results are confirmed by the multivariate analysis (logistic regression model) performed.

Conclusions: Pre-donation hypertension without organ damage should not be considered an absolute contraindication for live kidney donation. A non negligible proportion of donors develop de novo hypertension after donation. In most cases, hypertension in live kidney donors was not associated with a greater increase in blood pressure nor a relevant decrement in filtration rate after donor nephrectomy. However, long follow-up with serial monitoring of blood pression and renal function is mandatory for these donors.

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PP_124 ENHANCING STEATOTIC LIVER PRESERVATION: A COMPARATIVE STUDY OF CONVENTIONAL AND MODIFIED SOLUTIONS

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Background: Maintaining the viability of steatotic livers during transplantation is crucial for minimizing the detrimental effects of ischemia-reperfusion injury. This study explores the intricate biochemical profiles of liver homogenates and perfusates derived from Zucker obese rat livers following 24 hours of cold storage at 4°C. The investigation evaluates several preservation solutions, including the University of Wisconsin (UW), Histidine-Tryptophan-Ketoglutarate (HTK), IGL-2, and a modified version of IGL-2 (IGL-2M) optimized for greater stability at room temperature.

Methods: Male Zucker obese rat livers are preserved for 24 hours at 4°C using UW, HTK, IGL-2, and IGL-2M solutions. A SHAM control group undergoes identical procedures without the application of preservation solutions. Perfusates are collected through an exhaustive washout with Ringer's solution, and liver tissue samples are obtained for analysis. Measured parameters include ALT, AST, GLDH, lactate, nitrites and nitrates, uric acid, syndecan, SDH, succinate, pH, homocysteine, ferritin, ATP, OXPHOS, 4HNE and glucose.

Results: Preservation with HTK results in significantly higher levels of transaminases (ALT, AST), GLDH, and uric acid compared to other solutions. IGL-2M exhibits a distinct biochemical profile, showing a notable increase in nitrites and nitrates relative to IGL-2. Livers stored in UW demonstrate elevated syndecan levels, potentially indicating greater glycocalyx shedding. Both IGL-2 and IGL-2M display comparable SDH release, suggesting similar performance between these formulations.

Conclusions: The biomarkers identified in this study offer valuable tools for assessing liver condition through perfusate and tissue analysis. IGL-2 and IGL-2M achieve promising results, characterized by reduced inflammation and improved preservation of key biochemical markers. Further research to validate these markers is critical, as they hold significant promise for advancing evaluation methods for steatotic livers prior to transplantation.

PP_126 COMPARATIVE OUTCOMES OF DECEASED AND LIVING DONOR LIVER TRANSPLANTATION BY GRAFT-TO-RECIPIENT WEIGHT RATIOS

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Background: Liver transplantation is a critical procedure for patients with end-stage liver disease, and the graft-to-recipient weight ratio (GRWR) plays a significant role in post-transplant outcomes. This study aimed to compare the survival outcomes and risk factors associated with deceased donor liver transplantation (DDLT) and living donor liver transplantation (LDLT) with varying GRWRs in patients with a Model for End-Stage Liver Disease (MELD) score of 35-40.

Methods: We conducted a retrospective analysis of 338 liver transplant recipients, divided into three groups: DDLT, LDLT with GRWR < 1.0, and LDLT with GRWR ≥ 1.0. Baseline demographics, clinical characteristics, and donor information were collected. Survival analysis was performed using Kaplan-Meier curves, and risk factors for graft and overall survival were identified using multivariable Cox regression models.

Results: The study included 191 DDLT recipients, 69 LDLT recipients with GRWR < 1.0, and 78 LDLT recipients with GRWR ≥ 1.0. Significant differences were observed in recipient age, sex, BMI, etiology of liver disease, ICU stay, and donor characteristics among the groups. Kaplan-Meier analysis showed a significantly higher graft survival rate in LDLT with GRWR ≥ 1.0 compared to DDLT and LDLT with GRWR < 1.0 (p = 0.011). Multivariable Cox regression showed that LDLT with GRWR≥1.0 showed superior graft survival (HR=0.3348, CI=0.137-0.818, P=0.016) compared to DDLT.

Conclusions: LDLT with a GRWR ≥ 1.0 provides superior graft survival compared to DDLT and LDLT with GRWR < 1.0 in patients with high MELD scores. The CTP score, etiology of liver disease, and donor characteristics are crucial factors influencing post-transplant outcomes. These findings support the consideration of GRWR in donor selection and highlight the need for careful preoperative assessment to optimize transplant success.

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PP_128 HEPATOBILIARY VIABILITY CRITERIA DURING LONG-TERM NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) is used to preserve and evaluate donor livers prior to transplantation using hepatobiliary criteria for viability assessment. This study aimed to explore the value of established, point-of-care hepatobiliary viability criteria for clinical NMP during experimental long-term NMP (>24 h; LT-NMP) and assess whether interventions could improve cholangiocellular viability parameters.

Methods: Human livers donated for research purposes underwent LT-NMP using a modified Liver Assist (XVIVO, Groningen, the Netherlands) perfusion device, including adjusted oxygenators and gas mixer, continuous renal replacement therapy, and continuous monitoring. Livers were assigned to three intervention groups to observe the effect of no bile salts, bile salts (Sodium taurocholate, Merck Life Science N.V., Darmstadt, Germany) supplementation, or bile salts plus secretin (ChiRhoStim?, ChiRhoClin, Inc. Burtonsville, USA) administration on cholangiocellular viability parameters (e.g., biliary pH, bicarbonate and glucose).

Results: Nine human donor livers underwent NMP for 7 days. After initially excellent viability criteria results, a decline was seen after 12 hours of NMP to a (near) acceptable range (Figure). Despite fluctuations, overall stability in values was maintained throughout perfusion. Bile salts administration significantly increased the volume of bile production ($p<0.01$), with secretin further enhancing this effect ($p<0.01$). Secretin also induced a higher bicarbonate excretion into the bile, leading to a higher bile pH.

Conclusions: Most livers maintained hepatobiliary viability criteria within the (borderline) acceptable range during LT-NMP, suggesting that this protocol can maintain biliary viability and function in ex situ perfused donor livers for 7 days. Administration of bile salts improved bile production, while response to secretin administration may serve as an additional viability criterion to assess cholangiocyte function.

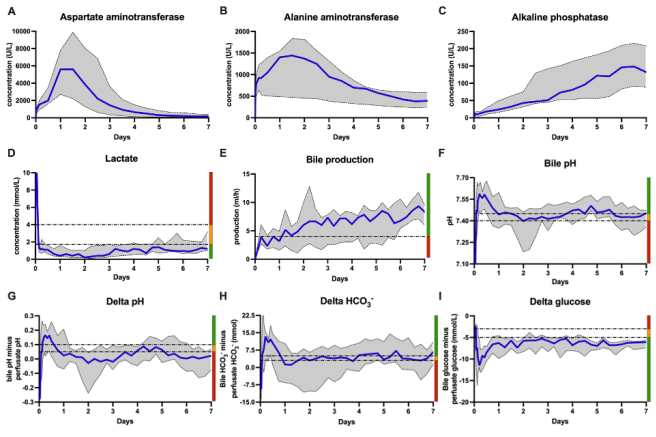

Figure: Hepatic and biliary function markers and hepatobiliary viability criteria
Panel A-C: The hepatic markers aspartate aminotransferase and alanine aminotransferase, and the biliary function marker alkaline phosphatase. **Panel D-E:** The hepatocyte viability criteria lactate and bile production. **Panel F-I:** The cholangiocyte viability criteria bile pH, delta pH, delta HCO_3^-, and delta glucose.
Median values (blue line) with interquartile range (grey area) for n=9 livers. The horizontal black interrupted lines display the ranges of acceptable viability criteria, which is also reflected by the colors vertically displayed at the right (green is acceptable/good; orange is suboptimal/borderline; red is not acceptable).

PP_132 REDUCING KIDNEY DISCARD: CAN NMP PARAMETERS PREDICT THE TRANSPLANT SUCCES OF HARD-TO-PLACE KIDNEYS?

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Background: In the U.S., 25% of donor kidneys are unused, due to inefficiencies in organ allocation and reluctance to utilize high-risk organs. Normothermic machine perfusion (NMP) offers a sustainable approach to improving kidney utilization, reduce cold ischemia, and provide insights into organ viability. Clinically meaningful NMP viability criteria would facilitate organ rescue. However, limited use makes defining viability criteria challenging. Here, we present preliminary data from the OPTIMAL study—the first U.S. NMP study—evaluating correlations between perfusion parameters and short-term transplant outcomes of hard-to-place donor kidneys.

Methods: Donor kidneys (n=23) that exhausted UNOS allocation were transported to a preservation center (34 Lives, *PBC*) using hypothermic machine perfusion (HMP), where they underwent 120 min of acellular subnormothermic machine perfusion, before transport to the transplant center using HMP (Fig 1A). Donor data, preservation parameters, and early post-transplant outcomes were collected. Pearson correlation analysis evaluated 108 variables against recipient estimated glomerular filtration rate (eGFR) and serum creatinine (sCr) at 7- and 30-days post-transplant.

Results: Correlation analysis identified 12, 17, 18, and 9 variables significantly associated with 7-day sCr, 7-day eGFR, 30-day sCr, and 30-day eGFR, respectively (Fig 1B). NMP parameters showed the greatest correlation with outcomes, whereas donor and HMP variables exhibited limited correlation. Perfusate and urine gas values during NMP were primary contributors to 7-day sCr (Fig 1C), while 30-day sCr correlated with NMP hemodynamics (Fig 1D). Delayed graft function and primary non-function rates were 18% and 0% respectively.

Conclusions: These findings demonstrate that NMP parameters show stronger correlations with outcomes compared to donor characteristics and HMP parameters. 7-day sCr correlated with perfusate and urine gas values, while 30-day sCr linked to hemodynamics, suggesting distinct markers for immediate and short-term outcomes. Although limited by a small dataset and short follow-up, these results highlight the feasibility of NMP to safely enhance utilization of hard-to-place kidneys, reduce organ discard and promote sustainability in organ transplantation.

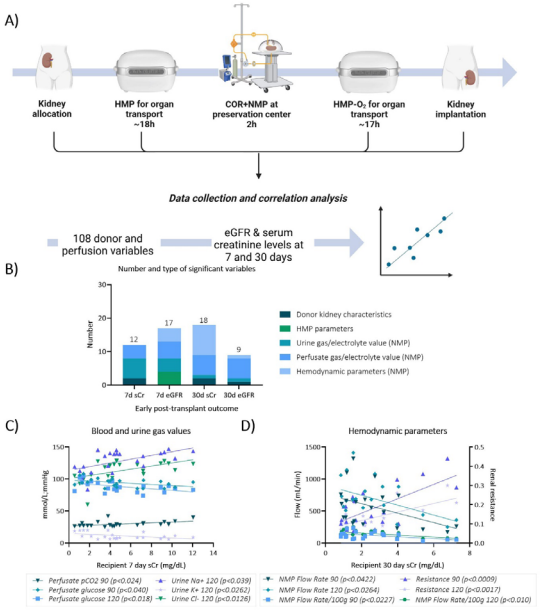

Figure 1. A) Schematic representation of kidney allocation, perfusion, and transplant process. Kidneys were transported to and from the preservation center using hypothermic machine perfusion (HMP). At the preservation center, kidneys underwent controlled oxygenated rewarming (COR) and (sub)normothermic machine perfusion (NMP) for 120 minutes. Data was collected throughout and used for correlation analysis. B) Number of significant variables detected that correlate with recipient transplant outcome and type of variable. C) Perfusate and urine gas values measured during NMP that significantly correlate with recipient 7-day serum creatinine (sCr). D) Hemodynamic parameters measured during NMP that significantly correlate with recipient 30-day sCr. 90=90 minutes of NMP; 120=120 minutes of NMP.

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PP_133 ASSESSING THE RESPONSE TO ANTIMIR-21 IN HUMAN MODELS OF KIDNEY ISCHAEMIA-REPERFUSION INJURY

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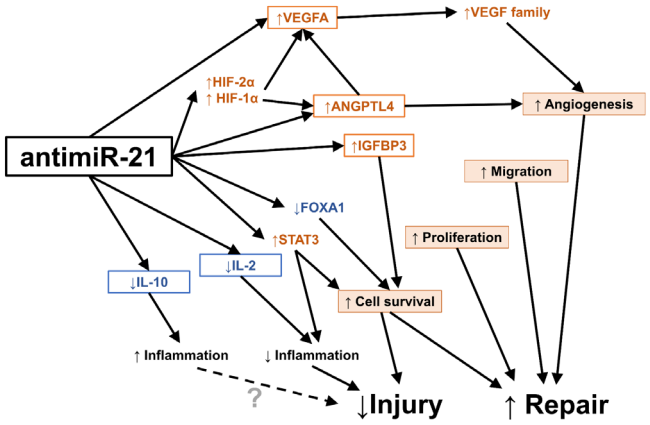
Background: Therapies that target ischaemia-reperfusion injury (IRI) in kidney transplantation have the potential to improve graft survival, so benefiting recipients and those on the waiting list. MicroRNAs (miR) are potential targets through which to modulate these injury pathways and rodent studies suggest blocking miR-21-5p is beneficial in kidney IRI. We delivered a miR-21-5p inhibitor (antimiR-21) to human in vitro and whole organ ex vivo models of kidney IRI to explore the response in human cells.

Methods: Human kidneys declined for transplantation were used to isolate proximal tubule epithelial cells (PTEC; n=4) or as pairs for normothermic machine perfusion (NMP; n=5). To mimic IRI in vitro, isolated cells were incubated in 1% O_2 for 24 hours before return to normal conditions for 24-48 hours of reoxygenation. 40 nM antimiR-21 or control was added to cell media at reoxygenation. End reoxygenation cell lysates were matched with normoxia controls. Pairs of kidneys were perfused ex vivo for 24 hours with NMP using urine recirculation and either antimiR-21 or control. Samples were analysed by bulk RNA sequencing (PTEC) and liquid chromatography mass spectrometry-based proteomics with data independent acquisition (PTEC and kidneys). miR-21 levels were quantified before and after perfusion. Apoptosis was quantified by flow cytometry for PTEC and TUNEL stain for kidney pairs. Immunoassay measured secreted cytokines.

Results: AntimiR-21 delivered at reoxygenation for 24 hours upregulated certain miR-21 targets on RNA and protein level data from PTEC in vitro and reduced miR-21 expression in perfused kidneys. In vitro, antimiR-21 had an opposing effect to hypoxia-reoxygenation on gene expression and predicted pathway activity. The figure shows a summary of in vitro findings and potential effects. AntimiR-21 did not increase apoptosis. 24 hours was not sufficient to detect changes in protein expression downstream of antimiR-21 in perfused kidneys.

Conclusions: This data supports a potentially reparative effect of antimiR-21 in human PTEC exposed to IRI in vitro. In addition, antimiR-21 treatment during 24 hours of NMP effectively reduced miR-21 expression. Future work will analyze stored matched kidney samples using single-cell RNA sequencing to further assess downstream effects.



PP_134 LIVER TRANSPLANT IN PRIMARY SCLEROSING CHOLANGITIS - DO MACHINE PERFUSIONS CHANGE OUTCOMES?

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Background: Primary sclerosing cholangitis (PSC) is a chronic liver disease affecting especially the biliary tree, for which transplantation is the only definitive treatment for end-stage liver disease. In PSC patients the average age of diagnosis and transplant is during early adulthood, hence the ideal need for long-lasting and/or straightforward grafts: the choice of the right liver could prevent worse outcomes as well as need for re-transplantation. The recent need to increase marginal graft usage (from both cardiac and brain death) was possible thanks to the spread of machine perfusion techniques, as they mitigate ischemia-reperfusion injury and improve transplant outcomes. The aim of this study is to evaluate whether the use of machine perfusions can change outcomes in either DBD and DCD livers for PSC recipients.

Methods: This single-centre retrospective analysis includes all patients who underwent liver transplantation for primary or recurrent PSC between 2022 and 2024. The primary outcomes considered were early allograft dysfunction (EAD) and acute rejection, alongside with biliary complications (anastomotic and non-anastomotic strictures) and vascular complications.

Results: 72 patients were included, out of which 2 needed re-transplant. The use of machine perfusion was more relevant in the DCD group (p value <0.001), with less perfusion time. Early allograft function was similar despite the different types of graft (p value = 0.121) and machine perfusion (p value = 0.899). Acute rejection incidence was higher in DBD grafts, but statistically relevant in the machine perfused DCD livers (p value = 0.028). Overall complication incidence was higher in DBD grafts, but there was no statistical difference correlated to machine perfusion.

Conclusions: Machine perfusion improves outcomes for DCD grafts, reducing early allograft dysfunction and overall complications. While DBD grafts showed a higher incidence of complications, the findings suggest that machine perfusion could optimize the use of marginal grafts in PSC liver transplantation.

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PP_135 COLD COMFORT: VIABILITY TESTING IN AUSTRALASIA'S FIRST HYPOTHERMIC OXYGENATED MACHINE PERFUSION (HOPE) PROGRAM

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Background: Viability assessment is lacking for liver grafts receiving HOPE. Recently, perfusate FMN has been proposed as a viability marker. The aim of this study was to provide real-life data on the use of FMN as a viability marker for liver grafts undergoing HOPE in New Zealand.

Methods: This is a single centre retrospective study. Extended criteria-DBD and DCD grafts were perfused with D-HOPE using the Xvivo LiverAssist™ device. Samples of the perfusate were prospectively collected every 30 min. and retrospectively analysed with fluorometry. Recipients were monitored post-operatively for clinically significant non-anastomotic biliary strictures (NABS).

Results: 50 livers were treated with HOPE from 2022-2024 (nDCD = 19, nDBD = 31). There was no primary non-function cases. Clinically significant NABS was seen in no DBD and five (26%) DCD grafts. All patients with NABS experienced graft loss: 3 were retransplanted and 2 died. 30 grafts had FMN sampled during perfusion (nDCD = 11, nDBD =19). FMN levels demonstrated a predictive value for NABS at 30 and 60 min. with AUCs of 0.760 (p=0.029) and 0.670 (p=0.302), respectively. Summation of FMN levels taken at 30, 60 and 90 min. yielded the best AUC for NABS prediction - 0.788 (p=0.049). DCD grafts alone had a predictive value for NABS at 30 and 60 mins. with AUCs of 0.857 (p=0.003) and 0.750 (p=0.141). FMN at 30 and 60 min. showed excellent predictive value for 6m patient survival with respective AUCs of 0.914 (p<0.001) and 0.901 (p<0.001). FMN concentrations at 30 min. significantly correlated with both the L-Graft7 (p = <0.001) and CCI scores (p=0.038). Using 60 min. FMN cut-offs from the recent study by Eden (2024), two high risk grafts were identified. However, only one developed NABS. The other four patients with NABS had low risk FMN values. Combining FMN risk categories with clinical scores, such as UK-DCD and BAR scores, only reclassified one patient appropriately.

Conclusions: Perfusate FMN during the first 90 mins. of HOPE is a reasonable predictor of graft function and clinical outcomes. Kinetics within the first 90 mins. may be considered, as opposed to a single measurement at 60 mins. Our real-life experience shows that FMN cut-offs alone are not reliable enough to discard a graft and combination with donor and recipient risk factors should be contemplated in future studies.

Figure 1

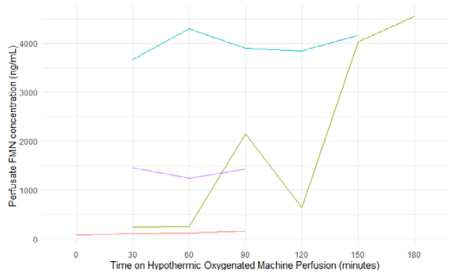

Figure 1: Perfusate flavin mononucleotide (FMN) concentration kinetics, obtained during hypothermic oxygenated machine perfusion. Each line represents the grafts that developed ischaemic cholangiopathy.

Table 1: Cases of clinically significant non-anastomotic biliary strictures treated with D-HOPE in New Zealand

Patient	Patient age	Donor type	fWIT (mins)	CIT (mins)	WIT (mins)	Diagnosis and clinical significance	Outcome	FMN concentration after 60 minutes of perfusion (AU)	Risk score for FMN concentration at 60 mins ^
1	64	DCD	21	279	21	Initially diagnosed incidentally on ERCP for anastomotic problem. Patient later developed graft dysfunction.	Re-transplant	257	Low
2	58	DCD	24	288	25	Biochemical graft dysfunction	Re-transplant	No data	n/a
3	58	DCD	6	337	25	Recurrent cholangitis	Re-transplant	511	Low
4	55	DCD	22	318	38	Biochemical graft dysfunction	Death	8589	High
5	26	DCD		408	51	Initially diagnosed incidentally on ERCP for anastomotic problem. Patient later developed graft dysfunction.	Death	2497	Low

^ as defined by Eden et. al. Assessment of liver graft quality during hypothermic oxygenated perfusion: the first international validation study. 2024. J Hep.

fWIT = functional warm ischaemic time, CIT = cold ischaemic time, AU = arbitrary units, mins = minutes

PP_136 HTK IS ASSOCIATED WITH HIGHER POST-REPERFUSION SYNDROME: TIME FOR A GLOBAL RETHINK?

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Background: With the increasing use of marginal grafts and longer cold ischaemia time (CIT), optimizing organ preservation solutions is more critical than ever. Recently, a shortage of University of Wisconsin (UW) solution led to a temporary shift to histidine-tryptophan-ketoglutarate (HTK) solution for flushing and preserving deceased donor livers across the United Kingdom. This pan-UK multi-center study aims to compare the outcome of liver grafts perfused with UW solution versus HTK solution.

Methods: Retrospective observational study of consecutive deceased donor liver transplants (DDLTs) performed at all centers in the UK between November 2022 and May 2023.

Results: Of the 478 DDLTs during the study period, 224 were UW and 254 were HTK perfused. There was no difference between the two groups in terms of donor and recipient demographics, type of graft (DBD/DCD), cold and warm ischaemia time, and usage of machine perfusion. There was an increased incidence of Post-Reperfusion Syndrome (PRS - drop in mean-arterial pressure >30% for >1 min within 5 mins of reperfusion) in the HTK group (34.7% vs. 24.4%; p=0.014) in per-protocol analysis, with two-fold higher rate of severe PRS (asystole/arrhythmias/need for continuous vasopressors) in HTK group (21.3% vs. 11.6%; p=0.004). There was no difference in primary non-function and early allograft dysfunction, however significantly prolonged hospital stay was observed among HTK group as compared to UW group (15 vs. 14 days, p=0.019) with similar 3-month graft and patient survival. On multivariate analysis, HTK use is an independent predictor for PRS. Use of normothermic regional perfusion (NRP) during retrieval is shown to significantly decrease incidence of PRS (p=0.008).

Conclusions: HTK solution appears to be inferior to UW solution in deceased donor liver graft preservation. There is an emergent need for the global transplant community to solve the concerns of preservation solution shortage and usage for optimal outcome.

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PP_138 CENTRAL HEMODYNAMICS IN KIDNEY DONORS FOLLOWING NEPHRECTOMY

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Background: While long-term changes in brachial blood pressure (bBP) after kidney donation have been reported, data on aortic BP (aBP) are scarce. aBP is associated with cardiovascular events, with numerous studies suggesting it offers greater prognostic value compared to bBP. The present study investigated central hemodynamics in kidney donors post-nephrectomy.

Methods: This is a cross-sectional study of 107 kidney donors with at least one year follow-up, who attended the Outpatient Donor Clinic of our hospital from 02/2023 to 02/2024, and underwent 24-hour ambulatory bBP and aBP monitoring with Mobil-O-Graph device. Study population was divided into four subgroups based on ambulatory SBP phenotype: Phenotype I: Normal systolic bBP (bSBP) and systolic aBP (aSBP), Phenotype II: Normal bSBP and abnormal aSBP, Phenotype III: abnormal bSBP but normal aSBP, Phenotype IV: abnormal bSBP and aSBP.

Results: The study population consisted of 70 women. Mean age was 62.4±9.8years. After a median follow-up of 3.2 (1, 24) years, mean eGFR was 61.1±13.2ml/min. Mean bSBP and aSBP were 118.96±11.48 mmHg and 109.36±10.23 mmHg respectively. Among donors, 28% had hypertension, 20.6% were obese and 32.7% were tobacco users. The number of donors classified as having phenotypes I, II, III and IV were 89, 0, 2 and 16 respectively. Gender, age at time of donation and examination and smoking did not differ across phenotypes. Phenotype I was significantly associated with the absence of diabetes and obesity (p=0.003 and p=0.006 respectively). Dyslipidemia or carotid intima media thickness (IMT)≥0.6mm were associated with phenotype IV (OR4.774, 95% CI (1.240-18.380), p=0.023 and OR:5.922, 95% CI(1.242-28.242), p=0.026 respectively). In multivariate logistic regression analysis obesity was the only factor that correlated with phenotype IV(p=0.031), while its absence was associated with phenotype I (p=0.007). No correlations were observed between different phenotypes and eGFR, time since donation or medications.

Conclusions: The current study suggests a low prevalence of hypertension early after kidney donation. A modifiable factor, such as obesity, was linked to increased bSBP and aSBP post-nephrectomy. These findings emphasize the importance of thorough evaluation and lifelong medical surveillance of kidney donors.

PP_139 A CONCEPT REDESIGN OF CENTRAL NORMOTHERMIC REGIONAL PERFUSION FACILITATES HEART FUNCTION ASSESSMENT

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Background: Thoraco-abdominal normothermic regional perfusion (TA-NRP) raises controversies. Bi-phasic Recovery Implemented in Donor organs Guided by Extracorporeal circulation NRP (BRIDGE NRP) is a redesigned TA-NRP, that avoids interventions on the aortic arch, while cerebral circulatory arrest remains undisturbed. In BRIDGE NRP cardiac output (CO) depends mainly on abdominal venous return, that limits and obscures the attainable upper limit of CO during loaded heart action.

Methods: The basic BRIDGE NRP can be redesigned by adding a 'windkessel device' (WKD) -comparable to the output side from the Cardiac BioSimulator® from LifeTec Group™-, to the left-left-shunt to divert CO of the left ventricle (LV) via the WKD to the venous reservoir (VR).

Results: Extracorporeal circulation (ECC) provides abdominal NRP (aNRP) and thoracic NRP independently. ECC hot shot during the primary phase of NRP ensures coronary and pulmonary reperfusion. The heart is first recovering in an unloaded condition. The right atrium (RA) drainage is during NRP converted from the primary RA-cannula (pRAcan) to the additionally inserted long venous cannula (LVC). The pRAcan is consecutively converted to become access for venous return. A loaded heart action occurs in the secondary phase, converting the ECC from a thoracic veno-arterial-assist to the Active Venous Return (ActVR) gradually. The tip of the LVC is repositioned below the diaphragm, and the inferior cava is closed. The right ventricle starts generating CO. Drainage from the LV is reduced, the LV begins generating CO. The WKD is gradually opened to convey LV CO to the WKD. ECC hot shot is ceased eventually. The aNRP shunt provides continuous flow to abdominal organs, adjustable by a variable flow resistor. Pulsatile flow from the LV is diverted via the WKD to the VR. The team directs the level of CO via the centrifugal pump. The final condition of NRP is depicted in the figure.

Conclusions: The BRIDGE NRP WKD concept actively directs CO. The WKD provides adjustable LV afterload, while the VR offers a volume buffer. While aNRP is maintained at a constant level, BRIDGE NRP WKD serves as a dynamic cardiac assessment tool. The circuit is donor-lung independent. The WKD is not yet clinically available and needs further testing in an animal model.

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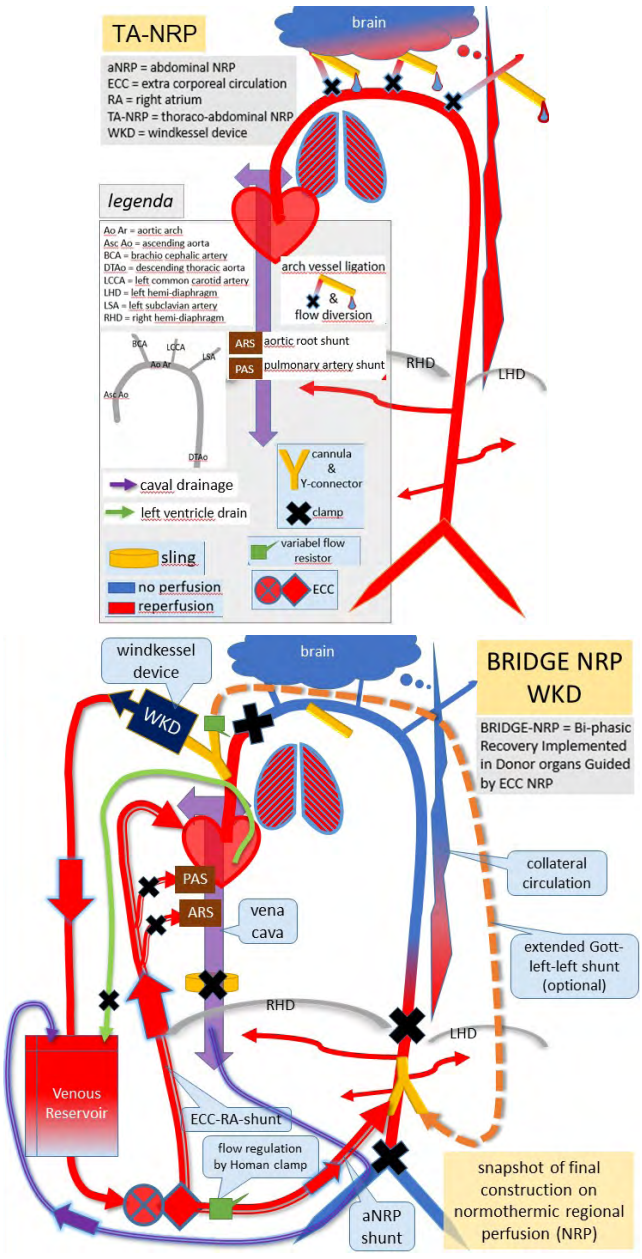

PP_140 INVESTIGATION OF THE SAFETY AND EFFICACY OF MIROCOCEPT IN REDUCING DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANTATION

Fayyad Jaradat[1], Alima Rahman[2], Abdel Douiri[3], Roseanna Greenlaw[4], Jonathon Olsburgh[5], Peter Friend[6], richard a.smith[7], Steven Sacks[8], Theodoros Kassimatis[9]

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Background: Delayed graft function (DGF) affects up to 50% of kidney transplants and is mostly a result of ischaemia-reperfusion injury (IRI). DGF is associated with inferior graft and patient outcomes and prolonged hospitalisation. Local complement activation in the renal tubules seems to play a pivotal role in IRI. We have developed Mirococept, a cytotopic complement inhibitor, that can be administered to the donor kidney ex vivo prior to transplantation. After administration, Mirococept is retained in the donor organ, thereby minimizing the risk of systemic side effects. Previous work in a porcine kidney model showed that Mirococept at 80mg induces maximum tissue saturation. This is equivalent to 120mg in the human kidney. The EMPIRIKAL-2 trial aims to identify the most safe and efficacious dose of Mirococept to reduce DGF rate in deceased-donor kidney transplantation (KT).

Methods: EMPIRIKAL-2 is a UK-based phase IIa multi-centre double-blind randomised controlled trial (RCT) with an initial safety run. The purpose of the safety run is to assess the tolerance of each of the three proposed Mirococept doses (60, 120 or 180mg), before the RCT begins. Three patients will be assigned to each treatment dose, starting from the lower dose. The safety run will be considered successful if at least one dose can be taken forward to the RCT for comparison to placebo. If safety is met, 144 participants (36 per arm) will be randomised to all doses meeting the safety criteria or placebo on a 1:1:1:1 basis. The primary endpoint is DGF, defined as the requirement for dialysis during the first week after transplantation. Secondary endpoints include the rate of decline in creatinine, DGF duration, primary non-function, acute rejection rates and 1-year graft and patient survival. Immunosuppression therapy, antibiotic and antiviral prophylaxis will be administered as per local centre protocols. Enrolment in the safety run and the RCT is estimated to take approximately 4 and 12 months respectively. Patients will be followed-up for 12 months.

Results: We aim to present preliminary results of the safety run at the ESOT meeting.

Conclusions: The EMPIRIKAL-2 trial will evaluate the efficacy of a locally acting complement inhibitor in reducing DGF in KT.

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PP_141 CONTROLLED OXYGENATED REWARMING PRIOR TO NORMOTHERMIC MACHINE PERFUSION OF EXTENDED CRITERIA LIVERS

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Background: Shortage of suitable donor livers has led to utilization of extended criteria (EC)-livers, which carry higher post-transplant risks. Ex-situ dual hypothermic oxygenated machine perfusion (DHOPE) and normothermic machine perfusion (NMP) linked by controlled oxygenated rewarming (COR; DHOPE-COR-NMP) enables viability assessment prior to transplantation and has shown excellent outcomes. COR is a complex and dynamic phase during the DHOPE-COR-NMP protocol and we illustrate our experience, providing insights on what to expect during rewarming of the liver.

Methods: Data from DHOPE-COR-NMP procedures (August 2021-May 2024) were collected. Livers underwent 2 hours of DHOPE, 1 hour of COR, and at least 2.5 hours of NMP. Graft viability was assessed based on predefined criteria. During perfusion, hepatic artery (HA) and portal vein (PV) flows and pressures were recorded. Perfusate samples were analyzed for pH, partial pressure of carbon dioxide and oxygen (pCO2, pO_2), base excess (BE), bicarbonate (HCO_3^-), electrolytes (Na^+, K^+, Ca^{2+}, Cl^-), glucose and lactate. Post-transplant outcomes were collected.

Results: 35 DHOPE-COR-NMP procedures were performed, and 22 livers were transplanted (63% utilization). There were no cases of primary non-function (PNF), PV or HA thrombosis. One non-anastomotic stricture, three anastomotic strictures (NAS) and three biliary leakages occurred. Perfusion parameters during COR are shown in Figure 1. Perfusate flows, corrected for liver weight and pressure, increased during rewarming. pH increased from below 7.0 to 7.2, and pCO_2 and pO_2 decreased towards physiological levels. BE increased to -10 and after 15 minutes HCO_3^- slightly increased towards the end of COR. Due to activation of Na/K-ATPase, Na^+ levels increased, while K^+ levels decreased. Ca^{2+} and Cl^- levels remained relatively stable. An increase in glucose was observed throughout rewarming. Lactate increased up to 45 minutes, after which transplanted livers showed an earlier and steeper decrease in lactate at 60 minutes (p=0.0085).

Conclusions: We provided insight in the dynamic COR phase, demonstrating patterns during rewarming and differences between transplanted and non-transplanted livers at the end of COR. Outcomes of these EC-livers were excellent, with no PNF and one case of NAS.

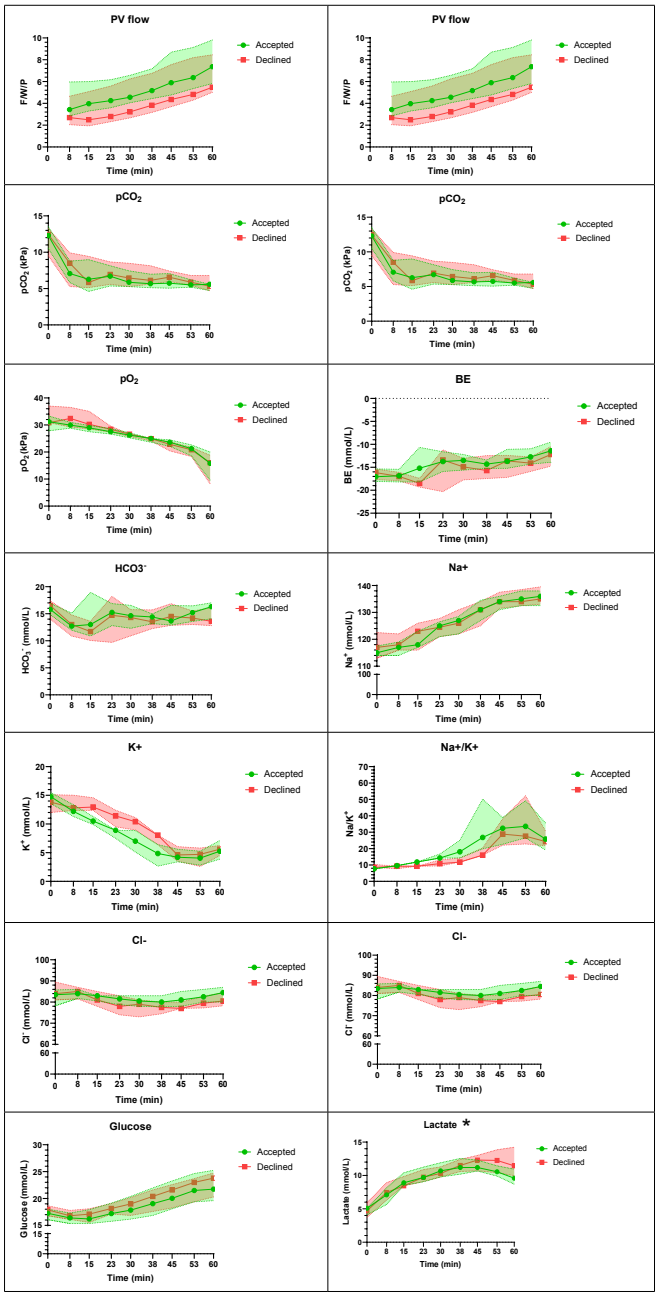

Figure 1 - Hepatic artery (HA) and portal vein (PV) flow corrected for liver weight and pressure. pH, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2), base excess (BE), bicarbonate (HCO_3^-), sodium (Na^+), potassium (K^+), sodium/potassium ratio (Na^+/K^+), calcium (Ca^{2+}), chloride (Cl^-), glucose and lactate.

Presented as median and interquartile range (IQR).

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PP_142 APPRAISAL OF THE ODC (ORGAN DONOR COORDINATOR)-BASED ORGAN DONATION, AND TRANSPLANTATION PROGRAMME IN GREECE

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Background: Deceased donation rates in Greece significantly lag behind leading European countries (5.71 ±1.42 donors per million population during 2001-2021). Recently, the Hellenic Transplantation Organization (HTO) has implemented several policies along with nationwide awareness campaigns in order to improve DBD (Donation after Brainstem Death) rates. The employment of ODCs (organ donor coordinator) at several hospitals for the early identification, assessment and referral of deceased donors, brain death confirmation, organ retrieval, and training of intensive care unit (ICU) professionals was an important measure. The aim of the study is to evaluate the activity of ODCs, in terms of several donation rates.

Methods: Retrospective data provided by the HTO were analyzed. The analysis refers to the three-year period after the employment of ODCs, whereas for some donation rates data before ODCs employment were also used, comparing the same time period.

Results: The employment of ODCs in 13 hospitals was associated with gradual improvement of all donation indicators. Firstly, there was an increase in the rates of brain death identification by 43%, and 60% during the second, and third respectively, compared to the first year of ODCs' presence. There was also an improvement in potential, and eligible donor referral by 43%, and 37.5%, respectively, during the second year, and by 31%, and 108%, respectively, during the third year. As ODCs have attained special training in approaching the potential donor's family, and marginal donors were also accepted, a consequent increase in the rates of actual deceased organ donors by 20% and 129% during the second and third, respectively, was documented. Finally, an increase in actual donors by 64% was noticed after ODCs employment, as compared with the previous years, for the same timeframe.

Conclusions: The ODCs programme, funded by Onassis Foundation, had positive results, as donation indicators steadily increased, even in hospitals with previous null organ procurement. Interestingly, the consolidation of ODCs network had a broader positive impact on donation activity in Greece, leading to a sustainable organ donor and transplantation framework.

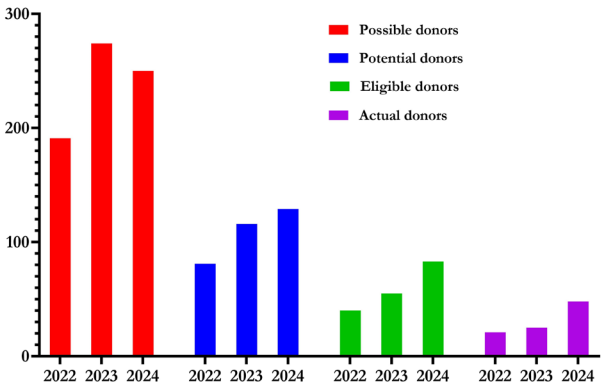

Figure 1. Donation rates during the period after ODCs employment

PP_143 DEVELOPMENT OF A MAGNETIC RESONANCE IMAGING PROTOCOL FOR EX-VIVO ASSESSMENT OF DECEASED DONOR HUMAN KIDNEYS

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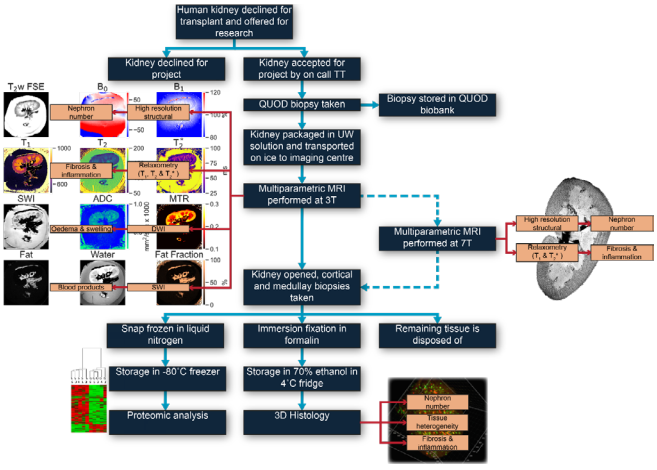
Background: In the UK deceased donor kidney viability is currently assessed using donor age, medical history, and estimated glomerular filtration rate, but these have limited predictive power resulting in potentially viable donor organs not being transplanted. The development of a rapid, non-invasive, assessment method of deceased donor kidney quality, ex-vivo, prior to transplant, would give clinicians confidence in determining the viability of donor kidneys. Here, we outline a Magnetic Resonance Imaging (MRI) protocol to study whole human kidneys that have been declined for transplant, integrating MRI measures with 3D-histology and tissue proteomics to develop an assessment protocol of deceased donor quality.

Methods: The research pathway of a declined kidney is shown below. The kidneys are retrieved for transplant but later declined and offered for research through the Quality in Organ Donation (QUOD) programme. Preparation mimics clinical practice; kidneys are flushed to remove any blood, bagged in University of Wisconsin solution and transported on ice. All kidneys are scanned on a 3T MRI system in a head coil. The MRI protocol collects high resolution structural, relaxometry, Apparent Diffusion Coefficient (ADC), Susceptibility-Weighted Imaging (SWI), magnetisation transfer ratio (MTR), fat/water, and field mapping scans. After MRI acquisition, the kidneys are cut lengthwise, and 24 punch biopsies taken from both the cortex and medulla. Half of these are formalin fixed for 3D-histology analysis; the other half are snap frozen for proteomic analysis.

Results: To date, fifteen kidneys have been imaged and biopsies taken. The images acquired from a representative subject are shown above. SWI data is especially effective for detecting any remaining blood products that should have been flushed at retrieval.

Conclusions: An MRI protocol has been developed to allow the assessment of donor kidneys, with samples subsequently being collected for validation via histology and proteomics. This work aims to establish a framework to allow non-invasive, whole kidney, assessment and potentially facilitate future donor kidney evaluations.

Acknowledgements: We acknowledge the funding support of Kidney Research UK (KS_RP_002_20210111), and the support of the NIHR Nottingham Biomedical Research Centre.



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PP_146 DEVELOPMENT OF AAV VECTOR BASED GENE THERAPY USING LIVER NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) enables liver preservation under close-to physiological conditions and thus, may serve as a platform to treat livers *ex situ*. Liver-directed adeno-associated virus (AAV) gene therapy is a promising option for the treatment of genetic liver diseases, but highly-specific AAV vectors are lacking. We herein utilized the NMP platform to optimize AAV vector-based gene therapy protocols.

Methods: Porcine livers (n=4) were procured and subjected to NMP (organOx Metra) for 48h. 3h after start of NMP, YFP-labelled AAV3B ($2x10^{13}$ vector genomes (vg) per kg liver) was applied into the perfusate. Serial perfusate samples during NMP were analysed for conventional liver viability parameters (lactate, AST, ALT, LDH) and complement factors. Tissue biopsies were taken pre virus application, after 3h, 24h and 48h, and immediately processed for real-time confocal microscopy to assess YFP signal, or cryopreserved for quantification of AAV3B gDNA levels.

Results: All livers could be successfully normothermically perfused for 48h, with lactate clearance present and low liver transaminases and LDH, suggesting stable perfusion and organ function. YFP-AAV3B application did not induce complement activation or an inflammatory response, as perfusate C3 and C4 as well as IL-6 levels remained low. AAV transduction was successful detected by YFP signals in immunofluorescence microscopy of tissue biopsies taken after 24h and 48h of NMP, but not as early as 3h. These results could be confirmed by quantification of AAV3B vector genomes.

Conclusions: AAV application during liver NMP is reasonable and do not induce adverse effects. This indicates the liver NMP model to be an excellent platform for the development of AAV-based gene-directed therapies.

PP_148 PROSPECTIVE EVALUATION OF RENAL FUNCTION IN LIVING KIDNEY DONORS DURING THE FIRST YEAR POST-DONATION

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Background: Living kidney donation plays a vital role in increasing transplant rates, particularly in countries with organ shortage. The altruistic principle of organ donation requires minimizing potential risks following nephrectomy. This study evaluated the renal function of living kidney donors during the first year after nephrectomy and examined potential influencing factors.

Methods: We prospectively studied 112 kidney donors followed at our Outpatient Donor Clinic between January 2021 and November 2023. Estimated glomerular filtration rate (eGFR) pre-donation was compared with eGFR at 3-, 6-, and 12-months post-donation. Associations between renal function and donor demographic factors and comorbidities were examined.

Results: Among 112 kidney donors, 34 (30.4%) were men, with a mean age of 61.16±10.14 years and a mean BMI of 27.12±3.85 kg/m2. Pre-donation eGFR values showed significant gender disparities, with men exhibiting lower levels than women (81.91±16.36 vs. 93.08±14.08 ml/min, respectively, p<0.001). A significant decline in renal function was observed 3 months post-donation, with eGFR decreasing by 29.3 ml/min (from 89.71±15.60 to 60.39±16.46 ml/min, p<0.001). After the first trimester, eGFR values stabilized and showed marginal improvement at 12 months (63.71±16.9 vs. 60.39±16.46 ml/min, p<0.001). Hypertensive donors demonstrated lower eGFR values both pre-donation (80±12.13 vs. 93.65±15.02 ml/min, p=0.025) and at one-year post-donation (59.38±15.29 vs. 65.65±17.4 ml/min, p=0.045). In contrast, gender, age, and tobacco use did not affect renal function at 12 months after donation. Donors with BMI≥ 30 kg/m2 had higher eGFR values than those with BMI<30 kg/m2, both pre- (93.05±15.64 vs. 90.98±15.35 ml/min, p<0.001) and one-year post-donation (71.27±20.6 vs. 61.40±15.08 ml/min, p=0.019).

Conclusions: Although kidney donation leads to sub-duplication of renal mass, donors' renal function does not decline proportionately, due to compensatory hyperfiltration by the remaining kidney. While the initial reduction in eGFR is expected and acceptable, it is typically followed by stabilization or slight improvement. The increasing number of elderly donors and those with comorbidities, highlights the importance of lifelong monitoring by transplant centers.

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PP_149 IMPACT OF PRESERVATION FLUID ON DECEASED DONOR ORGAN UTILISATION AND OUTCOMES

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Background: In the UK, University of Wisconsin solution (UW) is the most common fluid used for preserving deceased donor abdominal organs. Due to a manufacturing problem, UW was unavailable in the UK for 2023. As a result, Histidine-tryptophan-ketoglutarate solution (HTK) was used as an alternative. We hypothesised that there was no difference in organ utilisation and outcomes between solutions.

Methods: All proceeding deceased abdominal organ donors in the UK utilising UW (01/01/22-31/12/22) or HTK (01/01/23-31/12/23) were included. Transplant rates (transplanted/retrieved) were reviewed for kidney, liver and pancreas grafts. Post-transplant outcomes up to 90 days were analysed, including survival, delayed graft function rates, eGFR, and length of hospital stay, as at 05/06/24.

Results: 2626 donors were considered (1345 UW; 1281 HTK). Overall, there were lower transplant rates with HTK in kidney (UW 88% v HTK 86%; p=0.01), liver (80% v 76%; p=0.02), but not pancreas transplant (47% v 51%; p=0.3). In kidney recipients, immediate graft function was decreased significantly (73% v 67%; p=0.003) and median 3-month eGFR was lower (43 IQR: 32-56 v 41 IQR: 30-56; p=0.02) in the HTK cohort. When risk-adjusted, this rise in delayed graft function was borderline significant (p=0.06). Pancreas recipients had a significantly longer median days in hospital post-transplant with HTK (12 IQR: 9-19 v 15 IQR: 12-22; p=0.02). For liver transplant, there were no differences in any outcome. For all organs, there were no significant differences in any survival rates at 90 days (Table 1).

Conclusions: When UW was unavailable in the UK in 2023, the use of HTK over 12 months provided the opportunity to compare outcomes after UW or HTK preservation in unselected donors. This study showed no differences in outcomes after liver transplant but suggested marginally reduced graft function in HTK-preserved kidneys. Both solutions remain excellent in the preservation of abdominal organs for transplant.

Table 1 90 day unadjusted survival rates following first adult transplant, by perfusion fluid

Perfusion fluid	Number of transplants	Graft survival (95% CI)	Patient survival (95% CI)	Transplant survival (95% CI)
Kidney				
UW	1670	97.2 (96.3-97.9)	98.7 (98.0-99.2)	96.4 (95.4-97.2)
HTK	1460	96.0 (94.9-96.9)	98.8 (98.0-99.2)	95.4 (94.2-96.4)
Log-rank p-value		0.06	0.91	0.13
Pancreas				
UW	104	92.3 (85.2-96.1)	98.9 (92.5-99.8)	92.3 (85.2-96.1)
HTK	90	90.0 (81.7-94.7)	96.5 (89.6-98.9)	88.9 (80.3-93.9)
Log-rank p-value		0.54	0.22	0.39
Liver				
UW	695	95.7 (93.8-96.9)	97.0 (95.4-98.0)	94.1 (92.1-95.6)
HTK	589	95.0 (93.0-96.5)	96.6 (94.7-97.8)	93.9 (91.6-95.5)
Log-rank p-value		0.59	0.66	0.83

PP_150 ASSESSMENT OF BLOOD PRESSURE IN KIDNEY DONORS POST-NEPHRECTOMY. A CROSS SECTIONAL STUDY

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Background: Living kidney donation addresses the increasing demand for kidney transplants, especially in countries with a shortage of available grafts. Although it leads to physiological alterations that may elevate blood pressure (BP), the long-term impact of donation on BP is not well defined. The present study aimed to investigate determinants of BP in kidney donors after nephrectomy.

Methods: In a cross -sectional study, we included 107 kidney donors who were under regular follow up in the Outpatient Donor Clinic of our hospital, with a minimum of one year after nephrectomy. BP was assessed using both office measurements and 24-hour ambulatory blood pressure monitoring (24hABPM). Potential factors influencing BP were examined.

Results: Our cohort consisted of 70 women. The mean age was 62.4±9.8years and the mean eGFR was 61.1±13.2ml/min/1.73m2. Subjects were followed for a median time of 3.2 (1, 24) years. Among kidney donors, 28% had hypertension (HTN), 20.6% were obese (BMI>=30 kg/m2) and 32.7% were smokers. Among hypertensive donors, 60% were non-dippers, 26% were reverse dippers, and 10% had masked HTN. Donors with a history of HTN had a significantly higher BMI (28.8 ± 3.8 vs. 26.6 ± 4, p=0.03) and lower 25(OH) Vitamin D levels (23.1±8.7 vs. 29.1±11.4, p=0.03) compared to normotensive individuals. In univariate analysis, office and 24hABPM systolic BP (SBP) were strongly associated with obesity (p<0.001 and p=0.001, respectively). The same trend was observed for diastolic BP (DBP) using both methods (p=0.01 and p=0.01, respectively). Moreover, 24h, daytime, and nighttime SBP were inversely correlated with eGFR (p=0.017, p=0.01, and p=0.01, respectively), while no significant correlations were found between diastolic BP, dipping profile and eGFR. In multivariate analysis, obesity emerged as an independent factor not only for brachial SBP but also for aortic SBP (p=0.001 vs p=0.001 respectively), compared to eGFR (p=0.158 vs p=0.274 respectively).

Conclusions: In this cohort of living kidney donors, obesity, a modifiable factor, seems to have a stronger association with blood pressure than eGFR. Long-term medical monitoring following kidney donation is essential for promoting a healthy lifestyle and ensuring effective blood pressure management.

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PP_151 OUTCOMES AND EXPERIENCE IN ORGAN DONATION: RESULTS FROM A TERTIARY HOSPITAL WITH NO PRIOR ACTIVITY IN ORGAN PROCUREMENT

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Background: Because of increasing demands for organ transplantation, governments are developing strategies to strengthen their donation programs worldwide. In Greece, the implementation of a National Initiative for Transplantation and Organ Donation has resulted to doubling the number of Donors after Brainstem Death (DBD) from 5.71 in 2021 to approximately 10 donors per million population in 2024. The General Hospital of Thoracic Diseases of Athens is a Tertiary Hospital with no prior procurement activity and lack of a Trauma Department which has a total of 82 ICU beds (50 of which were added during the recent pandemic). Since April 2022 an Organ Donor Coordinator (ODC) has been appointed to our hospital. This study aims to document donation outcomes and characteristics of eligible DBD donors in our hospital after the assignment of an ODC.

Methods: Data of all eligible DBD donors from April 2022 to December 2024 were recorded and retrospectively analyzed.

Results: Fourty-two (50% male) eligible DBD donors were identified. Thirty-three (78.5%) were Greeks and 9 (21.5%) of foreign nationality. Twelve eligible donors were over 60 years old (up to 77y). The most frequent causes of death were: endocranial hemorrhage (50%), raptured aneurysm (14%), post-cardiac arrest encephalopathy (19%) and ischemic stroke (7%). In 21.4% of cases, Death by Neurological Criteria was confirmed into 3 days, in 47.6% between 3 to 7 days and in 31% after 7 days from detection. Consent rate in organ donation was 62%, being 73% (24 out of 33) among Greek families and 22% (2 out of 9) among foreign families. From 26 actual donors 69 solid organs (6 hearts, 2 lungs, 50 kidneys, 12 livers) and 42 corneas were retrieved. Religious beliefs and language barriers to communication were the reasons for foreign family refusal of donation, while among Greek families, the main reasons were intra-family miscommunication and fears of body alteration.

Conclusions: The Organ Donor Coordinator´s activity, raising awareness and supporting hospital professionals, in association with the increase of ICU beds have led to the significant donation rate in a hospital with no prior experience. The refusal rate among Greek families approached global data, however there is still enough room for further improvement.

PP_152 PRECONDITIONING OF ENDOTHELIAL CELLS WITH A NEDDYLATION INHIBITOR PROTECTS THEM AGAINST ISCHEMIA-REPERFUSION INJURIES

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Background: Long-term allograft survival, notably in kidney transplantation, is mainly limited by the occurrence of chronic antibody mediated rejection and aspecific fibrosis, the latter favored by ischemia-reperfusion injury (IRI) and by the use of organs from extended criteria donors of from donors after cardio-circulatory death. The graft endothelium is highly sensitive to IRI that causes chronic damages and increases its immunogenicity. Thus, a better preservation method and the treatment of organs prior to implantation (so called "graft preconditioning") constitute a major clinical challenge to improve graft survival.

Methods: We have evaluated the protective potential of neddylation blockade by MLN4924 as a graft preconditioning method in an *in vitro* ischemia-reperfusion model on microvascular endothelial cells (ECs). ECs were preconditioned for 3h at 4°C with 10 µM MLN4924 and subsequently switched back to 37°C in the presence of TNFα and IFNγ to mimic sterile inflammation, and resulting protective, inflammatory, and thrombotic cell responses were evaluated.

Results: We found that preconditioning of ECs with MLN4924 blocked the induction of ICAM-1, VCAM-1, E-Selectin, HLA I and HLA II molecules at their surface, and inhibited the release of IL6 and RANTES upon TNFα/IFNγ stimulation or upon aggression by activated T CD4 and T CD8 cells. This resulted in inhibition of T cell adhesion to ECs, as well as inhibition of EC-mediated allogenic T cell activation (non-professional antigen presenting cell properties). MLN4924 preconditioning also inhibited the expression of the prothrombotic molecules Tissue Factor and SERPINE 1 by ECs, suggesting an anti-thrombotic effect. It also increased in the expression of the complement inhibitor CD55 at the surface of ECs. Finally, MLN4924 treatment for 24h at 4°C in hypoxia (0% O2, model of cold storage) strongly diminished EC death by apoptosis in the hour following return to 37°C in normoxia (model of reperfusion).

Conclusions: Altogether, these results suggest that graft preconditioning by neddylation blockade during cold storage will protect graft ECs against IRI and reduce their immunogenicity, and has thus implications for the reduction of rejection and chronic changes that impair graft survival in the longer term.

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PP_153 COMPARATIVE ANALYSIS OF TRANSCIPTOMIC AND PROTEOMIC RESPONSES IN KIDNEY GRAFTS UNDERGOING NORMOTHERMIC PERFUSION

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Background: A shortage of donor kidneys has increased the use of marginal grafts, highlighting the need for better viability assessment to improve transplantation success. Normothermic machine perfusion (NMP) provides an opportunity to evaluate kidney function under near-physiological conditions before transplantation, enabling dynamic observation of organ function. This study aimed to clarify how transcriptomics and proteomics relate during NMP, providing insights into ex vivo kidney physiology and identifying potential biomarkers to improve graft viability assessment and predict transplant outcomes.

Methods: Thirty pigs underwent double nephrectomy, randomized to receive either 75 minutes of warm ischemia or no ischemia, followed by NMP. Renal biopsies were collected at pre-NMP, 1 hour, 2 hours, 3 hours, and 6 hours for transcriptomic and proteomic analyses. Only genes present in both datasets were included. Correlation analysis and unsupervised clustering were performed to assess transcriptome-proteome relationships, focusing on the impact of ischemia and perfusion on kidney physiology.

Results: Transcriptomics and proteomics analyses revealed distinct temporal patterns throughout the NMP process. Of the 5,600 overlapping gene-protein pairs, 27% showed positive correlation between mRNA expression and protein abundance, 5% showed negative correlation, and 68% exhibited no clear correlation. The proteomic changes typically lagged behind transcriptomic changes, with an average delay of 3 hours. This temporal delay indicates that mRNA expression changes precede the protein synthesis process. Approximately 20% of gene-protein pairs exhibited similar expression trends, clustering together in unsupervised clustering analysis, suggesting a synchronized response to ischemia and NMP conditions in these genes.

Conclusions: Proteomic changes lagged behind transcriptomic changes during NMP, with an average delay of 3 hours. This suggests that transcriptomics is a more reliable marker for assessing graft viability during the early stages of NMP. When eventually transformed to point-of-care biomarkers, early transcriptomic alterations may provide rapid insights into the graft's condition, whereas proteomic changes require more time to become evident.

PP_154 OUTCOMES WITH LARGE-FOR-SIZE GRAFT IN DECEASED DONOR LIVER TRANSPLANTATION: INSIGHTS FROM A HIGH-VOLUME CENTRE

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Background: Large-for-Size (LFS) grafts pose challenges in paediatric liver transplantation, but their impact on adult deceased donor liver transplantation (DDLT) is understudied. This study assesses short- and long-term outcomes of LFS grafts in adult DDLT at a high-volume liver transplant (LT) centre.

Methods: A retrospective review of primary LTs at King's College Hospital (2016–2023) evaluated outcomes based on graft-to-recipient weight ratio (GRWR). Patients were grouped into GRWR <2.0 and ≥2.0 (LFS grafts).

Results: Of 1560 transplants over 8 years, 1160 were analysed after excluding regrafts (n=101), super-urgent transplants (n=106), and missing graft weights (n=193). LFS grafts (n=576) were from younger (51.3 vs. 54.5 years; p=0.001), predominantly male donors (58.8% vs. 49.4%; p=0.001). Recipients were less often male (55.8% vs. 64.2%; p=0.003), weighed less (71.9 vs. 86.9 kg; p<0.001), and had lower BMI (25.2 vs. 29.3 kg/m²; p<0.001). LFS grafts were more often DCD (31.8% vs. 21.1%; p=0.001) with shorter CIT (150 vs. 170 mins; p=0.007). Outcomes showed no differences in PNF, early graft loss, or vascular/biliary complications. However, LFS recipients required more renal support (6.2% vs. 3.4%; p=0.020) and had longer ICU stays (5.2 vs. 3.9 days; p=0.009), though hospital stays were similar (15 vs. 14 days; p=0.20). One- and five-year graft and patient survival were comparable. In regrafts (data for 54/101), LFS grafts showed worse 5-year survival (90% vs. 10%; p<0.001). For super-urgent cases, outcomes were unaffected by LFS grafts.

Conclusions: LFS grafts may increase renal support needs and ICU stays, likely due to abdominal compartment syndrome. Caution is advised when using LFS grafts for redo transplants. Understanding GRWR can aid in optimising donor-recipient matching for better outcomes.

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PP_155 THE PIG AS A TRANSLATIONAL MODEL FOR RENAL NORMOTHERMIC MACHINE PERFUSION: INSIGHTS FROM TRANSCRIPTOMICS AND PROTEOMICS

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Background: Normothermic machine perfusion (NMP) is increasingly being explored as a platform for preserving and functionally assessing donor kidneys. However, detailed insights into renal physiology during NMP remain limited, especially regarding its translational relevance across species. Porcine kidneys are often used as a preclinical model to study the effect of NMP. Here, we aimed to investigate the pig as a model for human renal NMP by integrating transcriptomic and proteomic analyses.

Methods: Twenty discarded human and 60 pig kidneys were subjected to six hours of NMP. RNA sequencing and LC-MS/MS analyses were performed on cortical tissue biopsies taken before the initiation of NMP and at 1, 2, 3, and 6 hours of NMP. The differential expression of 50 predefined hallmark gene sets was analyzed, summarizing cellular processes to assess biological activity. By comparing the changes in protein and gene expression over time between human and pig kidneys, the interspecies differences in molecular responses to NMP were assessed.

Results: Over 6 hours of NMP, 48 out of 50 hallmark gene sets exhibited significant (adj.P<0.05) differential expression in the pig transcriptome, reflecting dynamic cellular changes during perfusion across almost all cellular processes. Importantly, all these transcriptomic alterations demonstrated a positive correlation between humans and pigs, with 30 out of 50 being significant (adj.P<0.05). This underscores a strong interspecies concordance in gene expression dynamics under NMP. In contrast, proteomic analyses revealed less pronounced concordance, with 39 out of 50 hallmark gene sets positively correlating, of which four were significant (adj.P<0.05). These were related to stress responses. This highlights a species-specific difference in protein regulation and post-transcriptional mechanisms.

Conclusions: Our findings suggest the pig is a robust and translationally relevant model for studying renal NMP, particularly at the transcriptomic level. These results provide a framework for understanding the molecular processes underpinning NMP and support using porcine models to optimize clinical kidney preservation and viability assessment strategies. Further study of proteomic divergences may reveal insights into species-specific adaptations during perfusion.

PP_156 IMPACT OF OXYGENATED HYPOTHERMIC MACHINE PERFUSION DURATION ON DECEASED DONOR KIDNEY TRANSPLANT OUTCOMES

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Background: Hypothermic machine perfusion (HMP) is the standard preservation method for deceased-donor kidneys in the Netherlands. For kidneys recovered from donors after circulatory death (DCD) aged 50 years or older, oxygenated hypothermic machine perfusion (HMP-O_2) has been proven to result in better outcomes compared to non-oxygenated HMP. Several studies have established that non-oxygenated HMP cannot be used to safely extend the duration of organ preservation, with each additional hour of HMP leading to worse post-transplant outcome. It has been suggested that oxygenation during HMP might allow a longer safe preservation time. Hence, this study aimed to evaluate whether the duration of HMP-O_2 influences transplant outcomes.

Methods: We retrospectively analyzed 1,777 deceased-donor kidney transplants performed in the Netherlands between 2014 and 2024. Of these, 547 kidneys underwent HMP-O_2, while 1,230 underwent non-oxygenated HMP. Multivariate Cox proportional hazards models and Kaplan-Meier survival analyses were used to assess the relationship between HMP-O_2 duration and graft survival.

Results: We found no significant association between HMP-O_2 duration and one-year graft survival (adjusted hazard ratio: 1.033, p = 0.339). Kaplan-Meier survival analysis similarly demonstrated that longer HMP-O_2 durations did not adversely affect graft survival. In contrast, longer durations of non-oxygenated HMP were significantly associated with an increased risk of graft failure (adjusted hazard ratio: 1.046, p = 0.003) and Kaplan-Meier analysis clearly confirmed this.

Conclusions: This study suggests that longer HMP-O_2 durations do not compromise kidney graft survival. These findings carefully support the potential of HMP-O_2 to reduce the urgency of nighttime surgeries by allowing a safe extension of the preservation time. Nevertheless, further research is needed to confirm these observations, evaluate other important outcome measures and also define an upper safe limit for HMP-O_2 duration.

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PP_157 GRAFT AND PATIENT OUTCOME OF KIDNEY TRANSPLANTATION FROM DECEASED ORGAN DONORS WITH PROTEINURIA

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Background: Kidney transplantation (KT) remains the preferred treatment among end-stage renal disease (ESRD) patients. Thorough evaluation of donors is important in order to properly select candidates for KT. Proteinuria was known to be a strong predictor of ESRD thus reservations have been made for deceased organ donors (DOD) having proteinuria. This study aims to evaluate the outcomes of post-KT recipients from DOD with proteinuria.

Methods: A retrospective cohort study of 176 DOD-KT recipients from January 1, 2015 to December 31, 2023 in which 23% were from non-proteinuric DOD and 77% from proteinuric DOD. Outcomes of DOD-KT recipients were analyzed, including renal function, proteinuria, and graft and patient survival up to 12-month post-KT.

Results: There was no significant difference on the 12-month post-KT mean creatinine, eGFR, proteinuria, patient, graft, and death-censored allograft survival among KT recipients receiving kidneys from proteinuric vs non-proteinuric DOD. The rejection rate was 2.2% within 12-month post-KT. At the end of the follow-up period of the study, 83% of the KT recipients from proteinuric DOD became non-proteinuric.

Conclusions: There is high incidence of pre-donation proteinuria among DOD with subsequent decline at 12-month post-KT. The graft, patient and death-censored allograft survival of KT recipients from proteinuric DOD is similar with non-proteinuric DOD. Using kidneys from DOD with proteinuria may benefit more patients and reduce waiting time among KT candidates.

PP_158 VISUALIZING GRAFT PERFORMANCE: DEVELOPING AN INTERACTIVE REGISTRY FOR MACHINE PERFUSION

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Background: Machine preservation (MP) for liver transplantation has steadily increased in recent years. However, research on key parameters including viability criteria and patient outcomes is hindered by low incidence seen within single institutions. We have therefore created the PUMP Consortium – combining real-time data collection and historic data collated within a multi-center registry for enhanced evaluation of clinical perfusion.

Methods: A core multidisciplinary team including surgeons, perfusionists, program coordinators, researchers, and computational scientists convened with software developers to create the PUMP platform. An iterative design model was utilized, constructing a framework to support relevant real-time feedback to the clinical team and facilitate data collection for future research. Appropriate regulatory departments were consulted to ensure patient and data protection throughout the process.

Results: Web-based and mobile platforms were developed simultaneously to promote efficient entry of basic graft information, perfusion parameters, and perfusate analysis. Generated graphics, benchmarked against historic cases in the registry, allow the surgeon to contextualize graft performance within previous recipient outcomes. These outcomes and detailed donor information can be updated post-operatively to enrich evaluation of subsequent perfusions [Fig. 1]. Clinical beta-testing has commenced at a single center, with prioritization of usability for accurate, timely data input and clear assessment by the surgical team. Additional features including user notifications and institutional workflow customization remain in the pipeline. Adoption at other centers will follow regulatory review.

Conclusions: The PUMP Consortium registry empowers clinicians and researchers to actively engage with perfusion data. Continued collaboration and iterative assessment are necessary to expand the database, promoting research and optimizing the impact of MP on clinical outcomes.

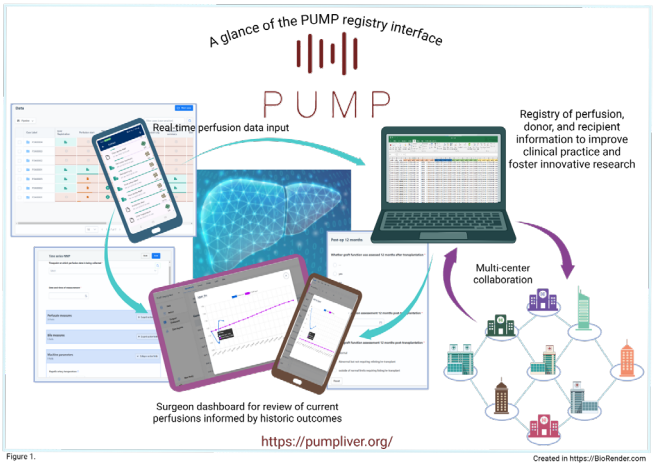

Figure 1.

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PP_159 PERFORMANCE OF MULTIVISCERAL GRAFTS DURING NORMOTHERMIC MACHINE PERFUSION

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Background: Machine perfusion has an increasing role in clinical transplantation with evolving research applications. Significant growth has occurred in liver and kidney preservation but to date little has been published regarding multivisceral en bloc perfusion. Previous iterations of this model at our department incorporated hypothermic perfusion and variations in graft procurement. Here, we describe early results from multivisceral grafts which underwent normothermic machine perfusion (NMP) alone with standardized graft and circuit composition.

Methods: The multivisceral graft containing the liver, kidneys, pancreas, spleen, and proximal bowel was procured en bloc from six swine and connected to a customized perfusion circuit [Fig. 1A]. Normothermic perfusion commenced with a blood-based perfusate with addition of albumin or STEEN for volume repletion as needed. Perfusion parameters were recorded and perfusate and biopsy samples were obtained for analysis.

Results: All grafts underwent at least 8 hours of NMP. The mean aortic flow was 1.37 ± 0.40 L/min with mean pressures sustained at 71.33 ± 5.29 mmHg. Elevated aortic resistance was noted during perfusion of graft 5, which improved after realignment with arterial inflow [Fig. 1B, C, D]. Evidence of organ function, including bowel peristalsis and urine production, was observed in all grafts, with bile produced by all but graft 6. All grafts exhibited lactate clearance during perfusion with mean lactate decreasing from 5.02 ± 1.53 to 1.69 ± 1.06 [Fig. 1E]. Levels of functional biomarkers varied during perfusion, with most downtrending at the end of perfusion [Table 1]. Post-perfusion microscopic architecture was preserved, particularly on liver and kidney histology [Fig. 1G-J].

Conclusions: Multivisceral perfusion can be achieved with evidence of preserved organ function up to 8 hours. Further analysis is required to characterize histologic and functional changes during the perfusion course. Future steps will investigate adjustments necessary to create a stable platform for extended evaluation of en bloc physiology and exploration of ex vivo therapeutics, with eventual translation into clinical machine perfusion.

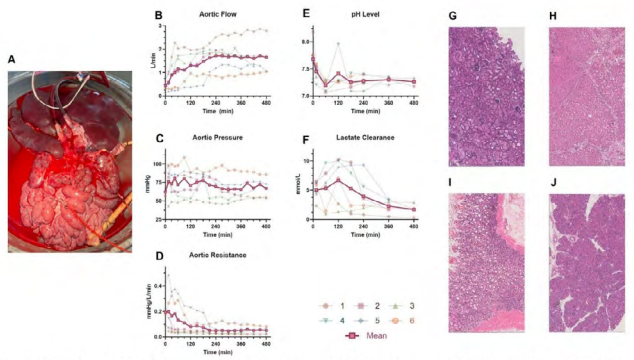

Figure 1. Multivisceral graft perfusion: A) gross image of multivisceral graft. Perfusion parameters: B) aortic flow; C) aortic pressure; D) aortic resistance; E) pH level; F) lactate clearance. Representative post-perfusion histology, 10x magnification: G) kidney; H) liver; I) proximal bowel; J) pancreas

Graphs and figure created in GraphPad Prism

Table 1. Functional markers during perfusion

	Baseline	240 mins	End
(units)	Mean (SEM)	Mean (SEM)	Mean (SEM)
AST (U/L)	148.5 (92.74)	900.7 (196.60)	885.3 (219.90)
ALT (U/L)	26.67 (2.93)	63.00 (11.05)	60.83 (12.98)
Amylase (U/L)	970.80 (143.40)	4662 (520.20)	5670 (1403)
Lipase (U/L)	596.40 (526.90)	1816 (505.70)	3683 (1443)
BUN (mg/dL)	8.17 (0.83)	24.50 (2.95)	36.17 (5.72)
Creatinine (mg/dL)	9.70 (1.23)	9.55 (3.62)	4.65 (0.72)
LDH (mmol/L)	568.80 (136.90)	1914 (258.90)	1719 (463.70)
Lactate (mmol/L)	5.02 (0.62)	3.94 (1.27)	1.90 (0.40)

Table 1. Perfusate analysis of functional markers at baseline, 240 minutes, and end of perfusion. Mean and standard error of the mean (SEM) calculated in GraphPad Prism. Abbreviations: aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), lactate dehydrogenase (LDH).

PP_160 PLASMA PROTEOME DURING NORMOTHERMIC REGIONAL PERFUSION SHOW REDUCED COMPLEMENT AND HIGH DETOXIFICATION LEVELS

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Background: Abdominal normothermic regional perfusion (NRP) is a retrieval technique which restores blood circulation to abdominal organs in donation after circulatory death (DCD). It allows an enhanced organ assessment and a more controlled retrieval by bridging asystole and organ procurement. Clinical data suggest improved transplant outcomes for NRP-DCD livers and kidneys compared to standard DCD donation. Despite the potential clinical benefit, little is known about the molecular changes induced by NRP. The aim of this study is to analyse changes to the donor plasma proteome during NRP in a cohort of clinical samples from UK DCD-NRP donors.

Methods: Multiple plasma samples from 10 DCD-NRP donors were collected at the end of donor management, prior to NRP (NRP DB) and at various timepoints during NRP (NRP 0h, NRP 1h, NRP 2h), processed and stored by the UK Quality in Organ Donation (QUOD) Biobank. Proteins were extracted from plasma, trypsin-digested and analysed by untargeted LC-MS/MS proteomics. Proteins were identified and quantitated using Proteome Discoverer 3.1 and differential expression of proteins over time was assessed by one-way ANOVA (Perseus 1.6.15.0). Enrichments in biological processes were analysed by String. Similarly, metabolites were extracted from the plasma samples and analysed by LC-MS/MS.

Results: A total of 759 proteins were identified in at least 70% of samples in each group and taken forward for analysis. Seventy-one proteins were significantly (FDR 0.05) differentially expressed between the end of donor management and end of NRP (Figure 1A), with 39 proteins increased and 32 decreased. The top three biological processes significantly upregulated were: cellular detoxification, generation of precursor metabolites and glycolysis, while complement activation and humoral immune response were significantly decreased (Figure 1B). Integrated Metabolomics analysis is currently underway.

Conclusions: This study describes plasma protein changes that occur after DCD donor management and during subsequent NRP, offering an initial insight into the molecular mechanisms that potentially relate to the clinical benefits of NRP. These results may help to better understand and enhance donor assessment prior to transplantation.

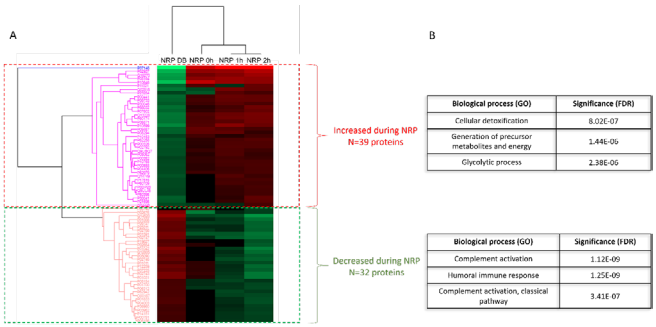

Figure 1. Heatmap of plasma proteins significantly increased (red) or decreased (green) over the course of NRP (A) and top 3 enriched biological processes in the two identified protein clusters (B). (A) N=71 proteins were significantly differentially expressed when comparing DCD NRP donor plasma collected at the end of donor management (NRP DB) and sequential plasma samples collected over the course of NRP (NRP 0h, NRP 1h, NRP 2h) (1-way ANOVA, FDR 0.05). (B) Gene ontology analysis of enriched biological processes showed a significant increase in cellular detoxification, generation of precursor metabolites and glycolytic processes and a significant decrease in complement activation and immune response over the course of NRP.

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PP_161 PGC-1 ALPHA PLAY A ROLE IN HYPOTHERMIC RENAL PROTECTION IN ISCHEMIA-REPERFUSION INDUCED RENAL FIBROSIS MICE MODEL

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Background: Hypothermia is recognized for its protective effects against acute renal injury caused by ischemia-reperfusion injury (IRI). However, its impact on renal fibrosis following IRI remains unclear. This study aimed to evaluate the protective effects of hypothermia on renal function and fibrosis and to elucidate the underlying molecular mechanisms.

Methods: A renal fibrosis mouse model was utilized to study ischemia-reperfusion injury. C57BL/6 mice were allocated into sham control and IRI groups (maintained at 37°C or 32°C). Kidneys were harvested on days 1, 3, and 7 post-IRI. Molecular pathways involved in renal injury and protection were investigated using histological analysis and cellular assays.

Results: Mice in the 32°C IRI group exhibited significantly reduced blood urea nitrogen (BUN) and serum creatinine (s-Cr) levels and improved histologic renal injury scores compared to those in the 37°C IRI group. Hypothermia significantly decreased TGF-β and α-SMA expression while increasing PGC-1α levels in kidney tissue. In HK2 cells, cold preparation enhanced PGC-1α expression and attenuated TGF-β-induced increases in α-SMA and type IV collagen. Knockdown of PGC-1α using siRNA abrogated these protective effects of cold preparation.

Conclusions: Hypothermia mitigates renal function decline and fibrosis in ischemia-reperfusion-injured kidneys. PGC-1α is a critical mediator of the protective effects of hypothermia in renal fibrosis following IRI.

PP_162 IMPACT OF PRESERVATION FLUIDS ON POST-PANCREAS TRANSPLANT COMPLICATIONS: UW VS HTK

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Background: Preservation solutions are used to maintain the organ intended for transplantation in optimal conditions from retrieval to reperfusion. University of Wisconsin (UW) is currently the most frequently used preservation fluid in pancreas transplantation (PT). Several studies have suggested that the use of Histidine-Tryptophan-Ketoglutarate (HTK) remains controversial, as it is associated with an increased incidence of post-transplant complications. This study aims to compare the outcomes of PT according to the preservation fluid used.

Methods: We compared outcomes of pancreatic grafts flushed and stored with either UW or HTK, using a prospectively maintained database from 09/2021 to 02/2024. Continuous variables are summarised with median and interquartile range and compared using the U Mann Witney test. Categorical variables are summarised with proportions and percentages and compared with the Chi-square test. Cox regression was used to identify risk factors for graft pancreatitis.

Results: 107 PT were performed. 3 patients were excluded from the study as they were transplanted during a transition period between UW and HTK. 104 patients (52 with UW and 52 with HTK) were included in the analysis. There were no significant differences in recipient demographics, donor age (31 vs 39 years, p=0.067), CIT (648 vs 669 min, p=0.132) or percentage of DCDs (14 vs 21%, p=0.296), although there was a trend towards older and DCD donors in the HTK cohort. Postoperatively, a significantly higher number of CT scans were performed (42.3 vs 57.7%, p=0.034) in the HTK cohort. Postoperatively, a significantly higher number of CT scans were performed (42.3 vs 57.7%, p=0.034) and numerically but not significantly higher rate of graft pancreatitis (7.7 vs 15.4%, p=0.365) was observed with HTK. Risk of graft pancreatitis was not independently associated with the type of perfusion fluid used (Table 1).

Conclusions: This single centre analysis found no significant differences in postoperative complications between UW and HTK. Further research with multicentre studies with larger sample sizes and longer follow-up periods is required to analyse the effect of the type of perfusion fluid on short- and long-term transplant outcomes.

	B	HR	P value	95% CI
Type of preservation fluid (UW/HTK)	-0.413	0.662	0.539	0.177-2.469
Recipient age	-0.004	0.996	0.904	0.929-1.067
Recipient BMI (m/kg^2)	-0133	0.876	0.238	0.703-1.091
Donor age	0.046	1.047	0.117	0.989-1.110
Donor BMI (m/kg^2)	-0.035	0.966	0.742	0.785-1.189
Donor type (DCD/DBD)	0.469	1.599	0.506	0.402-6.361
CIT	0.003	1.003	0.298	0.997-1.009
CRF	-0.004	0.996	0.730	0.977-1.017

Table 1. Cox proportional hazards regression analysis of risk factors for graft pancreatitis.

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PP_163 CANCER TRANSMISSION IN DECEASED DONOR ORGAN TRANSPLANTATION: AN AUSTRALIAN POPULATION-BASED LINKAGE STUDY

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Background: Cancer transmission-risks from deceased organ donors to recipients may be overestimated, as non-transmissions are rarely reported. We sought to estimate the transmission-risk for breast, prostate, colorectal cancers in deceased donors and identify missed opportunities for donation.

Methods: We linked all persons referred for consideration for deceased organ donation (actual donors and potential donors forgone) and transplant recipients, 2010-2018, with population cancer registry notifications, 1976-2018 in NSW, Australia. We assessed cancer transmission rates from actual donors and compared suspected cancer history during medical assessment with validated cancer registrations of potential donors forgone.

Results: Of 165 cancer histories identified in 993 deceased donors, there was one high-risk breast, six minimal-to-high-risk prostate, and no colorectal cancers. Organs from these seven donors were transplanted in 11 recipients (ten kidneys, one liver) with no evidence of "Proven/Probable" cancer transmission after a median 6-years' follow-up. Additionally, 169/3,588(5%) potential donors were forgone for a suspected cancer transmission risk. Of these, 6/169(4%) had no cancer registration, and 39/169(23%) had registered cancers of minimal-to-low- transmission risk. Accepting these 45 additional donors would have increased donation by 5%.

Conclusions: A balanced review of transmission and non-transmission events in organ donation could inform current risk assessments and improve donation rates.

PP_164 FLAVIN MONONUCLEOTIDE AS AN ADDITIONAL MARKER FOR LIVER VIABILITY ASSESSMENT

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Background: Ex situ machine perfusion is increasingly recognized as a strategy to optimize the utilization of donor livers for transplantation. Despite its potential, it would be useful to integrate criteria for evaluating mitochondrial function, which guarantees proper metabolic functioning of the organ. This study aims to validate the predictive potential of perfusate flavin mononucleotide (FMN) and nicotinamide adenine dinucleotide (NADH) during HOPE to enable the implementation of FMN-based assessment into clinical routine and to identify safe organ acceptance thresholds.

Methods: Livers were perfused under hypothermic devices HOPE (XVIVO); perfusate samples were collected at defined intervals (5, 30, 60 minutes and at the end of perfusion). FMN was quantified using fluorimetric analyses and absorbance-based, while levels were assessed exclusively through fluorescence. Additionally, liver biopsies from discarded grafts were assessed by immunohistochemistry (IHC). A correlation analysis was conducted between ELISA and fluorimetric measurements of FMN. Donors and recipients data were collected for clinical correlation.

Results: A total of 43 livers (76% DBD and 24% DCD), perfused in HOPE were analyzed. Mean perfusion time was 231 minutes. Mean donor age was 70.4 years. Overall, we had two patients deaths (due to sepsis) and one graft loss (due to vascular thrombosis): no significant correlation emerged between these outcomes and the levels of FMN and NADH. No correlation was found between FMN level and the need for CCRT or non-anastomotic strictures in DCD graft. Among the 43 livers analyzed, 5 graft (11.6%) were discarded due to hemodynamic and macroscopic appearances during HOPE: only these cases exhibiting elevated FMN (>1x10^{6}ng/ml) and NADH levels. IHC analyses on these discarded livers are going to be analyzed.

Conclusions: Dynamic liver perfusion emerges as a promising tool for assessing organ quality and predicting post-transplant function and outcomes. Real-time monitoring of FMN and NADH levels during perfusion confirms to represent a valuable addition to the clinical decision-making process for graft assessment: ELISA test validated the pattern observed in the fluorescence assay.

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PP_165 KINETIC ESTIMATED GLOMERULAR FILTRATION RATE IS A PROMISING MARKER OF KIDNEY GRAFT QUALITY

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Background: Biopsy findings play an important role in many algorithms aimed at estimating organ quality, but can lead to unnecessary organ discard. Moreover, kinetics of serum creatinine do not correlate with glomerular filtration rate (GFR) in donors with acute kidney Injury (AKI), which poses another challenge for evaluating organ quality. A new concept of Kinetic GFR (keGFR) was recently developed, representing an estimate of immediate GFR, that reflects "real-time" kidney function. (Chen et al., J Am Soc Nephrol, 2015) We hypothesize that KeGFR calculation performed in donors prior to organ procurement could add prognostic information of donor kidney graft quality beyond the current AKI classification or biopsy.

Methods: In this prospective study, procurement kidney biopsies were performed in 137 deceased donors between May 2021 and December 2022. AKI was defined by AKIN criteria. Mixed-effect linear models were used to predict eGFR at 1-year post-transplant. A donor biopsy score was calculated as a mean of cv, ah and IF/TA scores. The root Mean Square Error measure was used to compare model performance.

Results: AKI was present in 60 (43.8%) of donors. A multivariable model showed donor keGFR and donor biopsy score were the only independent predictors of eGFR at 12 months (β 2.14, SE 0.91, p = 0.02; β -5.32, SE 2.5, p = 0.03, respectively). Donor AKI nor terminal creatinine were associated with lower eGFR at 12 months (β -0.79, SE 2.42, p = 0,74; β 0.62, SE 0.66, p = 0.34). Next, model performance of models with keGFR and/or biopsy scores was evaluated. Performance of models using only keGFR and biopsy were similar (RMSE 18.67 vs. RMSE 18.68, respectively). Addition of both parameters into the model did not substantially improve prediction performance (RMSE 18.29).

Conclusions: Kinetic GFR is a good predictor of graft function post-transplant, which might challenge the use of kidney donor biopsies in the future.

PP_166 A REVOLUTIONARY MODEL FOR THE STUDY OF HUMAN LONG-TERM PERFUSION

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Background: Normothermic machine perfusion preserves organs ex vivo, maintaining aerobic metabolism and viability, having an immense potential for prolonged isolated organ studies and interventions, including physiological analyses, regenerative medicine, and gene product delivery. Stable long-term homeostasis is essential. Combining NMP with continuous kidney replacement therapy (CKRT) maintains hydro-electrolyte and acid-base balance.

Methods: Following a successful 17-day pilot perfusion, the platform was refined for stability and reproducibility. This study reports 5 liver perfusions lasting over 7 days, assessing performance via macroscopic evaluation, perfusate and bile analyses, and routine biopsies. Key metrics included lactate clearance, coagulation factor synthesis, injury markers, albumin, BUN, tumor markers, cytokines, FMN, and NADH. Additional analyses covered bile production, glucose, pH, transaminases, and tumor markers. Biopsies of healthy and tumor tissue were stained, analyzed for RNA integrity, and preserved for proteomic and transcriptomic studies.

Results: Five livers from CRLM patients were obtained at transplant after hepatectomy, flushed with room-temperature solution, and perfused at 37°C. Mean WIT was 15 minutes, and mean perfusion time was 196 hours with stable hemodynamics. Mean PV flow was 0.84 ml/min, HA flow 155 ml/min, and bile production 10 ml/h. Lactate clearance (<2.5 mmol/L) was achieved within 240 minutes, and hydro-electrolyte, ammonia, and pH were maintained. Over 7 days perfusion three cases showed elevated lactate and worsening hemodynamics, linked to microbial cultures (1 Gram-, 2 Gram+), as confirmed by histology. IL-6 was consistently elevated across cases, while FMN and NADH levels rose in late perfusion stages.

Conclusions: We introduced and demonstrated the feasibility of a new technique to expand the availability of human livers for experimental models. We adopted explanted diseased organs (CRLM) obtained at the time of hepatectomy to undergo long-term commercially available MP. We herein show the feasibility and reliability of the model for at least 7 days perfusion. This model will provide extra livers for in-depth and physio-pathological studies, opening promising avenues for high-level translational research.

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PP_167 NEW HOPE FOR INCURABLE LUNG DISEASES - ENDOTHELIAL CELL-BASED EX-SITU THERAPY

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Background: Ex situ lung perfusion (ESLP) was originally developed as alternative to static cold preservation and is now also established as promising tool for evaluating, recovering and optimizing marginal donor organs, especially by regenerative approaches. Since endothelium plays an important pathogenetic role in many lung diseases (e.g. pulmonary arterial hypertension (PHT)), we developed an endothelial cell-based ex situ therapy in which diseased native endothelium can be supplemented or even replaced by functional endothelium.

Methods: Using ESLP-relevant preservation solutions and concentrations of 17ß-estradiol (ES), disintegration of the native endothelial monolayer (EM) with subsequent integration of labelled endothelial cells (ECs) and subsequent viability, regeneration of cell-cell connections and the barrier functions of EM were analyzed. EC-specific nitric oxide, activation and thrombogenic state markers, also physiological reactivity to TNFα were analyzed by qRT-PCR. Optimal protocol was applied to ex situ perfused rat lungs. After disintegration, perfusion solution enriched with labeled ECs was delivered. FACS quantified labeled, non-integrated ECs at the end in perfusion solution. Lungs were fixed and subjected to cryosection technique or optical clearing for light-sheet microscopy (LSM) to detect integrated ECs.

Results: All perfusion solutions led to endothelial disintegration, enhanced by concentration-dependent ES addition. CDH5 immunofluorescence provided evidence for integration of vital, labelled ECs into native EM, whose confluence and barrier function were regenerated. qRT-PCR confirmed a physiologically non-inflammatory and antithrombogenic eNOS-producing EC layer. Labeled ECs were detected throughout the whole rat lung, including pulmonary microvasculature, while FACS showed that <1% of labeled ECs were washed out.

Conclusions: Demonstrating general feasibility enables establishment for specialized applications, such as using genetically modified ECs (e.g., eNOS-producing ECs in PHT) and transferring to other ex situ perfused organs (e.g., LAMA4 in DCM). Successful implementation expands the donor pool by treating marginal organs and enables transfer to autologous ex situ therapy, thus replacing transplantation.

PP_168 BARRIERS AND FACILITATORS TO PHYSICAL ACTIVITY FOR TRANSPLANT RECIPIENTS; THE ROLE OF SOCIAL NETWORKS

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Background: Research suggests that most transplant recipients do not meet the recommended amount and type of physical activity (PA), thereby limiting their wellbeing and long-term health. Transplant recipients are surrounded by a network of relationships (e.g., family, friends, medical professional) that may influence their PA and health-related behaviours (Fernández-Peña et al., 2018). Using Patient and Public Involvement and engagement (PPI), we explored the lived experiences of 26 transplant recipients in Australia and the UK and their support environment. Therefore, our main research question is: Using PPI what are the barriers and facilitators to PA of transplant patients, and what social and medical support structures can encourage PA?

Methods: A combination of social network analysis (Fernández-Peña et al., 2018; Merminod et al., 2022) and semi-structured interviews were used to triangulate the lived experiences of 26 transplant recipients.

Results: The findings indicate transplant recipients often discussed their transplant experiences with family, friends, partners, and healthcare professionals. In total 299 relations were identified by the 26 participants, whereby on average participants had 11.50 alters (SD = 4.90, range: 5-20) with whom they discussed their transplant experiences. Regression analysis suggest having more physically active network connections may increase transplant recipients' levels of PA (i.e., having one more alter that is physically active would lead to 531.98 addition MET). Most transplant recipients maintained or increased their level of PA post-transplant. Transplant recipients experienced various barriers to post-transplant PA (i.e., fear of injury, infection, lack of guidance), however positive experience of PA motivated transplant recipients to (re-)engage in PA. Connecting with other transplant recipients appeared to reduce isolation.

Conclusions: Social networks play an important role in influencing transplant recipients' level of PA. We are currently working with transplant recipients to create a PA framework and aim to share further results and conclusions at the ESOT congress in the summer.

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PP_170 BETWEEN BURDEN AND CONFIRMATION: THE INFLUENCE OF THANK-YOU LETTERS ON ORGAN DONATION COORDINATORS

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Background: Thank-you letters from organ recipients or from families in the organ donation process play an important and emotional role for both the writer and the recipient. They are a symbol of appreciation and connection. But what influence do these letters have on the treatment team, which is directly involved in the process of organ donation and transplantation on a daily basis? This study aims to analyze this on the basis of a survey of professionals.

Methods: A questionnaire with 16 questions was sent to two people from each of the transplant and organ donation teams in Switzerland. Five teams exclusively care for organ donors, three teams focus solely on organ recipients, and three teams support both organ donors and organ recipients (mixed teams). The questions relate to the emotional impact of the thank-you letters on them personally, on the team and on their daily work.

Results: Mixed teams or those that support organ donors and their families, deal with the thank-you letters more intensively compared to teams that exclusively support organ recipients. The answers were more emotional and more detailed. The coordinators feel joy and satisfaction when reading a letter. They are a confirmation, appreciation and motivation for their daily work as well as a sign of solidarity. Special letters – or those written after many years – remain particularly memorable. The same applies to letters from the donor family to the organ recipients. Those are a mixture of pain and loss, but also generosity and hope. Thank-you letters humanize the organ donation. Some coordinators find it difficult to contact the family to forward the letters, because they do not know what stage of the grieving process they are at. Letters are written anonymously, without blame and without expectations. The process in the centers varies in terms of procedure, timing, focus and attitude when it comes to talking to the organ recipients about the possibility of writing a thank-you letter.

Conclusions: Thank-you letters symbolize a bridge between life and death as well as between mourning and hope. The gratitude expressed in these letters highlights the positive aspects in the process of organ donation, which is often characterized by stress and emotional challenge. This is a resource and thus strengthens resilience of the professionals involved.

PP_171 FAT FILTER REDUCES LIPID LEVELS IN PERFUSATE OF STEATOTIC DONOR LIVERS DURING NORMOTHERMIC PERFUSION

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Background: The increasing prevalence of steatotic donor livers challenges transplantation due to their vulnerability to ischemia-reperfusion injury. Severely steatotic livers are often deemed unsuitable for transplantation. Long-term normothermic machine perfusion (LT-NMP) offers a platform to study and improve these organs. However, lipid release from the liver into the perfusate during NMP may cause fat embolisms in capillaries. We examined whether a fat filter can reduce lipid concentrations in the perfusate during LT-NMP paving the way for potential liver defatting in the future.

Methods: Four human donor livers allocated for research underwent LT-NMP using a red blood cell-based perfusate and parenteral nutrition with a modified Liver Assist device (XVIVO, Groningen, the Netherlands). Modifications included specialized oxygenators, continuous renal replacement therapy, and real-time monitoring for 7 days. A fat filter (Liposorber DL-50, Kaneka Medical Europe N.V., Eschborn, Germany) was applied twice (2 hours, days 4 and 7) for livers 1 and 2 or once (6 hours, day 7) for livers 3 and 4. Triglycerides and ApoB concentrations in the perfusate were measured at 12-hour intervals.

Results: Four human donor livers (median BMI donor 29 kg/m², median liver weight 2117 g) were successfully maintained on NMP for 7 days. Fat filter application on day 4 reduced median triglycerides from 2.62 to 1.29 mmol/L (-51%) and ApoB from 0.66 to 0.24 g/L (-70%). A subsequent fat filter application on day 7 decreased median triglycerides from 3.27 to 2.10 mmol/L (-36%) and ApoB from 0.79 to 0.24 g/L (-75%) (Figure).

Conclusions: Fat filter application during NMP effectively reduces triglyceride and ApoB levels in the perfusate. As these lipids are derived from the liver, the liver is expected to become less steatotic, a hypothesis under investigation. Further research is needed to assess the impact of perfusate lipid concentrations on the functional quality of these livers.

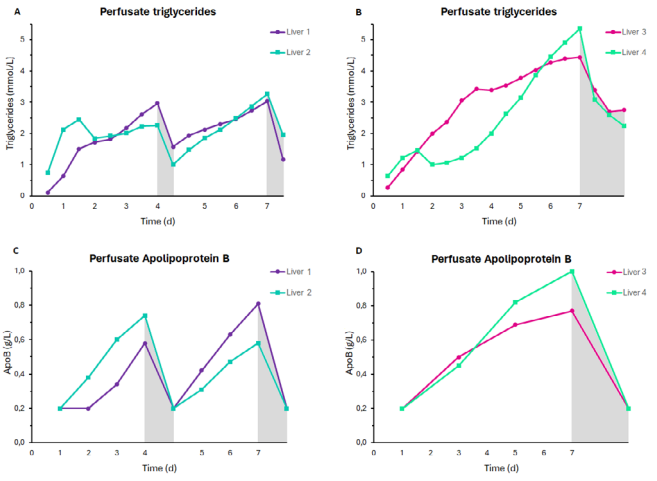

Figure: Concentration of triglycerides and ApoB in the perfusate of individual livers during long-term normothermic machine perfusion. The shaded gray area indicates the period which fat filters were applied.

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PP_173 DECISION SUPPORT TOOL TO AID RISK ASSESSMENT OF ACCEPTING VERSUS DECLINING A KIDNEY FROM A DONOR WITH CANCER HISTORY

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Background: The decision to accept a kidney offer from a donor with cancer history involves complex assessment of the risk of acceptance versus remaining on dialysis. Transplant clinicians and patients would benefit from tools to aid this decision-making. We aimed to develop a decision support tool for patients and clinicians comparing consequences of accepting versus declining a kidney offer from a deceased donor with reported cancer history.

Methods: We used data from the Australian and New Zealand Dialysis and Transplant Registry 2000-2019 to construct parametric models of time to transplant (generalized-F) and graft failure (2-knot spline). Mortality and cancer incidence were based on life tables (Australian Bureau of Statistics, Stats New Zealand), population-level data from Australian Institute of Health and Welfare, and published literature. We adjusted for age, sex, blood-group, previous transplants, comorbidities, kidney disease, dialysis time, kidney failure time, and donor characteristics (age, sex, pathway, Australian kidney donor profile index (KDPI), and cancer). Transmission risk by cancer site and type was based on clinical guidelines. A tool interface was developed using the R package 'shiny'.

Results: A web-app visualizing expected outcomes (Figure 1). For example, for a hypothetical donor (45y, male, DBD, KDPI 31%, glioblastoma) and recipient (50y, male, blood-group O, moderately sensitized, New South Wales resident, glomerular disease, transplant-naive, 2-years' dialysis) and the estimated risk of cancer transmission is 2%. Median waiting time for a better offer (KDPI < 31) is 2.3 months, with a chance of waitlist suspension (11%), de-novo cancer (0.1%) and death (1.1%) in that time.

Conclusions: A bespoke visualization of expected transplant outcomes and risks of remaining on dialysis may enable informed decision-making and better patient outcomes.

Figure 1: Screenshot of the decision support tool for a hypothetical patient and donor with cancer

PP_174 OPEN NEPHRECTOMY IN LIVING DONORS MAY STILL BE THE PREFERRED METHOD FOR KIDNEY TRANSPLANTATION IN YOUNGER CHILDREN

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Background: Although minimally invasive laparoscopic donor nephrectomy (LDN) has been established as the standard method for donor nephrectomy for adult recipients in recent years, there might still be a role for conventional open donor nephrectomy (ODN) in pediatric kidney transplantation (KTx). To investigate this, we compared the outcomes of LDN with those of ODN in pediatric patients.

Methods: A systematic literature search was conducted in Web of Science and Medline (via PubMed) databases, focusing on intraoperative data in donors and short-term postoperative outcomes in pediatric recipients following ODN and LDN. We used a subgroup analysis to compare these outcomes in recipients aged five years or younger.

Results: Of 816 retrieved articles, 14 studies involving 936 children receiving kidney grafts through ODN and 876 children receiving kidney grafts through LDN were analyzed. There were no significant differences in operation time, warm ischemia time, and blood loss among donors (P > 0.05). There were also no differences in the rates of acute graft rejection, delayed graft function, and one-year graft survival between pediatric recipients undergoing ODN and LDN. In the subgroup analysis, a random effects model indicated that the rates of delayed graft function and acute graft rejection were significantly higher in recipients aged five years or younger in the LDN group than those in the ODN group (odds ratio: 0.28; P = 0.016, odds ratio: 0.25; P = 0.027, respectively).

Conclusion: ODN may be the better donation method for kidney recipients aged five years and younger, where LDN resulted in a higher incidence of DGF and acute graft rejection episodes. Further studies on younger pediatric patients are needed to address the remaining uncertainties in this field.

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PP_175 LONG TERM FOLLOW-UP OF BILIARY COMPLICATIONS IN CDCD LIVER TRANSPLANTATION WITH NORMOTHERMIC REGIONAL PERFUSION

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Background: Liver transplantation (LT) after controlled donation after circulatory death (cDCD) is associated with a high rate of non-anastomotic strictures (NAS) ranging from 7 to 34%. The use of normothermic regional perfusion (NRP) has been shown to reduce the rate of NAS. However, long-term data from IDEAL-4 studies with systematic radiological follow-up are currently lacking.

Methods: This is a single-center retrospective study including all consecutive cDCD LT from January 2015 to January 2024. All cDCD LT were performed after mandatory use of NRP. The study aimed to determine the incidence, timing, types and treatments of biliary complications with a particular focus on NAS. A prospective protocol with at least one systematic magnetic resonance cholangiopancreatography (MRCP) six months after LT was applied to all patients. NAS was defined as any irregularity or narrowing of the lumen of the intrahepatic or extrahepatic donor bile duct in the absence of hepatic artery thrombosis. NAS was confirmed on MRCP by an expert radiologist and classified according to Croome et al. Biliary complications were classified according to the Clavien-Dindo classification (CD).

Results: A total of 84 cDCD LTs were included in the study with a median follow-up of 35 months. Median UK cDCD risk score was 3 with 20% of high-risk matchings (Table 1). One and 5-year overall graft and patient survival rates were 94%/83.5% and 95%/84.7%, respectively. Among recipients alive at 30 days, all but one underwent routine protocol MRCP after a median of 180 days [168 days-190 days]. Symptomatic biliary complications were observed in 25 patients (30%) of which 18 were anastomotic strictures (CD IIIb), 7 were bile leaks (n=4 CD IIIb, n=3 CD IV). Only one asymptomatic NAS (1.3%) with a low severity grade E was identified on MRCP at 6 months post-LT and did not require treatment (Figure 1). Importantly, no graft loss due to biliary complications or NAS was observed.

Conclusions: In this single-centre IDEAL-4 study on cDCD LT with NRP, the rate of NAS was < 2% and no graft loss or retransplantation due to biliary complications was observed. The use of NRP allows a low rate of radiological and clinical NAS similar to donation after brain death LT.

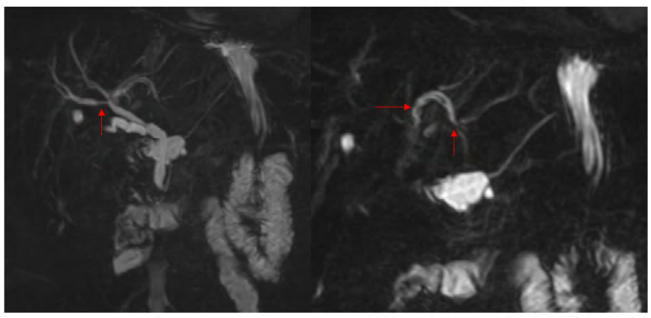

Figure 1: MRCP of the only patient with NAS (severity grade E according to Croome et al)

cDCD DONOR, GRAFT, RECIPIENT-RELATED CHARACTERISTICS		
		n=84
DONOR	Age (y)	54 (44,63)
	Sex male	62 (74%)
	BMI	23.9(21.9, 27.4)
	Intensive Care prior to WLST (days)	8(6,14)
	Cause of death (%)	
	CVA	14 (17%)
	Cerebral Anoxia	53 (63%)
	Trauma	17 (20%)
	Cardiac arrest recuperate	62 (74%)
GRAFT	TWIT (min)	32(28,38)
	FWIT (min)	24(20,27)
	AWIT (min)	18(16,22)
	A-NRP duration (min)	227 (204,239)
	CIT (min)	305(251,340)
	HOPE	13 (15%)
	Graft weight (g)	1540 (1310, 1800)
	AST last values before WLST	59.5 (36,73)
	ALT last values before WLST	49.5 (30,90.5)
	GGT last values before WLST	114 (57,219.75)
RECIPIENT	Recipient characteristics	
	Age (y)	57 (50,61)
	Sex male (%)	61 (75%)
	BMI	26.7 (23,30.2)
	MELD score	13 (10,18)
	TIPS	9 (11%)
	Transplant indication	
	HCC	45 (53.6%)
	Alcoholic	50 (60%)
	MASH	23 (27%)
	Biliary etiologies (PBC, PSC)	7 (8.3%)
	UK DCD Risk Score	3 (2,5)
	Low risk [0-5] (%)	67 (79.8 %)
	High risk [6-10]	17 (20.2 %)
	Futile [>10] (%)	0
	Liver transplantation details	
	Recipient Warm Ischemia (min)	37 (33,45)
	Intraoperative blood transfusions	0(0,2)
	Operation Time (min)	386 (334,438)
	complications and outcomes post LT	
	PNF	3 (3.6)
	Re-transplantation	3 (3.6%)
	Surgery < 90 days post LT	17 (20%)
	Dialysis < 90 days post LT for AKI	9 (11%)
	Symptomatic biliary complications	25 (29.76%)
	Asymptomatic NAS	1 (1.3%)
	HAT (%)	4 (5.2%)
	Recipient Survival 1 and 5 year	95% - 84.7%
	Graft Survival 1 and 5 year	94% - 83.5%

Median (Q1, Q3),
AKI : Acute Kidney Injury, A-NRP abdominal normothermic regional perfusion, AWIT : asystolic warm ischemia time, BMI : body mass index, CIT : cold ischemia time, CVA : cerebrovascular accident, FWIT : functional warm ischemia time, HAT : Hepatic Atery Thrombosis, HCC : hepatocelular carcinoma, HOPE : Hypothermic Oxygenated Perfusion, MASH : Metabolic dysfunction-associated statohepatitis, MELD : Model for End-stage Liver Disease, PBC : Primary biliary cirrhosis, PSC : primary sclerosing cholangitis, TWIT : total warm ischemia time, WLST : Withdrawal of life-sustaining therapy

Table 1: cDCD Donor, Graft and Recipient-related characteristics

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PP_177 IMPACT OF HEPATITIS B SURFACE ANTIGEN STATUS IN KIDNEY DONORS ON CLINICAL OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Clinical outcomes in kidney transplant recipients (KTRs) receiving graft from hepatitis B surface antigen (HBsAg) positive donor are still controversial because of a possibility of the transmission, reactivation, and renal and hepatic complications of hepatitis B virus.

Methods: We retrospectively analyzed the medical records of 6023 patients in the Korean Organ Transplantation Registry database between January 2015 and June 2020. We divided them into 2 groups based on the donor HBsAg status. We analyzed the impact of HBsAg status in kidney donors on clinical outcomes in KTRs.

Results: HBsAg positive donors are 139, and HBsAg negative donors, 5884. There were no significant differences in the baseline characteristics between KTRs with HBsAg positive donors and with HBsAg negative donors. There were no significant differences in the incidence of delayed graft function, de novo donor specific antibody, acute rejection at 6 months after kidney transplantation (KT), and allograft function from 1- to 5-year after KT. There was also no significant difference in the death-censored graft survival rate between them, but patient survival rate was significantly lower in the HBsAg positive donor KT compared to the HBsAg negative donor KT (P=0.002). However, causes of patient death were not associated with the HBsAg positivity of donors. In the subgroup analysis, we compared HBsAg negative KTRs to HBsAg positive KTRs from HBsAg positive donors. There were also no significant differences in the baseline characteristics between them. There were also no significant differences in the death-censored graft survival and patient survival rates.

Conclusions: Clinical outcomes in the HBsAg positive donor KT were comparable to those in the HBsAg negative donor KT. Therefore, the HBsAg positive donor KT might be an alternative strategy for organ shortage.

PP_178 OUTCOMES OF DCD LIVER TRANSPLANTATION AT HIGH-LEVEL TRANSPLANT CENTER: ANALYSIS OF PROGNOSTIC FACTORS

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Background: In the setting of organ shortage, donation after circulatory death (DCD) provides an opportunity to expand the donor pool of liver grafts. The use of the Normothermic regional perfusion (NRP) in sequence with ex situ hypothermic machine perfusion (D-HOPE) after the retrieval minimizes the rate of graft failure. However, use of DCD grafts still remains a marginal practice, above all in Italy.

Methods: From 2017 to 2024, 45 DCD LT were performed in our Centre in a setting of 20 minutes no-touch period of 20 minutes. Medium functional Warm ischemia time until normothermic regional perfusion (NRP) was 39 minutes. All grafts underwent hypothermic machine perfusion (D-HOPE). Clinical data of donor, recipient and postoperative period were collected. We analyzed prospective collected data with univariate and multivariate analysis (Cox regression analysis).

Results: Overall survival of DCD grafts was analyzed with Kaplan Meyer 87% at 5 years, with a significant difference between DCD Type 2 and type 3. At univariate analysis the presence of AntiHBc (p=0.04), high level of potassium (K) of the donor (p0.03), longer total Warm Ischemia Time (tWIT) of the graft (p0.03), blood and plasma transfusion during surgery (p0.02), INR at postoperative day (POD)1 (p0.02), ALT at POD1 (p0.02) and vascular complication (p=0.03). AntiHBc positivity and high serum K level of the donor showed a statistical correlation at multivariate analysis with worst survival outcomes.

Conclusions: Our analysis showed a great outcome in terms of patient survival, comparable with DBD grafts. In particular we found that AntiHbC positivity and high serum K level of the donor are important prognostic factors. Despite the small number of cases, our data encourage the use of DCD grafts after NRP-D-HOPE evaluation in a setting of long no-touch time. However, further analysis of prognostic factors are required to stratify the risk and improve recipient selection.

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PP_180 ADVANCING DECEASED ORGAN DONATION IN THE UAE: FROM 3 TO 320 DECEASED ORGAN DONORS THROUGH A QUALITY ASSURANCE PROGRAM

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Background: Since the regulation of deceased organ donation (DOD) in 2016, the UAE has shown strong dedication to advancing DOD practices. Federal Decree Law No. 25 of 2023 reinforced this commitment, aligning with the World Health Organization's resolution on increasing ethical access, availability, and oversight of transplantation. To address the multifaceted challenges of DOD, the UAE introduced a quality assurance program focused on standardization, evaluation, and continuous improvement.

Methods: The UAE adopted international best practices to establish a comprehensive DOD framework. Key components included standards and KPIs: Local health authorities defined benchmarks for facilities, professional roles, and procedures, such as neurological criteria assessment, early donor identification, and referral protocols. Mandatory KPIs in Dubai: Four performance indicators addressing structure, process, and outcomes were introduced to align with national standards. Donor Hospital Selection: High-potential hospitals were targeted for improvements. Collaborative Implementation: Local and international experts worked together to implement standards and assess effectiveness. External Audits: International assessors conducted audits to validate processes, identify gaps, and recommend enhancements.

Results: The program achieved significant outcomes, with a 30% increase in DOD activity in 2024 compared to 2023. The national donation rate rose from 5.5 donors per million population (DPMP) in 2022 to 9.1 DPMP in 2023 and 11.6 DPMP in 2024. Hospital audits revealed improvements in donor referral, compliance with UAE standards, and operational efficiency, highlighting the importance of continuous monitoring and capacity building.

Conclusions: The UAE Quality Assurance Program for DOD has established a systematic approach to enhancing organ donation practices. By integrating global best practices with rigorous performance evaluation, the program achieved notable progress in DOD outcomes. It serves as a replicable model for other nations seeking to improve organ donation systems through structured quality assurance initiatives.

PP_181 THE EFFECTS OF PRE-DONATION CARDIAC ARREST ON SHORT AND LONG TERM KIDNEY TRANSPLANT OUTCOMES

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Background: Donor selection in renal transplantation is important to optimize outcomes. Donor cardiac arrest and CPR is sometimes considered a risk for poorer transplant outcomes due to the risk of renal hypoperfusion and ischaemia, although there are no large studies to assess its effect. We therefore aimed to assess the effect of pre donation donor cardiac arrest on graft outcomes.

Methods: We performed a registry analysis of all deceased donor UK transplants between 2000 and 2022. Univariate and multivariate analyses were performed, and the outcomes measured were serum creatinine at 3, 12 and 60 months, DGF, PNF, and patient and graft survival. Subgroup analyses comparing DBD and DCD kidneys, and length of downtime were performed.

Results: A total of 36510 patients were included, with 24398 transplants from donors without cardiac arrest and 12122 from donors with previous cardiac arrest. After adjusting for potential confounders, there was a significant difference in creatinine at 3 months (156.5 vs 153.6 µmol/L, p<0.001), 12 months (149.8 vs 145.8 µmol/L, p<0.001), and 5 years (157.2 vs 152.7 µmol/L, p<0.001), with cardiac arrest donors having lower creatinine at each timepoint. There was a higher risk of DGF in the cardiac arrest group (Hazard ratio 1.13, p<0.001), but no difference in PNF (HR 0.91, p=0.23) Patient survival was similar between groups (HR 1.05, p=0.115), but graft survival was better in cardiac arrest donors (HR 0.91, p<0.001)(Figure 1).

Conclusions: Donor cardiac arrest in utilized organs does not negatively impact the outcomes of kidney transplants, and cardiac arrest alone should not be a factor in clinical decision making to decline such kidneys. There is a small but statistically significant difference in graft function and survival with cardiac arrest donors having better outcomes.

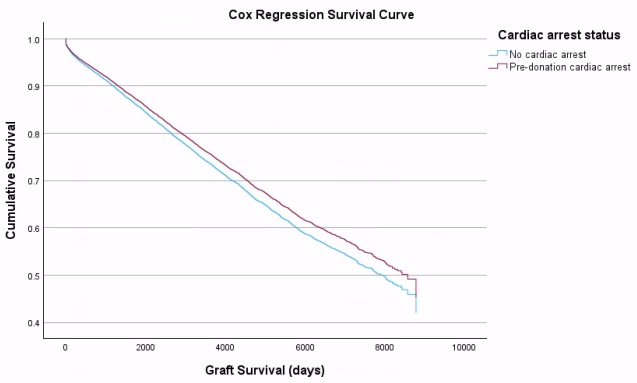

Figure 1. Multivariate Cox regression survival analysis of pre-donation cardiac arrest vs no cardiac arrest grafts.

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PP_182 HUMAN RECTUS FASCIA GRAFT PRESERVATION: IMPACT OF TIMING AND TEMPERATURE

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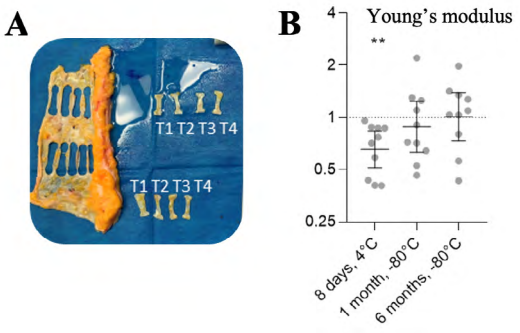
Background: Closure of the abdominal wall after abdominal transplantation (Tx) is a major challenge. During Tx a size-mismatch between donor and recipient might occur and these patients often have a hostile and contracted abdominal wall with loss of abdominal domain. Donor non-vascularized rectus fascia (NVRF) Tx provides a novel, promising technique to close the abdomen when primary closure is not feasible. In order to have on-demand availability of these grafts, this study investigates the impact of prolonged storage of NVRF on different temperatures.

Methods: The abdominal wall was procured en-bloc from human donors after organ donation (n=10). 6 male; age 56 (range: 26-68) with a BMI of 28 (range: 23-31); 6 DCD/4 DBD. After removing the muscle, NVRF was stored in sterile containers under different conditions: (T1) fresh tissue was stored in IGL-1 preservation fluid without antibiotics and analyzed within 39 hours; (T2) 4°C for 8 days in IGL-1; (T3) -80°C for 1 month (dry); (T4) -80°C for 6 months (dry) (Fig 1A). Endpoints were mechanical (uni-axial tensile testing), microbiological (Wilkens Chalgren and Sabouraud broth) and histological (hematoxylin & eosin and Masson trichrome staining) analysis. Data was normalized to fresh tissue and timepoints were compared to baseline with t-test.

Results: After 8 days at 4°C, the ultimate strength of the NVRF was reduced to 70% and the stiffness of the tissue was reduced to 66%. There were no indications for altered mechanical characteristics in NVRF stored at -80°C for 1 month compared to fresh tissue. After 6 months at -80°C, extensibility was slightly increased with 15% compared to fresh NVRF, but there were no indications for alterations in ultimate strength and stiffness (Fig 1B). Microbiological analysis showed absence of yeast contamination in all samples. Bacterial contamination was detected in 18/40 samples after different preservation methods. Histological evaluation showed no structural change after the different preservation methods.

Conclusions: Preservation of NVRF during 1 month at -80°C seems to be the optimal condition to maintain strength and integrity of the graft. This finding could result in a prolonged preservation of NVRF. A clinical trial is required to compare the different conditions.



PP_183 APPLICATION OF CUMULATIVE SUM MONITORING TO SURGICAL INJURY IN ABDOMINAL ORGAN RETRIEVAL

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Background: Maximum organ utilisation and good outcomes following organ transplantation is dependent on high-quality organ retrieval surgery. The grading system used by recipient units in the UK to report retrieval related surgical damage was updated in 2021 to a more objective scale. This allowed development of innovative cumulative sum (CUSUM) monitoring of organ loss due to retrieval damage within the National Organ Retrieval Service (NORS).

Methods: All kidneys, livers and pancreases retrieved for transplantation in the UK between 01/04/16-31/03/21 (baseline period) or 01/10/22-30/09/24 (monitoring period) were considered. Data were considered on a donor basis; donors having one or more organs lost due to surgical damage during retrieval being counted as a single donor event. All 10 NORS teams were compared to the national rate using observed-expected and tabular CUSUM charts.

Results: In the baseline period, 304/7226 (4.2%) of donors had an 'organ loss' event. Accordingly, the chart limit was set to 2.0 with monitoring for a doubling of organ loss. Monitoring reports began May 2023 on a quarterly basis. From 70 reports (10 teams x 7 quarterly runs), 2 signals from different teams were generated for detailed consideration. Donors in the monitoring period had an event rate of 4.0% (114/2878). Of those 114 donors, 107 (94%) had one organ lost, and 7 two organs lost (121 organs lost; 27/2758 left kidneys, 37/2744 right kidneys, 24/2128 livers, and 33/679 pancreases).

Conclusions: Introduction of a new damage grading system, along with a thorough review process, has allowed the development and implementation of CUSUM monitoring for organ loss due to retrieval surgical damage in the UK. This is the first real-time performance metric in Europe for retrieval damage that considers all abdominal organs, allowing for effective detection of potential issues within teams. The data confirm organ loss in the UK compares very favourably with international series.

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PP_184 DOES UTILIZATION OF NRP FOR DCD LIVER TRANSPLANTATION INCREASES RISK-TOLERANCE AROUND THE WORLD

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Background: Normothermic regional perfusion(NRP) for donation after circulatory death(DCD) liver transplant(LT) is a disruptive surgical innovation that has increased organ utilization and improved outcomes compared to static cold storage(SCS). Despite its swift uptake worldwide, a real-world assessment of NRP at an international level is lacking. We aimed to assess if the use of NRP increases risk-tolerance for donor-recipient matching.

Methods: All adult DCD LT from the United Kingdom(UK) and a single-center from the United States (US) were reviewed from 1/1/2017 – 31/3/2024 and 1/1/2017- 31/8/2024, for the UK and US cohorts, respectively. DCD LT was categorized by perfusion method: SCS or NRP. Donor, procurement, and recipient clinical characteristics were categorized by the UK DCD Risk Score (UKRS). Cases with missing UKRS were excluded. UKRS was compared between SCS versus NRP DCD LT among each cohort.

Results: There were a total of 162 DCD LT(51% NRP) in the US cohort and 689 DCD LT(28% NRP) in the UK cohort. When NRP was used in the US cohort, there was an increase in warm ischemia time(WIT) minutes(20±3 vs 24.5±4, p=0.003), a decrease in cold ischemia time(CIT) hours(4.8±1.4 vs 4.1±1.1, p=0.003), and the UKRS increased(3.7±0.9 vs 4.2±2.9,p=0.003). When NRP was used in the UK, WIT increased(26.8±7.6 vs 40.4±24.2, p<0.001),CIT increased(7.2±2.2 vs 8.6±2.3, p<0.0001),and the UKRS increased(5.4±3.1 vs 7.9±3.5, p<0.0001).

Conclusions: NRP facilitates an increase in risk-tolerance for donor-recipient matching irrespective of global geography as UKRS increased in both cohorts. The traditional definition of futility for DCD LT should be reconsidered in the modern era of perfusion technology. Establishing international collaborations will help transplant teams obtain mentorship in learning NRP techniques and recognize best practices. Global partnerships to benchmark data may improve accuracy of donor-recipient risk stratification.

Table 1. Donor, Procurement, and Recipient Characteristics of DCD LT: SCS vs NRP

	CU SCS	CU NRP	p-value	UK SCS	UK NRP	p-value
Number of transplants	79	83		494	195	
Donor Characteristics						
Age, years	43.8 (13.4)	42.5 (15.3)	0.73	50.8 (15.5)	51.6 (14.7)	0.5668
BMI, kg/m^2	29.0 (5.9)	28.6 (6.5)	0.76	25.6 (4.5)	26.6 (5.2)	0.0248
Procurement Characteristics						
Total WIT, minutes	20 (3)	24.5 (4)	0.003	26.8 (7.6)	40.4 (24.2)	<0.0001
Functional WIT (SBP <50), minutes	20.4 (4)	16 (3)	<0.001	16.6 (4.9)	24.1 (7.9)	<0.0001
CIT, hours	4.8 (1.4)	4.1 (1.1)	0.003	7.2 (2.2)	8.6 (2.3)	<0.0001
Recipient Characteristics						
Age, years	65(3)	52.9(9.3)	0.44	54.4 (11.0)	54.2 (10.6)	0.8368
Laboratory MELD-Na	20 (4)	20 (5)	0.75	14.9 (12.6)	17.7 (7.0)	0.0003
History of Previous Liver Transplant	0(0%)	5(6%)	0.11	7 (1%)	8 (4%)	0.0408
UK DCD Score						
Low Risk (≤5), n(%)	72 (91%)	66 (79%)	0.003	290 (59%)	59 (30%)	<0.0001
High Risk (>5 ≤10), n(%)	7 (9%)	14 (17%)		178 (36%)	93 (48%)	
Futile (>10), n(%)	0 (0%)	3 (4%)		26 (5%)	43 (22%)	
Overall	3.7 (0.9)	4.2 (2.9)	0.003	5.4 (3.1)	7.9 (3.5)	<0.0001

Means and Standard Deviations reported
CU, University of Colorado Hospital; UK, United Kingdom; DCD, donation after circulatory death; LT, liver transplant; SCS, static cold storage; NRP, normothermic regional perfusion; BMI, body mass index Kg/m²; WIT, warm ischemia time; CIT, cold ischemia time; Na-MELD, model for end-stage liver disease

PP_185 THE ITALIAN NRP-DCD SCORE. RE-DEFINING FUTILITY WITH THE USE OF NRP IN DCD LIVER TRANSPLANTATION

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Background: The 20 minutes no-touch period legally required for the declaration of death in Italy prompted the mandatory use of normothermic regional perfusion (NRP) which is very often followed by ex-situ machine perfusion (MP). Even if several scores have been developed to stratify the risk of graft loss in controlled DCD (cDCD), no one has been developed in a population characterized by extremely prolonged warm ischemia time (WIT) and evaluating the utility of NRP and MP.

Methods: A total of 431 consecutive liver transplants (LT) performed in 11 Italian transplant centers receiving a cDCD graft in the period september 2015-december 2024 were enrolled. Donors, NRP and recipients' parameters were prospectically collected and retrospectively analyzed. A new risk score was calculated on the basis of a regression analysis.

Results: After a median follow-up period of 13 months (Q1-Q3=6-28), 47 (10.9%) graft losses were observed within the first year after LT. Median donor age was 64 years (Q1-Q3=55-74), median WIT 48minutes (Q1-Q3=42-52) and asystolic time 25minutes (Q1-Q3=28-31).

Six variables were identified as predictors of graft loss and used to develop a risk score (NRP-DCD): decrease of lactates<35% during NRP (OR=1.977;p=0.049), increase ALT>100% during NRP (OR=2.021;p=0.037),ALT at commencing NRP>100IU/L (OR=2.092;p=0.025),pH reduction<5% during NRP (OR=2.071;p=0.031), no MP after NRP (OR=3.570;p=0.030) and recipient MELD>25 (OR=3.499;p=0.010). The NRP-DCD Score showed a better 1-year graft loss prediction (AUC=0.715;p<0.0001) than the UK-DCD Score (AUC=0.507;p=0.871). Stratifying the entire cohort in low (score 0-3), high (4-6) and futile (7-15) risk for LT, patients with low risk showed the best graft survival rates if compared with high (p=0.006) and futile (p<0.0001) cases. One- and three-years graft survival rates were 95.7 and 89.8% vs. 83.9 and 77.8% vs. 65.2 and 57.0%, respectively.

Conclusions: The Italian NRP-DCD score is able to detect high risk DCD donors and predict futile donor-to recipient match based on NRP parameters. With the use of NRP, donor age and asystolic time cannot be considered risk factors for a successful outcome.

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PP_186 NORMOTHERMIC MACHINE PERFUSION PUMP PARAMETERS PREDICT EARLY ALLOGRAFT DYSFUNCTION

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Background: Normothermic machine perfusion (NMP) is rapidly expanding the donor pool and can mitigate reperfusion injury, but aggressive donor utilization can be associated with early allograft dysfunction (EAD). We tested the ability of donor characteristics and NMP pump parameters to predict EAD.

Methods: Retrospective chart review was performed for all livers placed on NMP and then implanted at The Ohio State University. Discarded organs were excluded. Donor, recipient, and pump data were collected. ALT and AST were collected at the end of perfusion. The primary endpoint was EAD. EAD status was compared using Mann-Whitney U tests or Fisher Exact tests. A multiple logistic regression was used to determine odds ratios adjusting for covariates of interest.

Results: 112 livers were analyzed (45 DBD, 67 DCD). 46 recipients had EAD (41.2%) and 1 had primary non-function. In univariate analysis, donor BMI was associated with EAD (p = 0.0006). Pump parameters predictive of EAD included total bicarbonate given while the liver remained on pump (p = 0.0070), <10% decrease in glucose concentration by hour 3 (p = 0.0019), and perfusate ALT and AST (p = 0.0002 and p < 0.0001 respectively). In multivariate analysis, <10% decrease in glucose at hour 3 (OR 29.7, 95% CI 2.63-335), donor BMI (OR 2.34, 95% CI 1.10-4.97), total bicarbonate administered (OR 2.73, 95% CI 1.12-6.63), and cold ischemic time (OR 6.96, 95% CI 1.11-43.4) were associated with EAD. DCD donation was not associated with EAD (p = 0.2582). Recipients with EAD had longer ICU and hospital stays (p = 0.0443 and p = 0.0079 respectively). At 6-month follow-up, patients with EAD had lower graft and patient survival compared to patients without EAD (p = 0.0107).

Conclusions: In our institutional cohort, donor BMI, total bicarbonate given, lack of glucose utilization, and perfusate ALT/AST were associated with EAD. These donor and NMP pump parameters can be used to anticipate EAD and can aid in assessing recipient suitability for individual donor organs.

PP_187 COMPARATIVE OUTCOMES OF RENAL ALLOGRAFTS WITH PERSISTENT AKI STAGE >2 AND RESOLVED AKI: RETROSPECTIVE STUDY

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Background: The utility of deceased donor kidneys with acute kidney injury (AKI) remains debated due to concerns about graft function and patient outcomes. This study evaluates the outcomes of renal transplantation using kidneys from deceased donors with AKI compared to non-AKI donors. Between 2018 and 2022, 262 patients underwent renal transplantation at our center, with 41 receiving kidneys from AKI donors. Graft survival, patient survival, and graft function were analysed over a two-year follow-up period. The findings indicate that kidneys from AKI donors can provide acceptable outcomes, supporting their use to address the organ shortage.

Methods: This retrospective cohort study analysed data from 262 patients who received deceased donor renal transplants between January 2018 and December 2022. Donors were classified as having AKI based on the kidney disease: Improving Global Outcomes (KDIGO) criteria. Data collected included: • **Patient and graft survival** at two years. • **Graft function metrics** such as serum creatinine and estimated glomerular filtration rate (eGFR). • Incidences of complications, including delayed graft function (DGF) and acute rejection. Donors with AKI were further categorized into persistent AKI (stage ≥2) and resolved AKI groups to assess comparative outcomes.

Results: Among the 262 renal transplants, 41 donors were identified as having AKI. Of these, 21 had persistent AKI stage ≥2, while 20 had resolved AKI at the time of transplantation. Key outcomes over the two-year follow-up period include: Despite a higher proportion of DGF in the resolved AKI group, patient and graft survival rates were comparable across groups.

Conclusions: Deceased donor kidneys with persistent AKI stage ≥2 demonstrate comparable patient and graft survival rates to non-AKI donor kidneys. These findings support the utilisation of AKI donor kidneys to expand the donor pool and mitigate organ shortages. Further large-scale studies are warranted to validate these results and optimize transplant outcomes.

Outcome	Persistent AKI (n=21)	Resolved AKI (n=20)
2-Year Patient Survival (%)	95%	95%
2-Year Graft Survival (%)	100%	89%
DGF (%)	20%	35%
Acute Rejection (%)	4.76%	5%
Mean eGFR at 2 Years	62.8 ml/min/1.73m²	51.8 ml/min/1.73m²

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PP_188 NORMOTHERMIC REGIONAL PERFUSION ABROGATES WARM ISCHAEMIC INJURY IN DCD LIVER TRANSPLANTATION

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Background: Livers retrieved after circulatory determination of death (DCD) sustain significant ischaemic injury during functional and total warm ischaemic times (FWIT; systolic pressure <50 mmHg to in-situ perfusion; TWIT; withdrawal of life sustaining treatment to in-situ perfusion), reducing survival. It is unknown whether FWIT and TWIT reduce survival in NRP liver transplant. This paper compares effects of FWIT and TWIT on 1 year survival after standard DCD or NRP liver transplantation.

Methods: All adult first liver only transplants from adult DCD and NRP liver donors in the UK from 01/01/11 to 31/12/23 were included. Thoraco-abdominal NRP was excluded, as were grafts with ex-situ machine perfusion. FWIT and TWIT were considered in Cox regression models to assess association with 1 year graft and transplant survival.

Results: 1855 transplants were considered: 1633 DCD, 222 NRP. Figure 1 shows 1 year graft survival by method; NRP had significantly better survival than DCD (DCD 89.0% v NRP 96.2%, p=0.001). Results are shown in Table 1. Donor age and sex were not significantly different between cohorts (p=0.2 and p=0.4 respectively), nor were these statistics in recipients (Age p=0.3; sex p=0.07). FWIT and TWIT were 7 and 8 minutes longer in NRP donors (p<0.001). For every additional minute of FWIT or TWIT in DCD liver transplant, there were significant reductions in graft survival (p<0.05). In NRP livers, these effects did not reach statistical significance (FWIT p=0.3; TWIT p=0.5). In DCD livers, TWIT over 60 minutes led to significantly increased 1-year graft loss (p=0.015). There were an inadequate number of events to assess this statistic in NRP cases. Transplant survival showed similar findings (Table 1).

Conclusions: FWIT and TWIT are significantly deleterious to survival in UK DCD liver transplant, an effect which was not significant in NRP liver transplant. Data suggest that the damaging effects of FWIT and TWIT are mitigated by NRP, facilitating organ utilisation.

Figure 1 1 year liver graft survival, by method

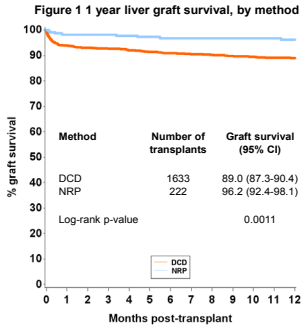

Table 1 Demographics and Cox modelling results by method

Variable		DCD N (%)	NRP N (%)	p-value	Overall N (%)
		1633 (100)	222 (100)		1855 (100)
Donor Age (years)	Median (IQR)	52 (39-63)	54.5 (41-63)	0.2180	52 (40-63)
Donor Sex	Male	1004 (61)	130 (59)	0.4443	1134 (61)
BMI (kg/m^2)	Median (IQR)	25.0 (22.6-28.0)	26.4 (22.8-29.7)	0.0017	25.1 (22.6-28.3)
Cause of death	Hypoxic brain	573 (35)	98 (44)	0.0425	671 (36)
	Stroke	777 (48)	98 (44)		875 (47)
	Other	283 (17)	26 (12)		309 (17)
TWIT (mins)	Median (IQR)	26 (22-31)	34 (29-42)	<0.0001	27 (22-32)
FWIT (mins)	Median (IQR)	16 (14-20)	23 (19-28)	<0.0001	17 (14-21)
Recipient Age	Median (IQR)	56 (49-62)	58 (50-62)	0.3431	57 (49-62)
Recipient Sex	Male	1088(67)	162(73)	0.0693	1250 (67)
Urgency	Elective	1626 (100)	219 (99)	0.1075	1845 (99)
MELD	Median (IQR)	14 (10-18)	14 (11-18)	0.2283	14 (10-18)
UKELD	Median (IQR)	53 (50-56)	54 (51-57)	0.0001	53 (50-56)
Cold ischaemia time (hours)	Median (IQR)	7.2 (6.1-8.3)	8.3 (6.6-10.4)	<0.0001	7.4 (6.2-8.5)

Graft Survival	DCD HR (95% CI)	p-value	NRP HR (95% CI)	p-value
FWIT; 1 minute increase	1.02 (1.007-1.024)	**0.010**	1.03 (0.985-1.081)	0.288
TWIT; 1 minute increase	1.007 (1.001-1.013	**0.043**	0.985 (0.940-1.034)	0.457
TWIT >60 min	3.004 (1.409-6.403)	**0.015**		
Transplant Survival				
FWIT; 1 minute increase	1.014 (1.005-1.023)	**0.024**	1.014 (0.966-1.064)	0.612
TWIT; 1 minute increase	1.006 (1.001-1.012)	0.063	0.987 (0.957-1.019)	0.338
TWIT >60 min	2.477 (1.165-5.265)	**0.039**		

PP_189 PATTERNS OF DECLINES ASSOCIATED WITH HIGH DONOR OFFERS AND UNIT LOGISTICS ACROSS LIVER TRANSPLANT UNITS IN THE UK

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Background: Organ discard rates have risen to 20% in the last decade. The number of extended criteria donors has increased but it is also reasonable to presume that decline rates are related to each centres capacity to deliver liver transplantation. In this study we reviewed the pattern of acceptance across units aligning this with logistical challenges.

Methods: Liver offering data for 15,463 UK deceased donors in the U.K between 2015-2023 was extracted from the UK Transplant Registry. A questionnaire was sent to each unit looking at on call rotas and changes in capacity during the week.

Results: 73,403 deceased donor liver offers were made to UK transplant centres between 2015 and 2023. The majority of offers (81.8%) were declined while an additional 7.6% were accepted but subsequently declined. The unadjusted offer decline rate by day of the week was lower on Monday and Tuesday (87.7% and 88.1% respectively) than on a Friday or Saturday (90.9% and 90.7% respectively). This difference was observed for named patient offers from donors after brain death (DBD) but not for donors after circulatory death (DCD). Different patterns in the transplant unit specific offer decline rates by day of the week were observed indicating different logistical challenges at each transplant unit. This was highlighted in the questionnaire responses. A median (IQR) of ten (8, 13) livers were offered per 48 hours and this reduced to 5 (3,7) for livers actually transplanted.

Conclusions: Offer decline rates remain high. Across transplant units specific offer decline rates by day of the week were observed indicating different logistical challenges. It is important to address this variation to ensure equity of access for all recipients and optimum utilisation of donor livers.

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PP_190 AMNIOTIC MEMBRANE-DERIVED HYDROGEL ENHANCES FUNCTIONALITY OF STEM CELL-DERIVED ISLET ORGANOIDS

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Background: Human pluripotent stem cells (hPSCs) are promising sources for generating islet organoids. Despite significant advances, producing fully mature beta cells remains challenging due to the lengthy maturation process and low differentiation efficiency. Prior studies have shown that individual ECM proteins significantly impact islets, and that critical ECM cues are often missing in pluripotent stem cell cultures. By addressing the absence of critical ECM cues, we can better harness the potential of hPSCs to generate fully mature islet organoids Our research focuses on designing an amniotic membrane-derived hydrogel (amniogel) to act as a "biological scaffold," recreating the native islet environment to promote stem cell derived beta cell maturation and pave the way for advanced diabetes therapies.

Methods: Islet organoids were generated from hPSC-derived pancreatic progenitors following Balboa et al.'s protocol and embedded in amniogel. Immunostaining of final stage islet organoids demonstrated that the majority of the cells co-expressed C-peptide+/NKX6-1+ and C-peptide+/PDX1+. These results were confirmed by analysing the transcriptional activities of pancreatic β cell-associated genes, which showed the expression of mature β cell markers such as C-peptide, NKX6.1 and MAFA. The function of islet organoids in vitro was assessed by a glucose-stimulated insulin secretion assay.

Results: Our findings demonstrated that amniogel facilitated efficient nutrient and metabolite exchange. Islet organoids maintained their viability, morphology and had improved in vitro function, as evidenced by higher glucose-stimulated insulin secretion levels, compared to those cultured on the conventional way.

Conclusions: These findings indicate that ECM from our amniogel support the viability and function of stem cell-derived islet organoids, offering a potential strategy for improving the efficiency and cost-effectiveness of beta cell production for diabetes treatment.

PP_191 DREAM TO REALITY: UAE ORGAN DONATION EXPERIENCE

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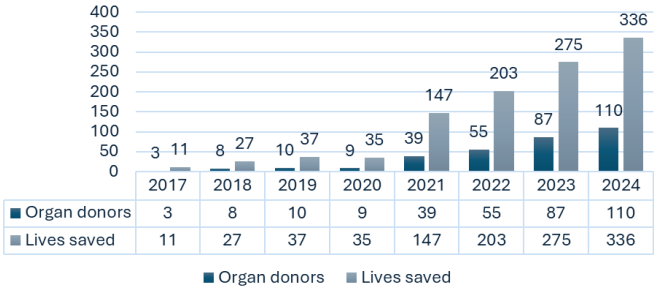
Background: Organ transplantation from deceased brain-dead donor (DBD) has been legalized in the United Arab Emirates (UAE) in 2016, which enabled the formal establishment of deceased organ donation program. The first multi-organ procurement and transplant from a brain-dead donation in the UAE took place on 15th July 2017. Subsequently the number of transplantation centers grew as previously only living related donations were being conducted in three kidney transplant programs in the country. The following year thoracic and abdominal and dedicated pediatric kidney transplant centers were set up.

Methods: A multi-pronged action plan was implemented by the UAE National Centre for Organ Donation and Transplant to increase organ donation and transplant rates among government and private health care sectors including various community awareness program across the country. A comprehensive educational program with specialized training provided to 10,000 health care professionals across the country to improve knowledge on brain death confirmation and management of organ donors to ensure high quality organs for transplantation. In addition, organ donation sessions were mandated for all new employees as part of hospital orientation. Dedicated organ donor coordinators visit hospitals to support early identification, organ retrieval including family support. In addition, implementation of organ donation referral pathways, policies, protocols, key performance indicators following the latest evidence-based guidelines to streamline process and practices.

Results: Currently seven centers perform kidney, four centers perform liver, and one center caters for heart, lung, and pancreas transplants. So far 320 organ donors which is equal to 9.5 donor per million population, saving over one thousand patients' lives between UAE and Kingdom of Saudi Arabia. The figure illustrates the growth of organ donation in the UAE since 2017.

Conclusions: Deceased donation is a time critical process that requires development of robust clinical governance pathways. UAE over the last few years made tremendous progress as the leading organ donation program in the middle east region.



	2017	2018	2019	2020	2021	2022	2023	2024
Organ donors	3	8	10	9	39	55	87	110
Lives saved	11	27	37	35	147	203	275	336

Organ donors Lives saved

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PP_192 EXPLORING SPECIALIST NURSE CONFIDENCE FACILITATING THE ORGAN DONATION PATHWAY ON EXTRACORPOREAL MEMBRANE OXYGENATION

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Background: With the increased use of Mechanical Circulatory Support (MCS) and Extracorporeal Membrane Oxygenation (ECMO) in critical care worldwide the number of UK centres asking us to explore deceased donation potential for ECMO patients is rising. Our Specialist Nurse (SN) workforce is recruited from a diverse range of specialties these SNs may not have had any prior exposure to ECMO or MCS. The aim of this study is to gain a national perspective of the confidence levels for our SN workforce when facilitating ECMO and MCS organ donors and if they have any experience within this growing area of critical care expertise.

Methods: Research governance approval was granted to launch a SN workforce survey to collate quantitative data about the experiences and confidence levels of SNs facilitating the organ donation pathway for potential donors on MCS or ECMO for both adults and paediatrics, prior experience of ECMO and MCS and teaching or training received. There was a free text box for further comments.

Results: The survey remains live with 64 responses. The results show that 57.8% of respondents feel not confident facilitating organ donation on ECMO and for paediatrics, 68.7%. 81.3% of respondents report no prior ECMO nursing experience, higher in paediatrics at 92.3%. Confidence facilitating organ donation on MCS shows a greater confidence gap than ECMO with 61% of respondents selecting not confident on the scale, paediatrics at 76.6%. 57.9% of respondents have no prior experience of MCS, even higher in paediatrics at 93.8%. 56.3% of respondents have had no adult ECMO training this rising to 70.3% for paediatrics. For no training or teaching in MCS the result was 68.8% and 78.1% for paediatric.

Conclusions: A training gap was expected, but the survey confirms that confidence in the majority is low for adult and paediatric ECMO and MCS organ donation facilitation and the majority of the SNOD workforce have no prior experience, additional comments welcome more training. The research group did not have an expectation of the MCS confidence gap being larger than the ECMO gap and this will aid the tailoring of education and training. The next phase of the project will be to engage with the SN workforce, build a robust overview of ECMO and MCS within organ donation nationally and look to provide quality education within this area of expertise.

PP_193 EVALUATING FMN AS A VIABILITY MARKER DURING ABDOMINAL NRP FOR LIVER TRANSPLANTATION: A PILOT STUDY

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Background: abdominal normothermic regional perfusion (aNRP) yields encouraging results after donation after circulatory death (DCD). In extended criteria DCD donors, aNRP enables evaluation of the liver to determine suitability to transplant, but universally accepted criteria remain lacking. Flavin mononucleotide (FMN) in perfusate and bile is proposed as biomarker in cold and warm ex-situ liver perfusion. We now analyze FMN in perfusate and bile to determine its potential as biomarker to predict postoperative complications in aNRP.

Methods: Between 2018 and 2023, 43 aNRP perfusions were performed. Livers were accepted based on our hepatocyte and cholangiocyte viability criteria. FMN values were retrospectively analyzed and correlated with perfusion parameters and clinical outcomes.

Results: Based on our acceptance criteria, 35 livers were transplanted and 8 livers were declined, based on hepatocyte criteria in 3, on cholangiocyte criteria in 1, and on combination of criteria in 4. FMN concentrations in the perfusate did not significantly differ between transplanted (0.91ug/ml, 0.52–2.65) and non-transplanted livers (0.79ug/ml, 0.43–1.01, p = 0.189). In this cohort, the incidence of overall biliary complications was 23% (8/35). The incidence of ischemic cholangiopathy was 6% (2/35). FMN levels in perfusate at 30 minutes (T30) perfusion were associated with the occurrence of biliary complications, with higher FMN T30 concentrations observed in livers that developed biliary complications (4.26ug/ml, 0.855–10.57) compared to those without (0.767ug/ml, 0.477–2.02, p = 0.038). Furthermore, there was a trend towards a significantly higher FMN concentration in bile between livers who developed overall biliary complications and those who did not 7.3ug/ml (4.41-11.38) vs 4.59ug/ml (3.03-6.96, p=0.09). The area under the receiver operating characteristic curve (AUROC) for FMN T30 in perfusate to predict overall biliary complications was 0.799, the AUROC for bile FMN was 0.732.

Conclusions: FMN concentration in the perfusate during aNRP at T30 shows promise as an early predictor of biliary complications. This pilot study has only few cases with overall biliary complications and a bigger cohort is needed to validate these results and adjust cut-off values for clinical guidance.

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PP_194 LUNG TRANSPLANTATION AFTER CIRCULATORY DEATH. A SINGLE-CENTER ANALYSIS

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Background: Since the implementation of controlled donation after circulatory death programs (cDCD), these donors reached 36.6% of all donations in 2022. The ISHLT registry showed that survival rates were similar to brain death donors (DBD). There is limited data on the development of chronic lung allograft dysfunction (CLAD) in DCD recipients. We present data on lung transplant recipients from DCD donors at Hospital Universitari La Fe.

Methods: Retrospective, descriptive, single-center analysis of lung transplant recipients from DCD donors (Maastricht 2A and 3) from January 2016 to November 2023. Recipient characteristics, development of PGD, acute rejection, CLAD, survival, and causes of death were reviewed. Mortality rates were compared with DBD data. Non-parametric variables were analyzed using Pearson's chi-square test, and survival was assessed using the Kaplan-Meier method.

Results: A total of 147 patients received lung transplant from DCD donors: 11 from uncontrolled DCD (uDCD) and 136 from cDCD. Bilateral 90.5%, single-lung 9.5%. By underlying disease, COPD 47.6%, interstitial lung disease (ILD) 33.3% and cystic fibrosis (CF) 6.1%. Mean age was 55 years range 7–71. PGD occurred in 35% of recipients (p<0.001). Fungal infections affected 100% of uDCD recipients (p<0.001). 17% of recipients met CLAD criteria (72% obstructive pattern, 16% restrictive, and 12% mixed). No significant association was found between PGD and the development of CLAD. Overall survival at one year was 85%, and at five years, 61%. Five-year survival was higher in the cDCD group (Maastricht 3) at 64%, compared to 54.5% in the uDCD group. Patients with COPD achieved the best five-year survival 70%, while those with CF had the worst outcome 21%. The primary causes of death were infectious complications 41.6%, cardiovascular 25%, and CLAD 13.9%.

Conclusions: This represents the largest single-center series of DCD lung transplant recipients to date. Overall survival rates are comparable to those reported in other series. Comparing DCD and DBD groups, survival rates were similar. Postoperative fungal infections occurred in 100% of Maastricht 2 patients. Patients with PGD had higher mortality, consistent with previously published evidence. However, we did not find an increased likelihood of developing CLAD among patients with PGD.

PP_195 VIABILITY ASSESSMENT OF DONOR LIVERS OVER 2 KILO FROM EXTENDED CRITERIA DONORS USING NORMOTHERMIC MACHINE PERFUSION

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Background: Sequential dual hypothermic oxygenated, controlled oxygenated rewarming and normothermic machine perfusion (DHOPE-COR-NMP) has been implemented for assessing the viability of extended criteria donor (ECD) livers. Steatotic livers are considered ECD livers due to a higher risk of post-transplant complications. Steatosis and other donor factors, such as gender, length and weight, influence liver size and weight. The aim of this study was to assess the viability of higher weight donor livers during DHOPE-COR-NMP and investigate the correlation between liver viability and the grade of steatosis.

Methods: Livers ≥2000 grams prior to perfusion (n=7), that underwent DHOPE-COR-NMP were 1:2 time-matched with 14 controls <2000 grams. Outcome parameters included viability assessment of hepatocellular and cholangiocellular function at 150 minutes of NMP and utilization rate. Vascular resistance corrected for liver weight (mmHg/mL/min/100g) of the hepatic artery (HA) and portal vein (PV) were calculated. Steatosis was graded based on liver biopsies taken prior to perfusion. Presented are median values and range.

Results: Liver weight was significantly different between groups (2470 (2160-3090) vs. 1340 (1150-1680), p<0.0001). The utilization rate was significantly lower in livers ≥2000 grams (1/7; 14% vs. 13/14; 93%, p=0.0009). Two heavy livers were declined based on hepatocellular function, three on cholangiocellular function and one on both. Vascular resistance was significantly higher in livers ≥2000 grams for both the HA (3.99 (1.55-5.09) vs. 1.49 (0.87-6.60), p=0.0056) and the PV (0.20 (0.12-0.29) vs. 0.10 (0.07-0.14), p=0.0001) (Figure 1). Six of the heavy livers had a steatosis grade of <5%, and one liver showed 15% steatosis. In the control group, three livers had an increased steatosis grade, with levels of 10%, 15%, and 20% in individual livers.

Conclusions: In conclusion, performing DHOPE-COR-NMP for ECD livers ≥2000 grams results in a low acceptance rate of only 14%, questioning the deployment of expensive machine perfusion resources for this category. These livers demonstrated an increased vascular resistance, which could not be attributed to the steatosis grade, but may serve as a target for pharmacotherapy.

Figure 1. Vascular resistance of the hepatic artery and portal vein.

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PP_197 THE PREDICTIVE VALUE OF THE GLYCOCALYX ALTERATION DURING PROCUREMENT FOR EARLY ALLOGRAFT DYSFUNCTION

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Background: Ischemia-reperfusion injury results from the lack of graft oxygenation. The glycocalyx is a membrane of glycoproteins covering the endothelium, which prevents interactions between blood elements and endothelial cells. When circulation stops, the glycocalyx detaches, exposing endothelial cells to inflammatory cells and cells' alteration. The aim of our study was to evaluate glycocalyx degradation from graft harvesting in the donor to organ reperfusion in the recipient. We assessed whether glycocalyx dynamics was a predictive biomarker of early graft function

Methods: This was a single-center observational prospective study at Paul Brousse Hospital from April 2022 to April 2023. All patients who underwent liver transplantation (LT) were included. Glycocalyx degradation was assessed during organ procurement, at the end of cold ischemia, and during LT in the graft's caval effluent, as well as in the recipient's peripheral blood. The primary endpoint was early allograft dysfunction (EAD) based on the MEAF score. We quantified: i) glycocalyx components: Syndecan-1 (Synd-1), heparan sulfate (HS), angiopoietin-1 (Ang-1), and angiopoietin-2 (Ang-2); ii) inflammation: TNF-alpha; iii) cell death markers. Correlations between histological lesions were analyzed.

Results: 48 patients were included. Sixteen patients (33%) had EAD with a MEAF ≥9. HS and synd-1 levels in the cava graft's effluent at the time of donor procurement were significantly higher in patients who developed dysfunction: [934 (691 – 1 165) vs. 584 (279 – 859) ng/mL, p=0.023; and 11 276 (10 293 – 18 729) vs 8 141 (4 905 – 11 143) pg/mL, p=0.009]. These patients also had significantly lower Ang-1 (1 374 pg/mL (317 - 5 867) vs. 4 246 pg/mL (1 965 – 9 204), p=0.034). The threshold at which these biomarkers levels predicted dysfunction was: 1) for HS: 887.4 ng/mL (AUC=0.71, IC 95% (0.54 – 0.88), p<0.05.); 2) for synd-1: 9594.85 pg/mL (AUC= 0.73, IC 95% (0.59-0.89), p<0.05); 3) for Ang-1: 2765.05 pg/mL (AUC= 0.69, IC 95% (0.52-0.86), p<0.05). No correlation was observed between ischemia-reperfusion histological lesions and these markers.

Conclusions: Early measurement of Synd-1, HS and Ang-1 during organ procurement may be predictive markers of liver graft function.

PP_198 SEX IMBALANCE IN LIVING KIDNEY DONATION AND CONSEQUENCES

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Background: Sex imbalance in kidney donation (KD) has been reported, with a predominance of female living kidney donors (LKD) and more men among recipients of those kidneys. More targeted research is needed to fully understand the influence of sex in long-term outcomes of donors and recipients

Methods: We retrospectively assessed the basal and follow-up characteristics of 2583 LKD, who donated a kidney in Catalonia between 2000–2023, and their recipients focused on differential characteristics according to sex. Data were obtained from the Catalan LKD Registry (RDVR) and the Catalonia Renal Patients Registry (RMRC). Recipient death and death-censored graft survival was evaluated according to donor-recipient (D-R) sex match.

Results: Of LKD included, 66% were women, in a similar proportion over time. Spousal donations were the most numerous (37.9%) compared to other relationships (p<0.001); largely wife-to-husband (73.6%) compared to husband-to-wife. More recipients were male (63.8%). At LKD, women were older (53.3±10.8 vs. 51.3±11.4 years-old;p<0.001). Although creatinine was lower in women (0.73±0.19 vs. 0.96±0.48 mg/dl;p<0.001), estimated glomerular filtration rate was similar. We found no differences in HTN, DM, dyslipidaemia or obesity. Ten years after donation, HTN was more frequent in men (22% vs. 15% women: p=0.002), with no differences in kidney function or other comorbidities. At follow-up, a similar proportion of deaths occurred in men and women (48 deaths, 2.8% vs.2%;p=0.22). Regarding recipients, 10-year patient survival was significantly worse with female-to-male D-R compared to male-to-male (82.8 vs. 90.9%). Ten-year death-censored graft survival was similar in all D-R combinations (male-to-male 86.5%; male-to-female 85.8%; female-to-female 83.2%; female-to-male 86.1%; p=0.89).

Conclusions: For the last 20 years, more women than men donated a kidney in Catalonia, with no change over time, and more men were LKD transplant recipients. The only difference at follow-up was an increased prevalence of hypertension in men post-donation. We found a recipient survival advantage in male-to-male LKD transplantation but found no differences in graft survival according to donor-receptor sex match. More sex-targeted investigation on living KD is needed.

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PP_200 DHOPE REDUCES BILIARY COMPLICATIONS IN LIVER TRANSPLANTATIONS FROM OLDER DCD DONORS: A RETROSPECTIVE ANALYSIS

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Background: Livers from donors after circulatory death (DCD) have an elevated risk of non-anastomotic biliary strictures (NAS), a significant cause of graft failure and higher recipient morbidity. Dual Hypothermic oxygenated machine perfusion (DHOPE) has demonstrated efficacy in reducing NAS but its benefits for older (age >60 years) donor livers remains unexplored. This study aims to evaluate the effectiveness of DHOPE in reducing NAS and other graft-related complications and improving survival outcomes from DCD donors aged 60 years and older.

Methods: This retrospective single-center study included patients who received liver transplants from older DCD donors between 01/2009 and 06/2024. Patients who received a DHOPE-treated liver were compared to those who received a cold stored donor liver. Primary outcome was the incidence of NAS within 12 months post-transplant. Secondary outcomes included anastomotic strictures (AS), early allograft dysfunction (MEAF score) and one-year graft- and patient survival.

Results: Of the 145 patients, 61 received DHOPE-treated DCD livers, and 84 received cold-stored livers. Median (IQR) follow up time was 45 (18-85) months. Donor risk index was higher in the DHOPE group (3.4 [3.2-3.7] vs 3.2 [3-3.5], *p=0.008*). Cold ischemia time was shorter in the DHOPE group (3.9 [2.9-4.4] hours vs 5 [4.4-5.8] hours, *p<0.001*), whereas total preservation time was longer in the DHOPE group (6 [5.6-7] hours vs 5 [4.4-5.8] hours, *p<0.001*). NAS incidence was lower in the DHOPE group (8% vs 26%, Log-rank *p=0.035*), Figure 1. There were no differences in anastomotic strictures or early allograft dysfunction. One–year graft- and patient survival were 80% and 82% in the DHOPE group and both 85% in the control group (log-rank *p=0.55* and *p=0.59*, respectively).

Conclusions: DHOPE significantly reduced NAS incidence in liver transplants from DCD donors aged 60 or older, supporting its use in this high-risk cohort. Further studies are needed to confirm these findings in larger populations.

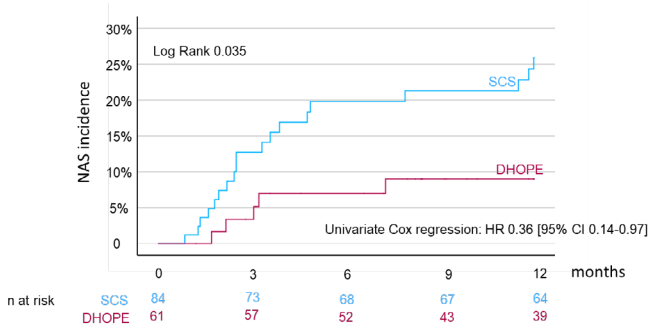

Figure 1. NAS incidence

Figure legend: NAS incidence was significantly lower in the DHOPE group compared to the SCS group(8% vs. 26%, log-rank p = 0.035).

Abbreviations: NAS=Non Anastomotic biliary Strictures, DHOPE=Dual Hypothermic Oxygenated Perfusion, SCS= Static Cold Storage

PP_201 PRELIMINARY COST-UTILITY ANALYSIS OF HYPOTERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION: PADOVA EXPERIENCE

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Background: By reducing ischemia-reperfusion injury and extending preservation times, the use of Hypotemic Machine Perfusion (HMP) not only increases the number of suitable organs but also improves graft quality, leading to better post-transplant outcomes. Beyond clinical advantages, MP has the potential to lower healthcare costs by reducing post-operative complications, hospital readmissions, and the need for re-transplantation.

Methods: The present analysis evaluates costs of HMP compared to static cold storage (SCS) in liver transplantation, focusing on the economic profile and clinical outcomes. We run a direct cost analysis of equipment costs, maintenance, and hospital resource utilization. In parallel, we arbitrarily selected early outcomes parameter as hospital stay ed re-operation rate as performance endpoint as preliminary probe of cost-effective analysis. Data was extracted from the 2023 cohort of liver transplant performed in our centers, 55 with SCS and 55 with HOPE.

Results: In our center the mean cost of the HMP comprehensive of machine, perfusate and perfusionist support is 10.370€. A shorter hospital stay (0,6days for ICU and 1,6days for ordinary stay) and a lower re-operation rate was observed in patients transplanted with HMP grafts.These parameters correspond to an economic benefit of approximately 2000€/patient for the HMP group. The reimbursement for liver transplantation in the Veneto region is 87.720€ and it also covers the cost of MP utilization.

Conclusions: This report represents only a preliminary investigation of HMP cost-effectiveness. We have a great benefit in terms of clinical outcomes associated with an economical benefit. The costs of the MP are not all covered by the economical benefit estimated. However, we considered only selected parameters of liver transplantation outcomes and further and more complete analysis needs to be done. In conclusion, HMP could represent a cost-effective strategy for liver transplantation. The combination of enhanced organ availability, improved patient outcomes, and potential cost savings positions MP as a transformative technology in the field of liver transplantation.

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PP_202 EX VIVO WARM KIDNEY PERFUSION IS ASSOCIATED WITH EXTENSIVE METABOLIC DERANGEMENTS

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Background: *Ex vivo* warm perfusion is a promising method for pre-transplant viability assessment and resuscitation of deceased-donor kidneys. To realize the full potential of warm perfusion, an in-depth understanding of *ex vivo* kidney metabolism, and how it differs from *in vivo* metabolism, is essential. Pathways involved in central energy metabolism are of particular interest, as energy depletion is a critical aspect of ischemia-reperfusion injury.

Methods: Paired kidneys were procured from laboratory pigs and randomly assigned to two experimental groups, one undergoing a minimal period of warm ischemia and the other 75 minutes of warm ischemia (n = 30 per group). Both groups were then preserved by *ex vivo* cold perfusion for 6 hours. Following cold preservation, kidneys underwent 6 hours of *ex vivo* warm perfusion. Cortical tissue samples were collected at three time points: *in vivo* just before ligating the renal vessels, after *ex vivo* cold perfusion, and after *ex vivo* warm perfusion. Metabolomics, transcriptomics, and proteomics analyses were performed on cortical tissue samples.

Results: Multi-omics analysis revealed that *ex vivo* warm kidney perfusion leads to enhanced glycolysis, decreased gluconeogenesis, and impaired tricarboxylic acid cycle activity, all with NAD^+ depletion as a common denominator. This depletion is associated with enhanced immune responses and cell death processes, and this is further exacerbated by ischemic injury. Additionally, we identified metabolic biomarkers that differentiate between injured and healthy donor kidneys.

Conclusions: *Ex vivo* warm kidney perfusion induces significant metabolic alterations that should be considered when optimizing perfusion strategies to support pre-transplant viability assessment and organ resuscitation.

PP_203 LACK OF FEMALE SEX HORMONES AND AGE WORSENS LUNG GRAFT STATUS AFTER BRAIN DEATH IN MENOPAUSAL FEMALE RATS

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Background: The limited number of available organs for transplantation is still a challenge, with long waiting lists, especially for solid organs as the lungs. Those are highly affected by brain death (BD), with females showing a higher inflammatory response, linked to the acute reduction of sex hormones. Additionally, with the aging of world population, the number of older donors is increasing. In this context, the study of menopause-associated changes in female donors gain importance. Thus, here we investigated menopause's effects in female BD rats, previously subjected to transitional follicular depletion and aging, on leukocyte influx to the lungs and inflammatory mediators release.

Methods: Female Wistar rats (8 weeks old) were divided in young (Y) and menopausal groups (M). The induction of menopause was based on administration of 4-vinylcyclohexene diepoxide (VCD, 80 mg/kg, i.p., 5 days/week) for 6 weeks. After follicular depletion, the rats aged for 10 weeks. Reduction in 17β-estradiol and increase in FSH serum concentrations confirmed menopause establishment. Thereafter, young and menopausal rats were submitted to BD by intracranial balloon catheter inflation and were maintained for 6 h under mechanical ventilation. Sham-operated rats served as controls. White blood cell (WBC) counts, bone marrow, and bronchoalveolar lavage (BAL) were analyzed and serum inflammatory mediators quantified. Lung tissue sections were evaluated and lung samples were cultured to assess inflammatory mediator release over 24 hours.

Results: WBC counts were reduced in both menopausal ($p=0.014$) and young rats ($p=0.011$) compared to Sham. Menopausal BD (M-BD) rats showed fewer blood granulocytes than young BD (Y-BD) rats ($p=0.01$). BAL in M-BD rats showed increased number of granulocytes compared to Sham ($p=0.018$) and Y-BD ($p=0.009$). Bone marrow cells increased in M-BD versus Y-BD ($p=0.035$). Serum IL-10 was lower in M-BD than Y-BD ($p=0.003$), while IL-1β and IL-6 increased in lung culture for both groups.

Conclusions: Menopause increases lung inflammation after BD, by higher leukocyte infiltration and reduction of IL-10. This inflammatory infiltrate can impact in the transplant result and further studies are necessary to understand and improve menopause donor management.

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PP_205 SIMULTANEOUS LIVER-KIDNEY TRANSPLANTATION: OUTCOMES WITH DONATION AFTER CIRCULATORY DEATH DONORS

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Background: Donation after circulatory death (DCD) donors represent a potential strategy to address the growing organ supply-demand discrepancy; however, limited data are available regarding outcomes of simultaneous liver-kidney transplants using these donors.

Methods: This study is a retrospective analysis of all patients who underwent liver-kidney transplantation at our center between 2019 and 2024. Baseline and outcomes of liver-kidney transplants from donation after circulatory death (DCD) donors were compared to those from donation after brain death (DBD) donors.

Results: During the study period, a total of 396 transplants were performed, 9% of which were double liver-kidney transplants. 36 simultaneous liver-kidney transplants were performed: 11 from DCD and 25 from DBD. DCD donors were younger, with a mean age of 41 years, compared to DBD, with no significant differences in BMI. From 2019 to 2024, 11 DCD and 25 DBD simultaneous liver-kidney transplants were performed. DCD recipients had a mean age of 54 years, a BMI of 28.32, and a MELD score of 24.36. In comparison, DBD recipients were older with a mean age of 56 years, a BMI of 26, and a MELD score of 22. Among all recipients, 33 underwent a first kidney transplant, and 3 received a second. The median cold ischemia time (CIT) was 12 hours for the kidney and 6 hours for the liver in both groups, while the functional warm ischemia time (FWIT) in the DCD group was 14 minutes. Delayed graft function (DGF) was observed in 54% of DCD kidney recipients and 48% of DBD kidney recipients. Among recipients with DGF, 3-year kidney graft survival was 53% for DCD versus 69% for DBD. Liver graft survival at 3 years was 100% in both groups, with early allograft dysfunction (EAD) observed in 27% of DCD recipients and 32% of DBD recipients. Patient survival at 5 years was 100% for both groups. Kidney graft survival at 3 years was 88% in the DCD group compared to 76% in the DBD group.

Conclusions: This study demonstrate that DCD donors represent a viable strategy to expand the donor pool in simultaneous liver-kidney transplantation, offering comparable outcomes in terms of overall patient and graft survival to DBD donors.

PP_206 OUTCOMES OF LIVERS WITH PROLONGED DURATION OF EX SITU NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic ex-situ liver perfusion (NESLiP) gives the opportunity to assess and modify marginal livers. Additionally, it also helps overcoming the time barriers by increasing the preservation time possible outside of static cold storage (SCS). NESLiP can be employed from the donor hospital until implantation or once the liver arrives at the recipient centre in a cold box. In this study, we discuss our experience of liver grafts subjected to prolonged NESLiP.

Methods: Retrospective analysis of livers undergoing NESLiP at our institute from May 2017 till January 2023. Patients were divided into two groups based on the duration of NESLiP (<10.5 hours [standard] and >10.5 hours [prolonged]) and outcomes compared. All livers underwent perfusion using a blood-based solution.

Results: There were 250 (DBD 115; DCD 135) livers undergoing NESLiP during the study duration that were subsequently transplanted. Sixty-two (24.8%) of these were perfused for more than 10.5 hours before implant with median 19.5 hours of total preservation. Comparing standard with prolonged perfusion livers, there was no difference in donor age (53 vs 48, p=0.248), sex (female = 51.6% vs 40.4%, p=0.163), BMI (27.6 vs 25.6, p=0.073), donor cause of death (p=0.562) or UK Donor Liver Index (1.6 vs 1.4, p=0.238). There was no difference in the number of DCD livers between groups (61.3% vs 51.6%, p=0.237). NRP was used in 38.1% of standard perfusion DCD livers compared to 26.3% of prolonged perfusion DCD livers (p=0.273). The cold ischaemic time was similar between groups (406 vs 410 mins, p=0.981). In terms of outcome, the MEAF score was similar between groups (3.8 vs 3.9, p=0.941) and did not correlate with perfusion duration (p=0.99). The incidence of early allograft dysfunction (11.7% vs 14.1%, p=0.8), primary non-function (1.6% vs 1.1%, p=0.99) and clinically relevant non-anastomotic strictures (11.3% vs 11.7%, p=0.99) were similar between the two groups.

Conclusions: Our experience suggests that prolonged NESLiP is safe. This further strengthens the role of this technology in aiding transplant logistics, viability testing and therapeutic delivery.

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PP_207 NORMOTHERMIC MACHINE PERFUSION OF STEATOTIC DONOR TRANSPLANT LIVERS

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Background: NMP offers potential benefits for improving outcomes of steatotic donor liver transplants compared to SCS. However, the biochemical and metabolic profile of the perfusate has not been comprehensively investigated. This study evaluates ex-situ biochemical, metabolic measurements and clinical outcomes of steatotic livers preserved with NMP from the COPE Liver NMP trial.

Methods: Donor livers with steatosis (*n*=48) were identified with pre-preservation biopsies showing mild (≥5% large droplet macrovesicular steatosis, ld-MaS) to severe steatosis (histopathologist score 1–3) and compared with matched lean controls (*n*=72). Of 120 donor livers, 105 livers were transplanted (steatotic NMP=21, steatotic SCS=12, lean NMP=46, lean SCS=26), 14 livers were discarded and one excluded due to ABO incompatibility. Perfusate samples collected at 15 min (P1), 60 min (P2) and end of NMP (P3) were assessed for hepatocellular injury, lipid and general metabolism. Clinical outcomes were compared between steatotic and lean donor livers preserved by NMP or SCS.

Results: Steatotic NMP livers showed significantly greater hepatocellular injury than lean NMP livers and AST levels followed a similar trend, **Figure 1A.** Triglyceride mobilisation was higher in steatotic livers at 15 min and 60 min (61.57±36.80 mg/dL vs. 34.68±19.35 mg/dL, *P*=0.001), alongside elevated fatty acid metabolism (3-OHB, *P*=0.001), **Figure 1B**. Steatotic livers demonstrated inferior lactate clearance, comparable glucose and lower insulin levels **Figure 1C.** CRP levels were similar, but FGF-21 release was non-significantly elevated in steatotic livers throughout NMP, **Figure 1D.** Clinically, recipients of steatotic NMP livers had significantly lower rates of PRS (14.3% vs. 50%, *P*=0.0267) and EAD (14.3% vs. 66.7%, *P*=0.002) compared to steatotic SCS livers. Peak AST was reduced (906 IU/L vs. 2479 IU/L, *P*=0.0126), comparable to lean SCS livers (*P*=0.649. Graft survival at 12 months was 90.5% for steatotic NMP livers vs. Steatotic SCS (88.3%)**.**

Conclusions: NMP reduces the risk profile of steatotic livers, achieving clinical outcomes comparable to lean livers preserved with SCS. By enhancing metabolic recovery and reducing IRI, NMP increases the utilisation of steatotic donor livers for transplantation.

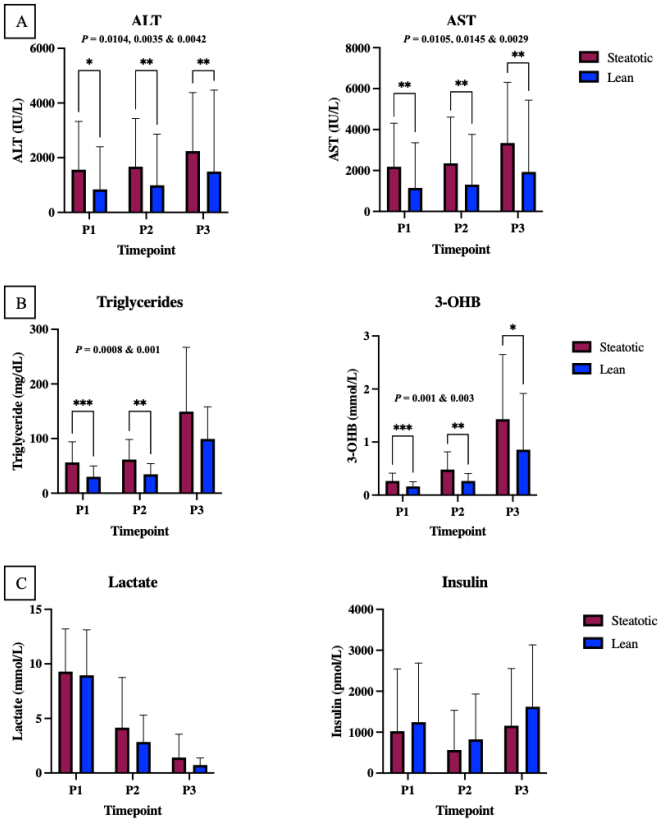

Figure 1A-D. Perfusate ALT and AST (A), triglycerides and 3-OHB (B), lactate and insulin (C) and CRP and FGF-21 (D) in steatotic compared to lean donor livers during NMP. Data presented as mean ± SD. *p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001.

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PP_208 THE ROLE OF HIF MODULATION AND DEFATTING IN DISCARDED STEATOTIC HUMAN LIVERS DURING NMP AND WHOLE BLOOD REPERFUSION

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Background: The hypoxia-inducible factor (HIF) pathway has been implicated in hepatic steatosis with the HIF-1a isoform providing a hepatoprotective effect through enhancement of liver fat metabolism and the HIF-2a isoform conversely promoting intrahepatic lipid accumulation. Pharmacological stabilisation of HIF-1a of steatotic livers during normothermic machine perfusion (NMP) may enable a greater proportion of livers to achieve ex-situ functional criteria for transplantation. We have previously reported dosing schedules for pharmacological HIF modulators including deferoxamine (DFO, a potent activator of both HIF-1a & HIF-2a) with selective HIF-2a inhibition using PT2385 (a HIF-2a dimerisation inhibitor) during NMP. The aim of the present study was to compare the effect of an established NMP defatting protocol (DeFat, comprising of insulin/glucose reduction, L-carnitine, NKH477 and lipid filter) with and without the adjunct of HIF modulators (DeFat-HIF, addition of DFO & PT2385) during ex-situ perfusion.

Methods: Six sequential discarded livers (DeFat, *n*=3 and DeFat-HIF, *n* =3) were perfused with pRBC using the OrganOx *metra* over 12h, flushed and reperfused for 6h with whole blood (ex-situ transplant model). Global hepatocellular function was measured using the LiMAx test. Macrosteatosis (MaS) was quantified using Visiopharm® digital image analysis software and blinded histopathologist report. HIF activation was determined through serial perfusate EPO measurements.

Results: Both groups demonstrated comparable lactate, pH, ALT and LiMAx test results with the exception of triglyceride/cholesterol mobilisation and glucose metabolism which was greater in the DeFat-HIF group (Figure1). The DeFat-HIF group had significantly higher levels of perfusate EPO following 12h of perfusion (233.7±107.2 miU/ml vs. 23.4±12.7 miU/ml, *P* = 0.03) and first 2h of reperfusion. A pronouced reduction in Ld-MaS was only observed in the DeFat-HIF group.

Conclusions: The DeFat-HIF protocol demonstrated a decrease in the presence of Ld-MaS and comparable perfusion biochemistry to the established DeFat protocol. The effect of these interventions on ischaemia-reperfusion injury remain to be elucidated.

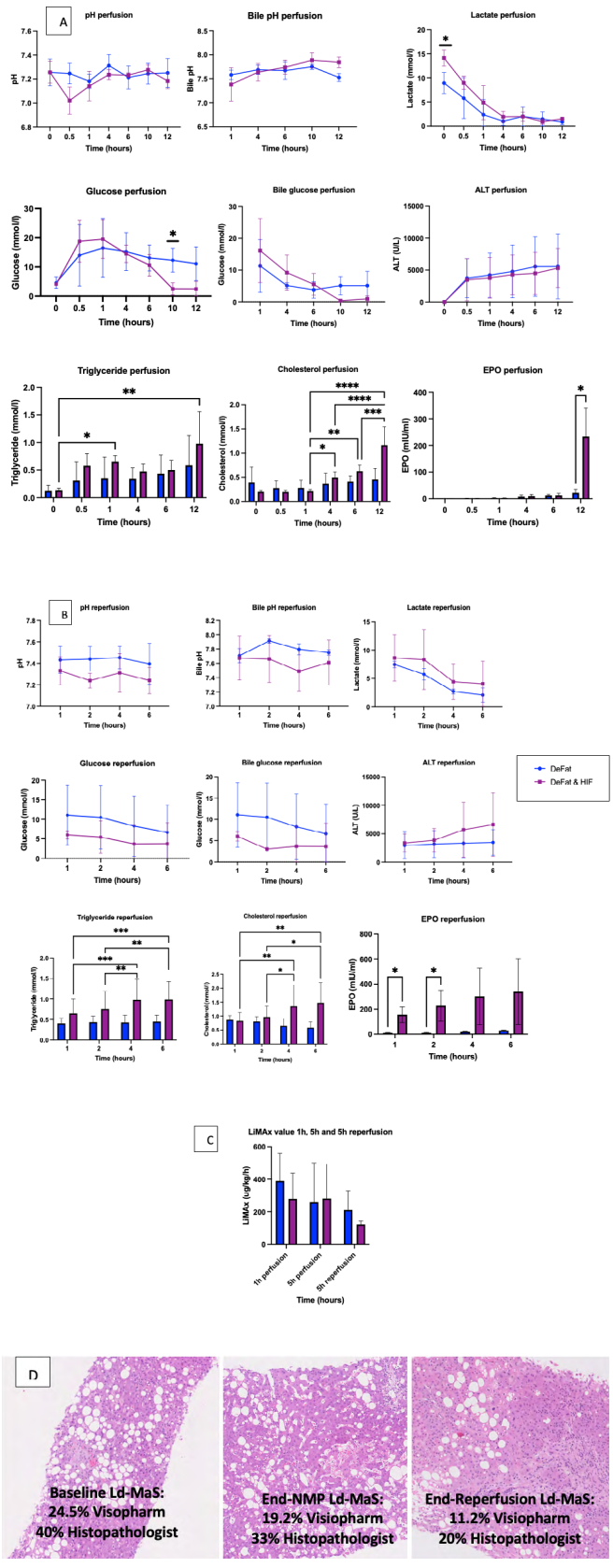

Figure 1: **[A]** Perfusion phase biochemistry, time '0h' signifies primed circuit prior to liver connection; **[B]** Whole blood reperfusion biochemistry, time '1h' signifies reperfusion at 1 hour following flushing of liver with UW solution and re-priming of the circuit with whole human blood; **[C]** Perfusion and reperfusion LiMAx values and; **[D]** Example of Ld-MaS reduction in DeFat-HIF group, H&E of Liver 5 shown (40X magnification). pH, lactate, glucose, ALT and EPO: multiple unpaired t-tests, data reported as mean ± SD. Triglycerides and cholesterol: 2-way ANOVA (Fisher's LSD) to compare difference per timepoint for each group. * $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$ and **** $P \leq 0.0001$.

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PP_210 ANTI-HMGB1 ANTIBODY INHIBITS PORCINE PULMONARY WARM ISCHEMIA-REPERFUSION INJURY INDEPENDENT OF INFLAMMATORY CYTOKINES

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Background: Strategies to reduce ischemia-reperfusion injury (IRI) may expand the use of extended-criteria or cardiac death donors and improve transplant outcomes. High-mobility group box 1 (HMGB1), a mediator of inflammation and cell injury, is a novel therapeutic target for IRI. However, data on the role of HMGB1 in pulmonary IRI in large animal models are limited. This study aims to investigate the role of HMGB1' in IRI and to evaluate the cytoprotective effects of anti-HMGB1 antibodies using our porcine lung warm IRI model.

Methods: Warm ischemia was induced in 12 CLAWN miniature swine by clamping the left bronchus, pulmonary artery, and veins for 90 minutes. The control group (n=5) received no treatment, while the HMGB1 Ab group (n=4) received 1 mg/kg of anti-HMGB1 Ab before reperfusion. An isotype control Ab group (n=3) received IgY Ab similarly. Lung function and structure were assessed via biopsy, X-ray, and blood gas analysis. Serum cytokines, including HMGB1 and IL-1β, were measured to evaluate inflammation and treatment efficacy.

Results: Serum HMGB1 levels increased following IRI, peaking at 14 ± 6 ng/ml two days post-reperfusion in the control group, while anti-HMGB1 Ab administration reduced levels to 0.9 ± 0.5 ng/ml. Two hours post-reperfusion, PaO_2 in the HMGB1 Ab group was 551 ± 19 mmHg, more than double that in the control group (266 ± 60 mmHg). Lung biopsy in controls showed significant alveolar endothelial damage, including edema, hemorrhage, and fibrin exudates at postoperative day 2 (POD2). In contrast, anti-HMGB1 Ab treatment improved histological findings, reducing PCNA-positive and TUNEL-positive cells. Systemic IL-1β levels peaked 24 hours post-reperfusion in both groups, with no significant difference (63 ± 26 vs. 62 ± 14 pg/ml). Isotype control IgY Ab showed no improvement in oxygenation or lung damage.

Conclusions: The findings of this study indicate that HMGB1 plays a significant role in the progression of lung IRI. The reduction of systemic HMGB1 via anti-HMGB1 Ab alone has been demonstrated to mitigate IRI independently of systemic IL-1β concentration in a clinically relevant large animal model. The targeting of HMGB1 may represent a novel therapeutic strategy for clinical ischemia-reperfusion injury (IRI) associated with lung transplantation.

PP_211 PERFUSATE PROFILING DURING HYPOTHERMIC OXYGENATED PERFUSION ENHANCES FMN ABILITY TO PREDICT LIVER FUNCTION

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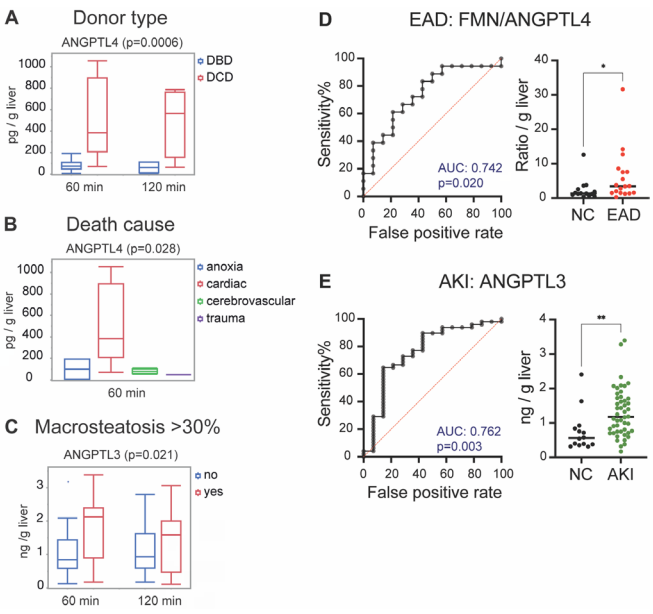
Background: Viability assessment during machine perfusion holds promise for predicting liver function after transplantation. While Flavin-mononucleotide (FMN) has emerged as a reliable biomarker of ischemia-induced mitochondrial injury, additional perfusate factors could better capture the endothelial damage elicited during the donation process. The study investigated the release of selected mediators during Hypothermic oxygenated machine perfusion (HOPE) of human livers.

Methods: We retrospectively included HOPE procedures performed on DBD-ECD and DCD donor livers from 2017 to 2020 at two Italian centers. Perfusate samples were collected hourly and stored. Biomarkers were measured using an automated rapid (<90min) immunoassay platform. The correlation between mediator concentration and transplantation outcomes was investigated.

Results: Eighty-nine donors were included, of whom 51 were DBD-ECD and 38 DCD. All grafts were successfully transplanted; 23 (26%) recipients developed early-allograft-dysfunction (EAD), while 52 (58%) experienced acute-kidney-injury (AKI). Release of Angiopoietin-like (ANGPTL) factors was higher in DCD compared to DBD donors and their concentration at 60min was associated with cardio-circulatory arrest duration. Perfusate ANGPTL4 and ANGPTL3 correlated with donor ALT. Higher ANGPTL3 levels were observed in livers with macrosteatosis exceeding 30%. FMN was the most informative biomarker for EAD (AUC 0.698). However, incorporating ANGPTL4 as a ratio further enhanced FMN predictive power (AUC 0.742). ANGPTL3 exhibited a good discrimination ability for AKI prediction (AUC 0.762).

Conclusions: Evaluating mediators during HOPE could allow a precise assessment of marginal grafts, while providing information for prediction of postoperative complications. Coupling ex situ perfusion with fast biomolecular profiling of the perfusate could enhance risk stratification of injured organs, in line with personalized medicine.



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PP_212 COMPARISON BETWEEN PARAFFIN AND RAPID CONFOCAL MICROSCOPY FOR PROCUREMENT KIDNEY BIOPSY RISK SCORES

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Background: Prognostic outcome models might help to minimize the discard rates of renal transplants from deceased donors. To this end, we have published 2-Step Scores for both delayed graft function and transplant loss with optional histology. With conventional paraffin PAS histology taking at least 3 hours excluding transport time, we tested whether fast, mobile confocal histology with portable VivaScope® systems might offer a viable alternative.

Methods: After omitting 17 biopsies with less than 12 glomeruli and 1 artery, we collected 14 zero-hour and 16 renal transplant indication (Tx) biopsies for a combined cohort. All biopsies were scanned in less than 10 min with a VivaScope® at 20x, rendering pseudo-HE images, then underwent our regular paraffin work-up. Banff Lesion Scores ct and cv were assessed on the granular ordinal scale and binary as (ct≤1 vs. ct≥2 and cv≤2 vs. cv3 together with the number of glomeruli as used in the previously published 2-Step Scores in a blinded fashion by an expert nephropathologist on the paraffin sections (P) and a VivaScope® scan (V). Additionally, we examined the ratio of globally sclerotic glomeruli. Fleiss' kappa-statistics, Kendall rank and Pearsons' correlation analyses compared P and V on the combined cohort.

Results: Between P and V, granular Banff ct correlated with a kappa of 0.513 (p=8.38e-05) and a Kendall's W of 0.706 (p=0.0694) on the combined cohort; binary Banff ct correlated with a kappa of 0.869 (p=1.92e-06).We had to exclude two more biopsies in which no artery was found in the scanning plane in V. Granular Banff cv correlated with a kappa of 0.109 (p=0.345) and a W of 0.677 (p=0.103) between P and V on the combined cohort, binary Banff cv with a kappa of 0.24 (p=0.204).The total number of glomeruli correlated between P and V with an R of 0.75 (p=2.3e-06), the number of globally sclerotic glomeruli with an R of 0.82 (p=4.1e-08) and the ratio thereof with an R of 0.86 (p=8.6e-10).

Conclusions: Instant, decentralized VivaScope® histology might deliver Banff ct and the number of glomeruli with sufficient accuracy for the 2-Step Scores to predict the risk of delayed graft function and 1-year death-censored transplant loss in deceased heart-beating donors. In contrast, VivaScope® assessment of Banff cv might not be accurate enough for the use in 2-Step Scores.

PP_213 SUPERIOR SURVIVAL OUTCOMES IN ABO INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANT THAN KIDNEY PAIRED DONATION

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Background: Incompatibility is one of the challenges of the transplant community. ABO incompatible (ABOi) living donor kidney transplant (LDKT) offers excellent results with respect to decease donor and dialysis, although worse than LDKT with compatible blood group (BG) (ABOc). But, the reality is that these couples would only have one ABOc in the Kidney Exchange Program (KEP). Our objective is to compare the ABOi LDKT with the ABOc LDKT in a national KEP (KPD LDKT).

Methods: Retrospective unicenter study (2010-2020) with a minimun of FU of 5 years. ABOi LDKT criteria for transplant was based on either IgM or IgG initial (<1024) and at-transplant (??8) isoagglutinin titters. KPD LDKT criteria were by immunological and BG incompatibilities, excluding in the analisys DES- treated patients. A comparative specific subgroup of KPD, included in KEP due to only BG incompatiblity (KPD*ABOi LDKT). After the initial main outcomes analysis, we focus in mortality approach in multivariant analysis. Ethics Committee approved the study.

Results: 352 of 772 LDKT were included in the study, meeting the inclusion criteria 112 LDKT (62 ABOi LDKT; 50 KPD LDKT, 19 KPD*ABOi LDKT). Females (p=0.001), higher cumulated dialysis vintage (p=0.013) and immune risk (p=0.004), and previous transplant (p=0.024) in KPD LDKT than ABOi LDKT in the same FU (71.86 ± 31.96 66.60 ± 32.14Mo, p=0.390). Higher graft loss was showed in KPD LDKT (34% vs 11.3%, p= 0.004) due to higher mortality (16% vs 3.2%, p=0.021), with no expected- higher any kind of rejection rate differences between both groups (p=0.564), either ABMR (0.494). In the survival analysis, higher recipient age (p=0.005), KPD LDKT over ABOi LDKT (p=0.021), KPD*ABOi LDKT over ABOi LDKT (p=0.007), and higher immune risk (p=0.056) were the risk factors associated to mortality in the univariant analysis; However, only recipient age (OR 1.10 [1.02-1.20], p=0.014) and KPD*ABOi LDKT over ABOi LDKT (OR 11.07 [1.61-75], p=0.014) were the associated factors in the multivariant analysis.

Conclusions: In our center, ABOi LDKT demonstrated superior patient survival than KPD LDKT. KPD LDKT recipients included in KEP due to BG incompatibility had higher mortality than ABOi LDKT recipients. Further multicenter analysis have to be done for stablish the recommendations in incompatible pairs.

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PP_214 HOPE AND USE OF EXPANDED CRITERIA DONORS IN LIVER TRANSPLANT FOR ACUTE AND ACUTE-ON-CHRONIC LIVER FAILURES

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Background: Liver transplant (LT) is an end of the line treatment for patients with acute liver failure (ALF) and Acute-On-Chronic Liver Failure (ACLF). Both have high mortality and the graft quality and waiting time until transplant are key factors for survival. Recent studies suggest that hypothermic oxygenated perfusion (HOPE) com improve graft quality and overall survival. We aim to evaluate the use of HOPE on waiting time, use of expanded criteria donors (ECD), complications and overall survival in patients with ALF and ACLF.

Methods: Retrospective study with LT in adults, for ALF and ACLF, between January 2020 and December 2023 for ALF and ACLF. The patients were separated in two groups: HOPE group and No HOPE group. Data from recipients, waiting time until LT, surgical technique, ischemia times, donors, pos-operative period, complications and mortality was recorded.

Results: A total of 30 patients were included, 18 with HOPE and 12 without HOPE. Median waiting time to transplant was significantly lower in HOPE group (3 vs 6 days, p = 0,037). In the HOPE group, 89% were ECD (89% vs 42%, p=0,006). Ischemic type biliary lesions (ITBL) were slightly higher in HOPE group (11% vs 8%). Overall mortality and vascular complications were lower in HOPE group, without significant differences. No statistically significant differences were found in recipient MELD-Na, surgical variables, ischemia times or peak enzymes and bilirubin.

Conclusions: Greater use of ECD, made possible with HOPE, reduces the waiting time to transplant, without significant increase in complications or mortality. This results are in line with previously results with HOPE use. Although this is a small sample, is the one of the greatest with LT in ACLF and ALF patients using HOPE. This study shows that HOPE may reduce waiting time until transplant by allowing the use of more ECD and expand the donor pool. This can be done without increasing both vascular and ITBL complications, as well as mortality.

PP_217 IMPACT OF PRE-DONATION HYPERNATERMIA AND MARKERS OF LIVER FUNCTIONS ON LIVER UTILISATION AND TRANSPLANTATION OUTCOMES

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Background: Assessment of liver function in deceased donors is essential for optimising transplantation outcomes. Pre-donation hypernatremia has been linked to early liver allograft dysfunction, but its impact on organ utilisation remains unclear. Similarly, the effects of elevated excretory and metabolic surrogate markers of liver functions on graft and patient survival warrant further investigation.

Methods: A retrospective cohort study was conducted using UK adult transplant registry data from January 2016 to December 2023. Donor serum sodium, bilirubin, gamma-glutamyl transferase (GGT) and lactate levels were categorised and analysed. Outcomes included liver utilisation rates, 1-year transplant and patient survival. The analysis plan included an interim exploratory analysis followed by a complete multivariate analysis stratified by donor type (DBD vs. DCD), adjusting for donor and recipient factors.

Results: Over the study period, 13,947 donors were offered, of which 6,706 (48.1%) livers were retrieved and transplanted (5,184 (77.3%) DBDs and 1,522 (22.7%) DCDs). The impact of categorised sodium, bilirubin, GGT and lactate levels on liver utilisation showed variability between the maximum and the latest recorded values pre-matching run. Kaplan Meier survival analysis pre-donation maximum sodium (>170) is significantly associated with lower 1-year patient survival (Fig.1). Pre-donation maximum lactate (>2.4) showed a significant association with inferior 1-year patient survival (Log-rank p=0.005).

Conclusions: This study highlights the importance of assessing pre-donation liver function markers in optimising liver transplantation outcomes. Interim exploratory analysis suggests that pre-donation hypernatremia and elevated lactate levels are associated with inferior 1-year patient survival. A complete multivariate analysis will be conducted to adjust for confounding factors, providing a comprehensive understanding of these associations.

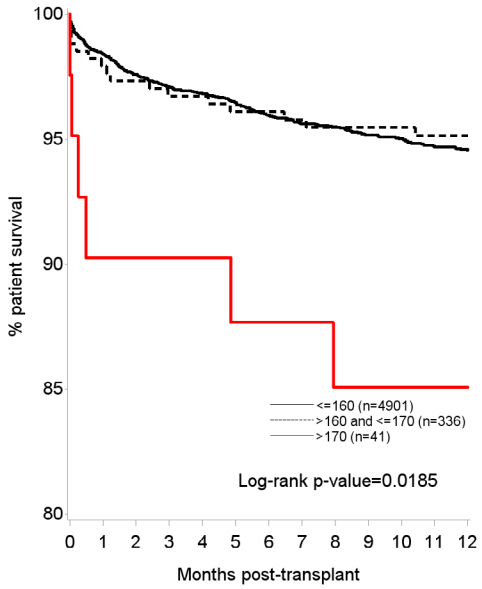

Fig. 1 – Kaplan Meier survival analysis of the impact of categorised pre-donation maximum sodium on 1-year patient survival.

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Donation, preservation & regeneration

PP_218 ANDROGRAPHOLIDE CAN POTENTIALLY RESCUE UNUSABLE EXTENDED CRITERIA DONOR LIVER GRAFTS

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Background: Extended criteria donor (ECD) livers have gained much attention in recent years as a potential solution to increase the availability of liver grafts available for patients with liver failure. This study aims to investigate the using Andrographolide (Andro) to improve the quality of donor liver grafts by reducing the fat content, enhancing the mitochondrial function, and inhibiting T cell induced inflammatory response.

Methods: Human hepatocytes were isolated from nine donor fatty liver grafts. Hepatic T lymphocytes were isolated from an additional 12 donors' liver perfusates. T lymphocytes and hepatocytes were treated with Andro at concentration of 5, 10, 25, and 50 μM. A CCK-8 assay was conducted to assess toxicity of Andro by measuring hepatocytes viability. Following treatment, free and total cholesterol levels were measured, lipid droplets were stained, and mitochondrial DNA copy numbers, along with expression of anti-oxidative genes were evaluated. Cytokine levels in T cells, including TNF-α, IFN-γ and IL-17, were assessed by flow cytometry.

Results: No toxicity was observed in hepatocytes at any of the variant doses of Andro (5, 10, 25, 50 μM). A higher dose of Andro (25 μM) reduced the level of free/total cholesterol, decreased the amount of lipid droplets, and increased the mitochondrial DNA copy numbers, as well as the mRNA expression of Peroxisome Proliferator-activated Receptor-γ Coactivator-1 (PGC-1α), Glutamate-Cysteine Ligase Catalytic Subunit (GCLC), Glutamate-Cysteine Ligase Modifier Subunit (GCLM), Heme Oxygenase 1 (HO-1) and NAD(P)H Quinone Dehydrogenase 1 (NQO1) ($p<0.05$). Additionally, Andro decreased the proportion of TNF-α or IFN-γ-producing T cells and reduced the mRNA expression of TNF-α and IFN-γ in T cells (5 μM, $p<0.05$; 10 μM, $p0.01$; 25 μM, $p<0.01$). Furthermore, Andro (25 μM) also lowered the protein level of TNF-α and IFN-γ in the supernatant of T cell culture ($p<0.01$).

Conclusions: Andrographolide has a significant potential to enhance the viability of ECD liver grafts and alleviate the shortage of grafts in the contest of human liver transplantation.

Infectious diseases, malignancies & long term challenges

PP_219 DIAGNOSTIC TEST ACCURACY OF DETECTING DONOR-DERIVED CELL-FREE DNA IN RENAL TRANSPLANT REJECTION

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Background: Recently, circulating donor-derived cell-free DNA (dd-cfDNA) has been utilised as a diagnostic biomarker in assessing allograft rejection and renal status. The biomarker is obtained through liquid biopsy. It is a non-invasive test that is relatively simple and safe. However, the accuracy of the test has yet to be established. The main aim of this study was to explore the diagnostic test accuracy using dd-cfDNA in detecting rejection in renal transplantation.

Methods: A systematic review and meta-analysis of diagnostic test accuracy studies were conducted in accordance with PRISMA guidelines, by searching all electronic databases MEDLINE via PubMed, EMBASE, Scopus, and Web of Science. All eligible studies reported sensitivity and specificity outcomes of dd-cfDNA in detecting rejection post-renal transplantation. The data analysis was performed using Review Manager (RevMan) Version 5.4.1 and MetaDTA Version 2.0.

Results: Twelve articles were included, comprising 1,599 samples analysed with a mixture of antibody-mediated rejection (ABMR) and T cell-mediated rejection (TCMR). When dd-cfDNA was above the 1% threshold, diagnostic accuracy revealed a pooled sensitivity of 62.1% (95% CI: 46.1% - 76.0%) and specificity of 81.9% (95% CI: 74.2% - 87.7%) in detecting unspecified rejection. A slightly higher pooled sensitivity of 75.3% (95% CI: 59.9% - 86.2%) and specificity of 82.1% (95% CI: 71.3% - 88.8%) were observed in ABMR rejection. Data were inadequate to allow for analytical comparison in TCMR rejection. The AUC for dd-cfDNA is better than serum creatinine in discriminating all allograft rejections.

Conclusions: dd-cfDNA test has a higher sensitivity and specificity in detecting AMBR than other allograft rejections. Future studies are needed to optimise the utility of dd-cfDNA in conjunction with other non-invasive tests in clinical practice.

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PP_221 MULTIDRUG-RESISTANT ORGANISM COLONIZATION IN LIVER TRANSPLANTATION: SURVIVAL AND RISK FACTORS

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Background: Patients with cirrhosis awaiting liver transplantation (LT) are at heightened risk of multidrug-resistant organism (MDRO) colonization due to frequent hospitalizations, antibiotic use, and immune dysfunction. This study aimed to evaluate the impact of MDRO colonization on short-term survival in LT recipients, with secondary aims of assessing epidemiological patterns and identifying risk factors for colonization.

Methods: We conducted a retrospective cohort study involving patients admitted for LT in the Liver Transplant Center Zagreb, Croatia, between 2021-2024. MDRO colonization was assessed through nasopharyngeal and rectal swabs at the time of LT. Clinical, demographic, and laboratory data were collected, including liver-disease severity scores for 65 consecutive patients.

Results: No significant difference in 60-day survival was observed between MDR-colonized and non-colonized patients, nor when comparing colonization at multiple sites or with multiple organisms. Colonized patients differed significantly from non-colonized in terms of etiology of liver disease (alcohol related liver disease (ALD) and HCC), leukocyte count, INR, albumin, sodium levels, MELD, CTP, SOFA scores, waiting time, number of ICU admissions before transplantation, and antibiotic use. In multivariate analysis, ALD emerged as the only significant factor, paradoxically reducing the likelihood of MDR colonization (OR= 0.139, 95% CI 0.03-0.64, p=0.011). The most common colonizers were multidrug-resistant Gram-negative strains (n=18), followed by vancomycin-resistant enterococci (n=10).

Conclusions: MDRO colonization did not impact shot-term survival in LT recipients, despite significant clinical and biochemical differences between colonized and non-colonized patients. The only independent risk factor for colonization identified was ALD, which surprisingly reduced the likelihood of MDRO colonization. These findings suggest that while colonization is associated with distinct clinical characteristics, its effects on short-term survival may be limited. Studies on larger, possibly multicentric cohorts, are needed to refine risk-stratification.

PP_222 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA WITH NO ACTIVE DISEASE OR A SINGLE SMALL TUMOUR

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Background: The risk of recurrent hepatocellular carcinoma (HCC) and HCC-related mortality post liver transplant (LT) is influenced by the number and size of active tumours at time of LT. This study assessed 5-year HCC-related mortality of subjects with a single active tumour ≤2 cm versus those with no active disease.

Methods: A retrospective cohort study was performed including adult patients transplanted for the indication of HCC between 1998-2018 at one Australian centre, and 2011-2018 at a second. Tumour burden was assessed on most recent pre-transplant imaging. Competing risks regression was used to assess 5-year HCC-related mortality post-transplant, with the competing risk of non-HCC related mortality. Secondary analysis was performed for single tumours of increasing diameters and 5-year HCC-related mortality.

Results: During the study period, 428 patients underwent LT for HCC. Amongst these, 152 patients had no active tumour and 108 patients had a single active tumour ≤2 cm. Of these two groups, 85% had HCC treatment prior to LT. There was no significant difference in 5-year HCC-specific survival in the presence of a single active tumour ≤2 cm vs no active disease (90.0% vs 95.4%, p=0.08). There was no significant difference in the cumulative incidence of HCC-related mortality between these two groups (LR 3.13, p=0.07), **Figure 1**. For a single tumour with diameter ≤3 cm, there was a significant increase in 5-year HCC-specific mortality compared to those with no active disease (**Table 1**). No difference between HCC recurrence (8.6% vs 13.0%, no active disease vs ≤2 cm, p=0.35) or time to recurrence (3.6 vs 1.8 years, p=0.40) was found.

Conclusions: This study demonstrates no significant difference in 5-year HCC-specific mortality for those with a single small (≤2 cm) tumour vs no active disease at the time of transplant. However, at a size of up to 3 cm, a single active tumour was associated with increased 5-year HCC-specific mortality.

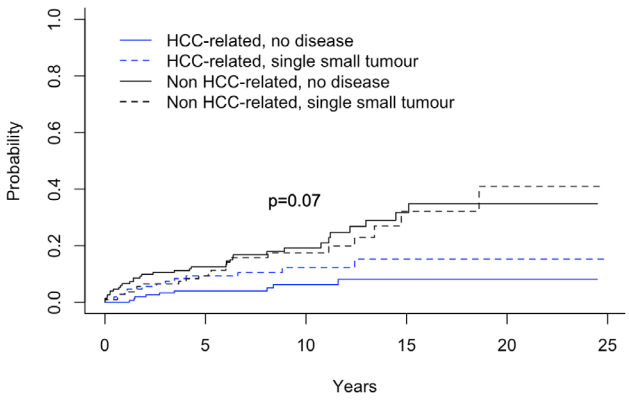

Figure 1. Cumulative incidence of HCC-related and non-HCC related mortality

	n	5 year HCC-specific mortality			HCC recurrence		
		n (%)	HR (95% CI)	p	n (%)	HR (95% CI)	p
No active disease	152	6 (3.9%)	N/A	N/A	13 (8.6%)	N/A	N/A
Single tumour ≤2 cm (vs no active disease)	108	10 (9.3%)	2.64 (0.98-7.10)	0.06	14 (13.0%)	1.62 (0.77-3.41)	0.20
Single tumour ≤3 cm (vs no active disease)	145	15 (10.3%)	**2.72 (1.06-6.98)**	**0.04**	20 (13.8%)	1.63 (0.81-3.28)	0.17
Single tumour ≤4 cm (vs no active disease)	167	17 (10.2%)	**2.70 (1.07-6.81)**	**0.04**	22 (13.2%)	1.58 (0.80-3.14)	0.19
Any size single tumour (vs no active disease)	178	18 (10.1%)	**2.67 (1.06-6.71)**	**0.04**	23 (12.9%)	1.57 (0.79-3.10)	0.20

Table 1.

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Infectious diseases, malignancies & long term challenges

PP_225 CURRENT STATUS OF ABO INCOMPATIBLE KIDNEY TRANSPLANTATION IN JAPAN - BASED ON STATISTICAL DATA -

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Background: In Japan, where there is a chronic shortage of organs, ABO blood-type incompatible transplants have been carried out since 1989 with the aim of expanding kidney transplants, and they account for 34.5% of living-donor kidney transplants in Japan. In recent years, even in cases where the anti-blood-type antibody titer is high, there has been a tendency for the transplant to take hold without antibody-related rejection due to ABO preoperative desensitisation therapy. We will examine the current situation of ABO incompatible kidney transplants in Japan.

Results: In Japan, the 5-year and 10-year survival rates of ABO living donor renal transplantation since 2000 are 96.7% and 91.8%, respectively, and the 5-year and 10-year survival rates are 96.6% and 89.6% (death censored), respectively, which are comparable to blood group matched renal transplantation. In 2021, 547 (35.6%) of living donor kidneys and 105 (87.5%) of donor kidneys were matched for ABO compatibility, and 310 (20.2%) of living donor kidneys were matched for incompatibility. Incompatible transplants were performed in 449 (29.2%) of the living kidneys. In a tally of special treatments for the 449 ABO-incompatible transplant cases of living kidney, splenectomy was performed in 2 cases (0.4%), plasma exchange in 366 cases (81.5%), immunoadsorption in 14 cases (3.1%), and immunoglobulin use in 55 cases (12.2%). The mean preoperative blood group antibody titers ranged from 16 to 32 times higher than that for blood group incompatible renal transplantation. There was no significant difference in renal transplantation success rates according to preoperative blood group antibody titers.

Conclusions: ABO incompatible kidney transplantation is increasing every year in Japan, where there is a chronic donor shortage. The proportion of PEKT is particularly high and often between married couples. There is no significant difference in blood group incompatibility between matched and matched recipients since 2000. There is no significant difference in the live-implantation rate between compatible and incompatible blood groups since 2000.

PP_226 MICROVASCULAR ULTRASOUND ASSESSMENT OF CHRONIC HISTOLOGICAL LESIONS IN KIDNEY ALLOGRAFTS

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Background: Chronic histological changes contribute to allograft failure and are seen on allograft biopsies. Using super-resolution ultrasound microvascular imaging, known as ultrasound localization microscopy (ULM) to track microbubbles (MBs) super-resolved images are generated of the microvasculature using ultrasound could be used. This study aims to compare ULM for noninvasive visualization and quantification of microvessel structures in kidney transplants with histology from the gold standard allograft kidney biopsies.

Methods: In each 9 kidney transplant recipients at 4-years post transplant, a 2.4 ml bolus of Lumason MB suspension (Bracco Diagnostics Inc., Monroe Township, NJ, USA) was administered intravenously, followed by a saline flush. Ultrafast plane-wave compounding imaging was performed using a commercial ultrasound scanner acquired beamformed in-phase/quadrature (IQ) data at a frame rate of 346 Hz. Quantitative metrics, including microvascular density (MVD), mean flow velocity (mV), and perfusion index (PI = MVD × mV), were calculated and compared to histopathological findings from biopsies done on the same day

Results: Spatial resolution of kidney microvessels enabled visualization microvasculature (Figure 1). The microvascular images demonstrated differences in vascularity in kidney allografts with varying degrees of histological injury by Banff scores. Quantitative microvascular metrics(MVD and PI) distinguished between allografts with mild injuries (Banff score ci/ct ≤ 1) and moderate/severe injuries (Banff ci/ct ≥2, Figure 1). A strong correlation was shown ULM metrics (MVD and PI) and the maximum Banff score (MVD: R = -0.91; PI: R = -0.90) correlating with increased microvessel rarefaction and decreased perfusion in patients with more severe injuries. Repeated ULM measurements for each patient also demonstrated strong correlation (r > 0.89).

Conclusions: This pilot study demonstrates that quantitative metrics derived from ultrasound microvascular imaging can effectively differentiate allografts with varying degrees of chronic histological injury. These findings underscore the potential of ULM as a robust, noninvasive tool for detection and routine monitoring of microvascular dysfunction in kidney transplants.

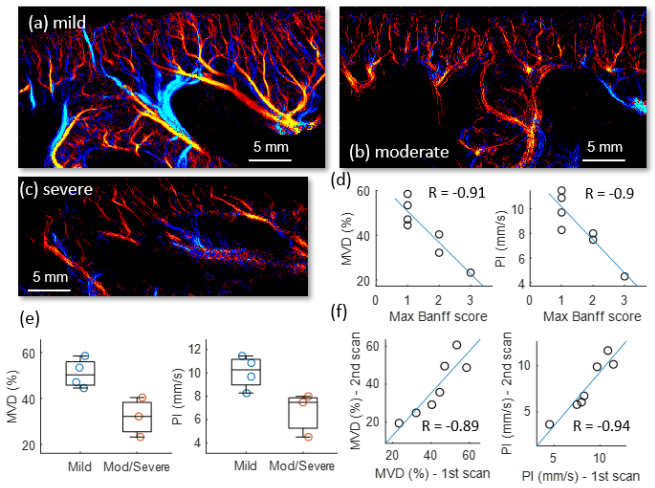

Figure 1.

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PP_227 TRABECULAR AND CORTICAL BONE LOSS POST TRANSPLANTATION: ASSOCIATION WITH EARLY BONE TURNOVER CHANGES

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Background: Bone loss and mineral abnormalities are common after kidney transplantation (KTx), increasing fracture risk and mortality. Traditional bone health assessments rely on biochemical markers of bone turnover and Dual-Energy X-ray Absorptiometry (DXA) to measure areal bone mineral density (aBMD). High-resolution peripheral quantitative computed tomography (HR-pQCT) provides additional insights into bone microarchitecture and volumetric bone density (vBMD) of cortical and trabecular compartments. This study evaluated bone turnover biomarkers, DXA, and HR-pQCT parameters over 1-year post-KTx, and assessed whether 3-month (3m) biomarker changes (Δdelta) predict 1-year (1yr) bone loss.

Methods: 75 patients were included in this prospective study (median age: 60.4 [52.1–65.8]), bone biomarkers (PTH, BALP, P1NP, TRAcP-5b, CTX, sclerostin) were measured at baseline (D0), 3m, and 1yr. DXA assessed aBMD at the lumbar spine (LS), hip, and radius, while HR-pQCT measured volumetric vBMD and bone microarchitecture at the distal radius and tibia.

Results: DXA revealed significant LS and femoral neck (FN) aBMD declines from D0 to 3m ($p < 0.03$), with partial LS recovery by 1yr. At 1yr, 30%, 29%, and 45% of patients showed significant bone loss at LS, FN, and ultradistal radius (UD) sites ($p<0.003$). HR-pQCT showed early declines in total (Tt) and trabecular (Tb) vBMD, as well as trabecular bone volume fraction (BV/TV) starting at 3m. Cortical (Ct) vBMD and cortical thickness (CtTh) also began declining at 3m, with significant reductions in all parameters by 1yr. Multivariate analysis identified ΔBALP at 3m as an independent predictor of LS loss at 1yr (OR 1.025; p=0.003). Baseline sclerostin predicted Ct vBMD loss (OR 5.651; p=0.01), and ΔBALP at 3m independently predicted Tt vBMD loss at 1yr (OR 1.283; p=0.0009).

Conclusion: Bone loss after KTx begins rapidly, with trabecular and cortical compartments significantly affected within 1yr. Early changes in biomarkers, particularly BALP and sclerostin, predict future bone loss, highlighting the importance of biomarker and imaging monitoring to identify high-risk patients and improve bone health outcomes.

Univariate analysis of parameters associated with decrease of BMD or HR-pQCT parameters over LSC

BMD loss at 1year over LSC cut off	Clinical and biological parameters	OR	Confidence interval		p–value
BMD lumbar spine loss ≥ 0.022 g/cm²	Delta 3m–D0 BALP	1.015	1.003	1.027	0.01
BMD total hip loss ≥ 0.027 g/cm²	Age	1.076	1.012	1.143	0.02
	PTH D0	0.994	0.988	1	0.04
BMD femoral neck loss ≥ 0.029 g/cm²	Native Vit D Prior Tx	0.189	0.061	0.587	0.004
BMD total radius loss ≥ 0.010 g/cm²	Age	1.068	1.015	1.124	0.01
	D0 CTX	0.999	0.999	1	0.04
	Delta 3m–D0 PTH	1.005	1.001	1.01	0.02
	Delta 3m–D0 CTX	1.001	1	1.001	0.03
	Delta 3m–D0 BALP	1.012	1.001	1.023	0.04
Total tibia vBMD loss ≥ 2%	BMI	1.132	1.008	1.272	0.04
	Delta 3m D0 BALP	1.131	1.024	1.248	0.02
Trabecular tibia vBMD ≥ 2%	Delta 3m D0 Calcium	0.027	0.001	0.582	0.02
Cortical radius vBMD ≥ 2%	BMI	1.174	1.039	1.325	0.01
	Active Vit D prior tx	4.371	1.171	16.311	0.03
	Sclerostin D0	2.727	1.144	6.499	0.02
	Delta 3m–D0 sclerostin	0.344	0.133	0.891	0.03
Cortical Thickness radius ≥ 2%	Delta 3m–D0 BALP	1.011	1	1.022	0.046
Cortical Porosity radius ≥ 2%	PTH D0	1.004	1.001	1.007	0.02
	P1NP D0	1.006	1	1.011	0.04
	Delta 3m–D0 P1NP	0.993	0.986	0.999	0.03

BALP: Bone alkaline phosphatase; BMI: body mass index; CTX: C–telopeptides; LSC: least significant changes; P1NP: Procollagen Type 1 N-Terminal Propeptide; PTH: parathyroid hormone; Tx: transplantation; Vit D: vitamin D

PP_228 PRE-TRANSPLANT SARCOPENIA AND ITS PROGRESSION POST-LIVER TRANSPLANT: IMPACT ON LONG-TERM SURVIVAL

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Background: Sarcopenia, defined as low skeletal muscle mass, is common in patients with end-stage liver disease (ESLD) awaiting liver transplantation (LT). It adversely affects survival both pre- and post-LT. While LT restores hepatic function, sarcopenia may persist or newly develop post-LT, increasing morbidity and mortality after LT. This study examines the long-term evolution of sarcopenia in LT recipients and its impact on survival and ICU/hospital stay.

Methods: This single-center retrospective cohort study analyzed 81 ESLD patients who underwent LT between 2009 and 2015. Sarcopenia was assessed by measuring the skeletal muscle mass index (SMI) via CT/MRI imaging at the L3 vertebral level pre- and post-LT, with follow-up extending up to 10 years. The pre-LT value was assessed at the time of listing for LT. Sarcopenia was defined by sex-specific thresholds (≤50cm²/m² for men, ≤39cm²/m² for women). Linear mixed models with restricted cubic splines assessed SMI changes, while the associations between pre-LT sarcopenia and clinical outcomes were analyzed using survival approaches (Cox model, Wilcoxon test, Fine & Gray model, Gray's) and Spearman correlations.

Results: Mean age at LT was 55±12 years; 53% of patients were male. Pre-LT, 61% were sarcopenic. No significant age difference was found between sarcopenic (54±12 years) and non-sarcopenic patients (55±12 years). Post-LT SMI declined early, partially recovered, and stabilized below baseline (Figure 1). Pre-LT sarcopenia was associated with reduced overall survival (Wilcoxon: p=0.016; Cox regression: HR 2.47, 95% CI 0.91-6.70, p=0.076) (Figure 2). Ten-year survival was 93% in non-sarcopenic patients versus 69% in sarcopenic patients. Sarcopenia did not significantly affect ICU/hospital stay.

Conclusions: Sarcopenia is highly prevalent among LT candidates and persists long-term, up to 10 years post-LT. Its association with reduced survival underscores the importance of routine sarcopenia assessment before LT. Targeted interventions such as physical rehabilitation and nutritional support may mitigate its impact on outcomes. Future research should focus on developing effective strategies to address sarcopenia and improve long-term health in LT recipients.

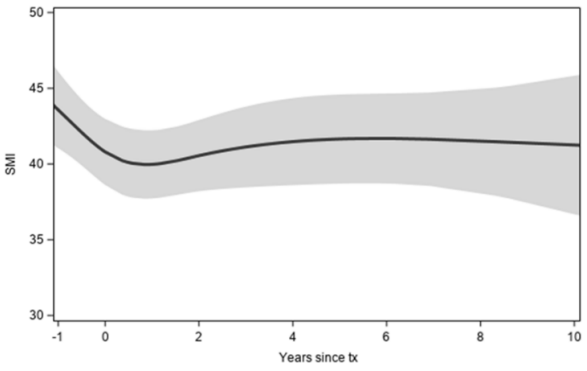

Figure 1. Longitudinal changes in SMI following LT.

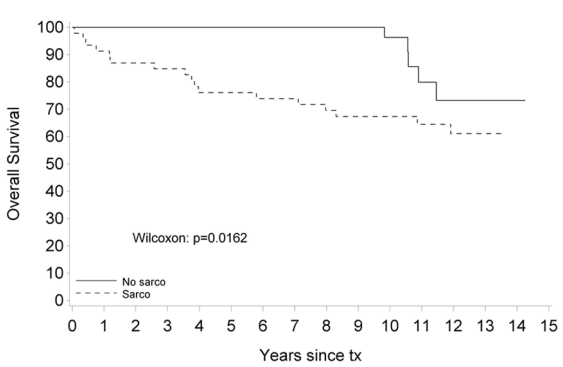

Figure 2. Kaplan-Meier survival curve showing the adverse impact of pre-LT sarcopenia on survival post-LT.

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Infectious diseases, malignancies & long term challenges

PP_229 IMPACT OF NUTRITIONAL STATUS AND BONE METABOLISM ON BONE FRACTURES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Previous studies reported that kidney transplant recipients (KTRs) had a higher risk of fracture than not only the general population but also patients on dialysis. The aim of this study is to investigate the roles of nutritional markers and bone metabolism–related serum biomarkers in fractures in KTRs.

Methods: We included 204 consecutive patients who underwent kidney transplantation at our institution and retrospectively reviewed their medical charts. The following nutritional markers were assessed: body mass index, Geriatric Nutritional Risk Index, Prognostic Nutritional Index, Controlling Nutritional Status, Nutritional Risk Index for Japanese Hemodialysis Patients, and Survival Index (SI). Additionally, bone metabolism-related serum biomarkers, including phosphorus, calcium, calcium phosphate product, intact parathyroid hormone (iPTH), alkaline phosphatase, hydroxyproline, 1,25-dihydroxyvitamin D, and osteocalcin, were evaluated. The cumulative incidence of fractures was investigated by focusing on nutritional markers and bone metabolism-related serum biomarkers.

Results: Fractures were found in 27 patients, and the regions of fractures included the hip (n=8), leg (n=8), arm (n=6), rib (n=4), and vertebrae (n=1). The age at surgery in the fracture group was significantly higher than that in the no-fracture group (P=0.018). Patients with fractures had a significantly higher risk of mortality than those without fractures (P=0.0018). The cumulative incidence of fractures was 4.6% at 1 year, 8.6% at 2 years, 12.3% at 3 years, and 15.5% at 5 years after the transplant during the median follow-up of 98 months. Multivariate analysis revealed that SI (a nutritional marker) <26.1 (HR 2.42; 95% CI, 1.14–5.16; P=0.022) and Serum iPTH level (a bone metabolism-related biomarker) ≥180 pg/mL (HR, 2.32; 95% CI, 1.01–5.30; P=0.046) were independently related to fractures.

Conclusions: Our findings suggest that nutritional status (SI) and bone-metabolism status (iPTH) may play important roles in determining the incidence of fractures in KTRs. Optimal management may be possible in clinical practice by stratifying the risk of fractures according to these markers. Further investigations are needed to establish the optimal strategy for fracture screening and monitoring in KTRs.

PP_230 URINARY METABOLOMICS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: End-stage kidney disease is optimally managed through kidney transplantation. However, the suboptimal function of the transplanted kidney can lead to imbalances in processes controlled by the kidneys, necessitating long-term monitoring of the graft's function and viability. Given the kidneys' high metabolic activity, a metabolomics approach is well-suited for tracking systematic changes in post-transplant patients and holds significant potential for monitoring graft function.

Methods: In this study, which follows the study on blood plasma, we analyzed morning and 24-hour urine samples from 55 patients who underwent primary kidney transplantation and were uniformly treated with immunosuppressants with a minimal follow-up of 50 months post-surgery. We assessed the relative levels of urinary metabolites detectable by NMR spectroscopy and investigated correlations between these metabolite levels and renal function.

Results: We observed rather unexpected independence of levels of urinary creatinine on serum creatinine as well as on allograft function expressed by eGFR. This observation allowed a very good agreement of outcomes from raw and creatinine-normalized data, consistent for both morning urine samples and 24-hour urine collections. The urinary levels of citrate and acetone were detected to be sensitive to allograft function, and the urinary levels of metabolites in combination showed promising prediction for kidney function, on the level of p-value: for 24 h pooled urine: 4.6×10^{-12} and morning urine: 5.36×10^{-9}.

Conclusions: Based on the results, we support the opinion of critical assessment of creatinine clearance when judging the filtration function of the allograft, where surely factors such as alterations in the tubular secretion of creatinine may play a particular role. As the next, urinary metabolomics can serve as an easily available supplement to prediction for allograft function in patients after kidney transplantation.

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PP_231 A QUALITY IMPROVEMENT PROGRAM IN MANAGEMENT OF KIDNEY TRANSPLANT DELAYED GRAFT FUNCTION

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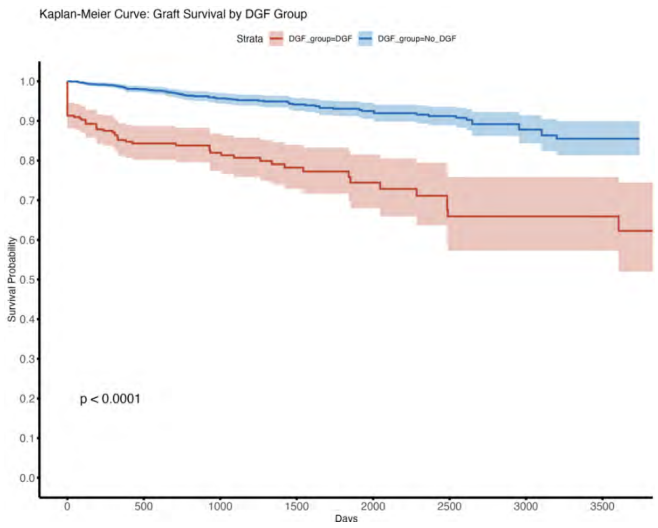
Background: Management of long delayed graft function (DGF) remains challenging due to heterogeneous pathophysiology and logistics. We developed a DGF protocol with dedicated clinics starting in April 2024.

Methods: This is a single-centre retrospective study of patients receiving both deceased and living donor kidney transplantation between 2007-2018. We determined factors associated with DGF duration, categorised as four groups (<14 days, 14-28 days, 29-90 days and >90 days). We studied the impact of DGF on death-censored graft function and patient survival. Finally, we performed a prospective pilot study (n=10, DGF lasting >28days) to see if the clinic improves outcomes.

Results: **Overview:** There were 299 (20%) recipients with DGF out of 1,509 transplants during the study period. Most patients had resolution of DGF by 14 days (n=211, 71%), while 13% (n=38) had resolution of DGF between 15-28 days and 16% (n=50) had DGF lasting >28days, out of which, 32 (67%) recipients had DGF lasting >90days. Of these, only 4 patients came off dialysis while 28 were declared primary non-function. **Baseline characteristics divided by DGF days**: With increasing number of DGF days, it was more common to see recipients being male, higher BMI and longer waiting time, while donors were older, higher donor risk index (DRI) and longer cold ischemic time. Multivariate analysis of donor and recipient factors associated with DGF were black recipients' ethnicity (1.81), higher DRI (0.72) and longer waiting time (<0.01). **Outcome of Survival**: Death-censored graft survival shows significant higher graft loss in DGF groups versus no DGF groups (Figure, p<0.01). On multivariate analysis, we observed DGF and male donor were associated with graft loss. Mean patient survival with DGF was significantly shorter (1,483 days) versus no DGF (1,903 days) (p<0.01). **Quality Improvement program and prospective pilot study**: We will describe the early result of our protocol in the newly started DGF clinic, where 7 out of 10 patients (DGF lasting >28days) successfully came off dialysis.

Conclusions: DGF is associated with significantly poor survival. Only 40% of patients who remain in DGF a month post-transplant recover function. Our pilot study suggests a dedicated DGF clinic may significantly improve the outcome of long DGF.



PP_232 CLINICAL PREDICTION MODELS IN ORGAN DONATION AND TRANSPLANTATION: THE GOOD, THE BAD, AND THE UGLY

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Background: Clinical prediction models for prognosis are an instrument of precision medicine to predict outcomes and support decision-making. Previous research criticized the quality of prediction models due to poor reporting and high risk of bias. How this applies to prediction models in organ donation and transplantation needs to be clarified. Therefore, this scoping review aimed to assess prediction models used in transplant centers in Switzerland and update clinicians on the transparency, quality of reporting, and risk of bias of these tools.

Methods: We used expert interviews and a survey with transplant clinicians to collect prediction models used in clinical practice in the context of organ donation and transplantation in Switzerland. We applied the reporting guideline for transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD+AI) and the prediction model risk of bias assessment tool (PROBAST). We performed a scoping review on whether prediction models were transparently reported, the risk of bias, and concerns regarding its applicability. The study had a registered study protocol (https://osf.io/ftxk8).

Results: Prediction models were named from kidney transplantation, liver transplantation, and intensive care. We identified a high risk of bias in several models due to unclear definitions of graft failure, lack of transparency in reporting outcome events, unjustified dichotomization of predictors, neglect of model calibration, and discrepancies between online calculators and published models.

Conclusions: The study highlights significant gaps in the transparency, reporting quality, and bias of clinical prediction models, potentially hindering graft survival predictions, donor eligibility, and resource allocation. Addressing these gaps with clear reporting and thorough validation is essential to improving outcomes and ensuring transplant practices meet high standards of precision medicine.

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PP_233 SPANISH EXPERIENCE WITH WEST NILE VIRUS:EPIDEMIOLOGY AND IMPLEMENTED MEASURES (2024)

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Background: West Nile virus (WNV) is transmitted by Culex mosquito bites to birds. In Europe, most of the cases are during the WNV circulation season, from June to November. There are well-documented cases of WNV transmission by organ transplantation.In Europe screening recommendations have been developed for donors in areas of high prevalence.

Methods: We describe our experience with the screening measures implemented in Spain to avoid the transmission through the organ transplantation for the 2024 WNV season.

Results: Every probable and confirmed WNV case is communicated by the CCAES and the National Epidemiological Surveillance Network to the Spanish National Transplant Organization. Once the first season case is confirmed the recommendations of the *Consensus Document of the Grupo de Estudio de la Infección en el Trasplante of the Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica and the Organización Nacional de Trasplantes on the Selection Criteria of Donors of Solid Organs in relation to Infectious Diseases* are applied. (Figure 1). The screening technique used for detection of viremia is by means of nucleic acid detection techniques with semi-automatic or automatic systems. The first case of WNV infection in 2024 was confirmed in April, before the beginning of the season. He was a boy with encephalitis in Sevilla(Andalucia region);the screening was implemented for every organ donors of this location. After,were affected, Huelva and Badajoz during the month of August. Caceres, Jaen, Cordoba and Cadiz in September. All of them are in the regions of Andalucia and Extremadura. At least 144 deceased organ donors were tested for WNV infection, most of them related with the province of Sevilla (n=68). The month with the highest number of WNV PCRs performed was October (n=32). Five deceased organs donors were contraindicated due to WNV clinical infection or PCR positive result, 4 in Sevilla and 1 in Caceres. There was no cases of WNV transmission through the transplant of organs.

Conclusions: WNV is already endemic in Spain and other European countries. Preventive measures and coordination among different departments are necessary in order to avoid the transmission of WNV infections through the organs transplanted, specially taking into account the severity of the infection in immunosuppressed patients.

For Deceased organ donors	For Living donors who have visited the affected area
Potential donors who have lived or visited the affected area within the 28 days prior to donation should be screened for WNV by RT-PCR.	Donation will be deferred for **28 days** after the return from that area.
Positive RT-PCR screening for WNV- Donation will not proceed	Otherwise, **screening by RT- PCR** must be performed
If there is no possibility to perform the RT-PCR screening, an individual risk assessment will be performed	

Figure 1-Preventive criteria applied

PP_234 DONOR-DERIVED CELL-FREE DNA TO MONITOR GRAFT INJURY AND ASSESS OUTCOMES IN KIDNEY TRANSPLANTATION

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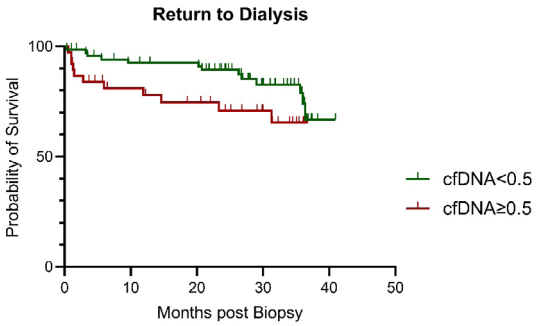
Background: We previously demonstrated that donor-derived cell-free DNA (dd-cfDNA) effectively discriminates active rejection, particularly antibody-mediated rejection, from other histopathological findings in kidney transplant recipients, supporting its utility in patient monitoring post-transplant (Benning et al., Transpl Int 2023). Elevated dd-cfDNA levels, however, are also observed in cases of non-rejection injuries, positioning it as a marker of general graft injury rather than a definitive diagnostic tool for specific causes.

Methods: To assess whether elevated dd-cfDNA predicts a greater risk of graft failure regardless of prior rejection diagnosis, we analyzed the clinical trajectories and outcomes of 106 kidney transplant recipients who underwent 108 allograft biopsies between November 2020 and December 2022. dd-cfDNA levels were measured at the time of biopsy, and patients were categorized into low-risk (<0.5%) and high-risk (≥0.5%) groups. Outcomes assessed included graft function over time, the need for additional biopsies, subsequent rejection diagnoses, return to dialysis, and patient survival.

Results: The median follow-up was 29.45 months (IQR: 20.98–35.6). Preliminary analysis indicates that among patients with dd-cfDNA levels <0.5%, 13/70 (18.6%) returned to dialysis, compared to 11 of 38 (28.9%) in the ≥0.5% group (*P*=0.24). Biopsy-proven rejection occurred in 6/70 (8.6%) patients in the low-risk group and 6/38 (15.8%) in the high-risk group (*P*=0.34). While these differences were not statistically significant, elevated dd-cfDNA levels were associated with a trend toward higher rejection rates and an increased likelihood of returning to dialysis (Figure 1), suggesting a potential link to greater graft dysfunction.

Conclusions: These findings underscore the potential of dd-cfDNA as a supplementary biomarker for monitoring kidney transplant recipients, enabling earlier detection of graft injury and enhancing clinical decision-making. Further investigation is required to confirm these trends and evaluate their clinical implications. De novo donor-specific antibody formation will also be evaluated in subsequent analyses.

Figure 1



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Infectious diseases, malignancies & long term challenges

PP_236 RISK FACTORS OF RENAL ARTERY STENOSIS AFTER KIDNEY TRANSPLANTATION: A META-ANALYSIS

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Background: Transplant Renal Artery Stenosis (TRAS) is a typical vascular complication that accounts for 75% of all vascular events following kidney transplantation. Post-transplant complications such as allograft dysfunction, allograft loss, and post-transplant hypertension have been attributed to transplant renal artery stenosis. This study aims to evaluate the risk factors related to TRAS after kidney transplantation.

Methods: A meta-analysis of studies that were published from inception until March 2023 was accomplished from the Science Direct and PubMed databases. Publications evaluating the prevalence of TRAS after kidney transplantation and assessing its risk factors were included in the study.

Results: Ten publications were included in the study. The incidence of TRAS was 1178 cases (2.84%) from 41,482 patients. Several variables relating to the occurrence of TRAS after kidney transplantation were examined. The variables that related to the development of TRAS were the history of hypertension [RR 1.07 (95% CI, 1.03-1.11), p = 0.0006, I^2 = 0%], diabetes mellitus [RR 1.16 (95% CI, 1.04-1.29), p = 0.007, I^2 = 24%], ischemic heart disease [RR 1.51 (95% CI, 1.26-1.82), p < 0.00001, I^2 = 0%], the incidence of DGF [OR 2.11 (95% CI, 1.31-3.38), p = 0.002, I^2 = 58%], high systolic [MD 10.98 (95% CI, 9.44-12.51), p < 0.00001, I^2 = 0%] and diastolic blood pressure [MD 7.64 (95% CI, 2.30-12.97), p = 0.005, I^2 = 85%], longer cold ischemia times [MD 4.40 (95% CI, 3.71-5.08), p < 0.00001, I^2 = 0%], and history of acute rejection [RR 1.84 (95% CI, 1.24-2.71), p = 0.002, I^2 = 0%]. While, variables that are not related to the development of TRAS including donor and recipient age, recipient gender and BMI, level of calcium, phosphorus, uric acid, and cholesterol, peak systolic velocity, CMV infection, smoking, number of hypertension drugs, the use of deceased donor and the duration of hemodialysis.

Conclusions: Several risk factors have been identified in the development of TRAS after kidney transplantation. However, further studies with large subjects are still needed to justify the findings in the recent study.

PP_238 CYTOMEGALOVIRUS INFECTION AND CORONARY ARTERY DISEASE IN LIVER TRANSPLANT RECIPIENTS

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Background: Cardiovascular disease contributes to a survival gap of liver transplant recipients compared to the general population. Positive cytomegalovirus (CMV) serostatus is associated with higher cardiovascular mortality in the general population. CMV reactivation and primary infections are common post-transplantation, but it is not known if they are associated with coronary artery disease (CAD). We aimed to determine if CMV DNAemia after liver transplantation is associated with subsequent CAD.

Methods: In the Danish Comorbidity in Liver Transplant Recipients (DACOLT) Study, we invited all liver transplant recipients in Denmark aged 20 or older for a cardiac computed tomography (CT). We included participants transplanted in 2011 and onward who were not retransplanted. We defined any calcified plaque as a coronary artery calcium score (CACS) >0, any stenosis as a maximum stenosis ≥1%, obstructive CAD as a maximum stenosis ≥50%, and extensive CAD as stenoses in >5 of 17 coronary artery segments. CMV surveillance followed a unified national protocol for a year after transplantation ensuring detection of subclinical CMV DNAemia.

Results: We included 247 liver transplant recipients, of whom 30% had CMV DNAemia after transplantation (Table 1). CMV DNAemia was not associated with any calcified plaque (OR 0.84 [95% CI: 0.49-1.46], P = 0.54), obstructive CAD (0.82 [0.29-2.28], 0.70), or extensive CAD (1.00 [0.40-2.50], 0.99). This was consistent after adjustment for traditional CAD risk (Pooled Cohorts Equation) and time since transplantation. Among those with any stenosis, 60% of those with CMV DNAemia had obstructive CAD compared to 45% without CMV DNAemia (Figure 1). However, this association did not reach statistical significance (1.87 [0.34-10.3], 0.47).

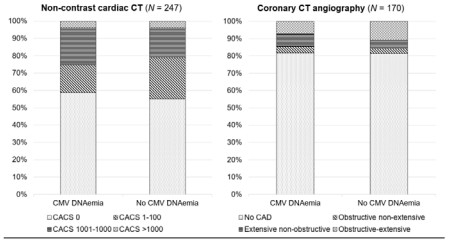
Conclusions: CMV DNAemia was not significantly associated with subsequent CAD in liver transplant recipients. Prospective studies are needed to assess if CMV infection is associated with plaque progression.

Table 1 Participant characteristics (*N* = 247)

Traditional cardiovascular risk factors	
Age, median years (IQR)	55 (47-62)
Male sex, n (%)	137 (56%)
Current smoking	28 (11%)
Hypertension	137 (56%)
Diabetes mellitus, n (%)	48 (19%)
Cytomegalovirus-related variables[a]	
CMV DNAemia after transplantation	75 (30%)
CMV disease after transplantation	28 (11%)
Positive recipient CMV serostatus	167 (68%)
Positive donor CMV serostatus	150 (61%)
Transplantation-related variable	
Years since transplantation, median (IQR)	4.2 (1.9-6.9)
Cause of transplantation	
Autoimmune liver disease	121 (49%)
Alcoholic or cryptogenic cirrhosis	52 (21%)
Hepatocellular carcinoma	21 (9%)
Fulminant hepatic failure	12 (5%)
Metabolic liver disease	10 (4%)
Hepatitis C virus	7 (3%)
Other	52 (21%)

CMV, cytomegalovirus. **IQR**, inter-quartile ratio. [a]Defined according to Ljungman et al., Clin Infect Dis. 2017; 64:87-91.

Figure 1 Coronary artery disease and cytomegalovirus DNAemia after transplantation



CAD, coronary artery disease categorised according to Fuchs A et al. Ann Intern Med. 2023; 176: 433-442. **CACS**, coronary artery calcium score using the Agatston method. **CMV**, cytomegalovirus. **CT**, computed tomography.

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PP_239 IS METABOLIC ACIDOSIS THE RISK FACTOR OF WORSE PROGNOSIS IN PATIENTS AFTER KIDNEY TRANSPLANTATION?

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Background: Metabolic acidosis (MA) frequently occurs in patients after kidney transplantation (KTx). Results of both experimental and clinical studies suggest that MA may contribute to faster progression of chronic kidney disease. Data on such relationship in KTx patients are limited. The aim of this clinical, single center, retrospective, observational study was to examine the relationship between MA and both patients' mortality and long term graft survival after KTx.

Methods: Blood [HCO_3^-] was measured in 486 patients (290 male; 196 female) aged 48.2±12.0 years at least one year after KTx and subsequently patients were observed up to 11 years. MA was defined at baseline of observation as the blood [HCO_3^-] concentration lower than 22 mmol/L.

Results: MA was diagnosed in 57 (12%) patients at baseline of follow-up. The Kaplan-Meier curves analysis have shown that patients with MA reach endpoints of follow-up earlier (log-rank p=0.002 for death and p<0.001 for dialysis or retransplantation and for cumulative endpoint p<0.001). In patients with MA the risk of starting dialysis therapy or retransplantation was significantly higher than in patients without MA [RR=2.00 (1.42-2.82), p<0.001]. In patients with MA the risk of death was significantly higher than in patients without MA [RR=1.61 (1.01-2.55), p=0.04]. The multivariable Cox regression analysis model has shown that baseline eGFR (HR=0.95 (0.94-0.97), p<0.001) and blood [HCO_3^-] (HR=0.92 (0.86-0.99), p=0.03) were negative predictors for initiation of dialysis therapy. Age (HR=1.09 (1.05-1.12), p<0.001) and diabetes mellitus (HR=2.12 (1.17-3.88), p=0.01) were positive predictors and blood [HCO_3^-] (HR=0.88 (0.81-0.97), p=0.009) was a negative predictor for death. Patients with metabolic acidosis were characterized by more pronounced eGFR loss in comparison to patients without metabolic acidosis (delta eGFR 3.4 vs. 2.4 ml./year/1.73 m^2, p=0.04).

Conclusions: 1. Metabolic acidosis is an important risk factor for increased mortality and progression of graft failure in kidney transplant patients 2. The prospective interventional studies with correction of MA will provide information whether treatment of MA improves the survival of both patients and transplanted kidneys.

PP_240 TORQUE TENO VIRAL LOADS DID NOT PREDICT SEVERE INFECTIONS IN STABLE KIDNEY TRANSPLANT RECIPIENTS

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Background: Torque teno virus (TTV) is a promising biomarker for immune monitoring and may be used to predict both infections and rejection early post-transplant. However, its role in stable kidney recipients (KTRs) beyond 1 year after transplantation is less clear.

Methods: This single-centre prospective cohort study included KTRs who are on stable immunosuppression for at least 3 months and had been followed up for at least 90 days. Baseline TTV viral loads clinical data and other biomarkers were collected upon recruitment. Primary outcome was severe infections defined as infections requiring hospitalization and secondary outcomes included biopsy-proven rejection (BPAR). Subjects were followed up until there was a change of immunosuppression.

Results: Of 165 recruited subjects, 151 with a median follow-up duration of 369 (interquartile range 303-443) days, were included (Table 1), of which 29 (17.8%) developed severe infections. Log transformed TTV viral loads (log TTV) were not associated with severe infections (odds ratio (OR) 1.21, 95% confidence interval (CI) 0.90-1.62, p=0.21), recurrent severe infections (OR 1.19, 95% CI 0.67-2.13, p=0.55) or time to severe infections (hazard ratio 1.20, 95% CI 0.93-1.56, p=0.17). Amongst the recruited patients, 25 patients underwent kidney allograft biopsy, of which 11 (44.0%) demonstrated BPAR. Log TTV was not associated with BPAR (OR 0.48, 95% CI 0.21-1.11, p=0.09), though patients with BPAR had lower log TTV compared to those without BPAR (4.79±0.86 copies/ml vs 5.76±1.48 copies/ml, p=0.05). On multivariable analysis (Table 1), log TTV was negatively associated with transplant vintage, absolute CD56 counts and cyclosporine-based and mTOR-inhibitor based regimens.

Conclusions: While TTV viral loads may be associated with clinical and laboratory factors related to degree of immunosuppression, they may not be able to predict admissions for infections and BPAR in stable prevalent KTRs.

Table 1. Univariable and multivariable analysis of factors associated with log transformed Torque teno virus viral load

Factor	Univariable analysis		Multivariable analysis	
	β coefficient (95% CI)	P value	β coefficient (95% CI)	P value
History of cirrhosis	2.80 (0.10, 5.51)	0.04		
Years since transplant	-0.02 (-0.03, -0.007)	0.003	-0.01 (-0.03, -0.002)	0.03
Tacrolimus-based regimens	0.80 (0.38, 1.22)	<0.001		
Cyclosporine-based regimens	-0.77 (-1.20, -0.33)	0.001	-0.74 (-1.18, -0.31)	0.001
mTOR inhibitor-based regimens	-0.90 (-1.70, -0.09)	0.03	-0.84 (-1.64, 0.05)	0.04
Absolute CD56 count	-0.001 (-0.002, -0.0002)	0.02	-0.001 (-0.002, -0.0001)	0.03

CI, confidence interval; mTOR, mammalian target of rapamycin

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Infectious diseases, malignancies & long term challenges

PP_241 CORONARY ARTERY CALCIUM SCORE PROGRESSION IN HEART TRANSPLANT PATIENTS

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Background: The coronary artery calcium score (CACS) is a well-established marker of coronary atherosclerosis with the absence of CAC indicating a low likelihood of obstructive coronary artery disease and a low risk of major adverse events. While CAC-scoring has been extensively studied in general populations, limited research has focused on its progression and clinical implications in heart transplant (HT) recipients. This pilot study aimed to evaluate the relationship between changes in CACS over time and clinical outcomes in HT recipients.

Methods: We included all adult HT recipients who underwent CT scans during annual checkup since 2018. Patients were categorized into 2 groups based on CACS over a 5-year follow-up period: (1) a stable CACS of 0 throughout follow-up and (2) any progression of CACS during follow-up period. Data on clinical outcomes (myocardial infarction (MI), percutaneous intervention (PCI) and death) during these 5 years were extracted from the electronic patient database and compared between the groups. Event rates were compared using the Chi-Squared Test and logistic regression was performed to evaluate the association between CACS progression and clinical outcomes.

Results: We included 103 HT patients (median age at transplant: 41 [IQR 22-52] years; 42 (41%) female). Median time between HT and first CT was 8 [IQR7-11] years. Of the total cohort, 49 (48%) patients were classified into group 1 and 54 (52%) patients into group 2. PCI was required in 1 (2%) patient in group 1 and 8 (15%) in group 2 (p=0.022). No patients experienced a MI. There was no difference in mortality between the groups (1 (2%) vs. 3 (5%) (p=0.356)). Patients in group 2 showed a marginally significant association with an increased likelihood of PCI, with an OR of 8.3 (95%CI 1.0-69.5, p=0.050).

Conclusion: CACS progression after HT is associated with a significantly higher likelihood of requiring PCI. No MIs were seen in both groups. There was no difference in mortality between patients with stable CACS and those with CACS progression during a five-year follow-up. These findings suggest that while CACS progression is linked to PCI, the impact on long-term clinical outcomes in HT patients remains unclear. The potential prognostic value of CACS as a possible therapeutic target post-HT needs further investigation.

PP_242 MANAGEMENT OF MULTI-DRUG RESISTANT ACINETOBACTER BAUMANNII INFECTION IN HEART TRANSPLANT RECIPIENTS

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Background: Acinetobacter baumannii (AB) is a Gram-negative, multi-drug resistant (MDR), nosocomial pathogen that causes ventilator-associated and bloodstream infections. It is particularly challenging in the early post-operative stages of heart transplants for intense immunosuppressant protocols and fragile conditions. We report the experience of our center in treating nosocomial MDR AB that provoked pneumonia and septic shock.

Methods: Eight heart transplant patients (7 males, 1 female; 46 ± 21 years, m ± SD) with positive hemocultures were included; 4 were in the ICU; 3 patients on mechanically ventilation, 1 required intubation; 3 patients were on extracorporeal membrane oxygenation (ECMO); 4 patients on continuous renal replacement therapy, 1 required it afterwards. 7 patients were already on antibiotics; the antibiotic protocol was antibiogram-based. Endotoxin blood level was measured with the Endotoxin Activity assay; if high (≥ 0.6 units) a cycle of Polymyxin B Hemoperfusion was performed; 6 patients were treated with iv Pentaglobin 0,25 g/Kg at 12 mL/h for 3 days, a solution containing 95 % immunoglobulins (IgG, IgM and IgA). 5 patients developed pancytopenia; we administered subcutaneous Filgrastim 48 MU for 3 days, an originator recombinant human granulocyte colony-stimulating factor. Immunosuppression was based on low dose of corticosteroids and tacrolimus serum levels were reduced to the lowest acceptable.

Results: Negative cultures were obtained after 14-45 days of therapy in all cases; antibiotics were suspended 20-30 days later. In every case we obtained normalization of leukocytes and flogosis, ECMO removal, independence from inotropes, respiratory weaning (3 patients after tracheostomy), recovering of renal function (no permanent treatment required). All patients are reported fine, leading an autonomous life 16 to 57 months after the events.

Conclusions: Management of MDR-AB is particularly challenging in heart transplant patients because of concomitant factors of fragility, such as recovering hemodynamics of the early transplant stages, and intense immunosuppressive strategies. The combined use of antibiogram-guided therapy, blood purification methods and modulation of immunosuppressants proved successful in managing these clinical scenarios.

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Infectious diseases, malignancies & long term challenges

PP_243 PERSISTENT FEVER IN A FORMER KIDNEY TRANSPLANT RECIPIENT: A CASE REPORT

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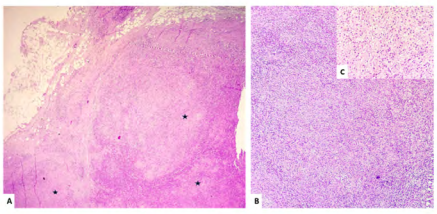
Background: An increased risk of lymph node pathology after transplantation has long been documented. The causes are varied posing a real challenge for differential diagnosis.

Methods: Commented clinical case

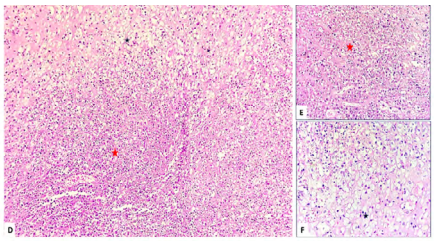
Results: We report our experience with a 30-year-old female patient who underwent kidney transplantation in 2006. She presented with nocturnal fever (38-39°C) and chills persisting for more than 15 days. Clinical examination was normal except for the presence of a hard, painful right inguinal lymphadenopathy. Investigations revealed lymphopenia at 580/mm³ and no evidence of CMV, BK virus, or EBV Infection. CT scan confirmed the presence of multiple inguinal lymphadenopathies. Histological examination of the full inguinal lymph node via excision biopsy, revealed disrupted follicular architecture with extensive inflammatory reaction, forming para-cortical nodules of variable size and shape extending to the cortex. These nodules were confluent, nearly destroying the lymph node, and composed of histiomonocytic cells, some small aggregates of foamy histiocytes, and large areas of non-tumoral, non-caseating necrosis rich in apoptotic bodies. Several diagnoses were considered, primarily infectious causes such as tuberculous lymphadenitis (endemic region), as well as neoplastic and immunological causes. However, they were excluded due to the absence of tuberculous markers, and normal infectious, neoplastic, and immunological workup. An Immuno-histochemical study showed reactive CD20, CD3, Bcl2, Ki67, and positive CD68, PS100 staining in clear nodules, with negative CD1a staining. The diagnosis of necrotizing histiocytic lymphadenitis, or Kikuchi-Fujimoto disease, was ultimately prioritised and confirmed based on the characteristic histological lesions. The inguinal localisation in this patient itypical, since the literature more commonly reports cervical involvement. The fever and lymphopenia resolved with symptomatic treatment alone (Antipyretic and antibiotics)

Conclusions: Necrotizing histiocytic lymphadenitis is a distinct clinico-pathological entity often described in Asia but rarely reported elsewhere. Definitive diagnosis is purely histological after ruling out other possibilities such as tuberculosis and tumoral proliferations.

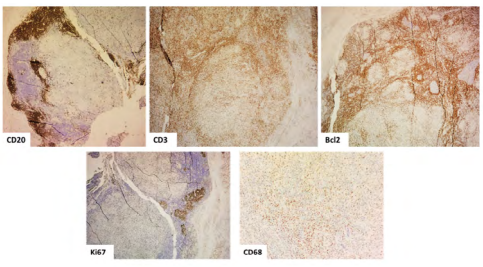
Note: Attached are photos of characteristic histological lesions of necrotizing histiocytic lymphadenitis.



Lymph node parenchyma, the site of an inflammatory reaction that almost completely erases the follicular architecture, made of light confluent clusters and nodules : black stars image **A** (HEx100).
The light nodules are composed of histio-monocytic cells: images **B** (HEx200) and **C** (HEx400).



Eosinophilic area of necrosis rich in apoptotic bodies: red stars images **D** (HEx200) and **E** (HEx400),
and some foamy histiocytes at the periphery of the necrosis: black stars images **D** (HEx200) and **F** (HEx400)



Reactive immunohistochemical profile (CD20, CD3 and Bcl2)
Low Ki67 in clear nodules, CD68-positive histiocytes in clear nodules

PP_244 PARENTHOOD AFTER KIDNEY AND LIVER TRANSPLANTATION: PERSPECTIVES FROM BOTH PARENTS AND THEIR CHILDREN

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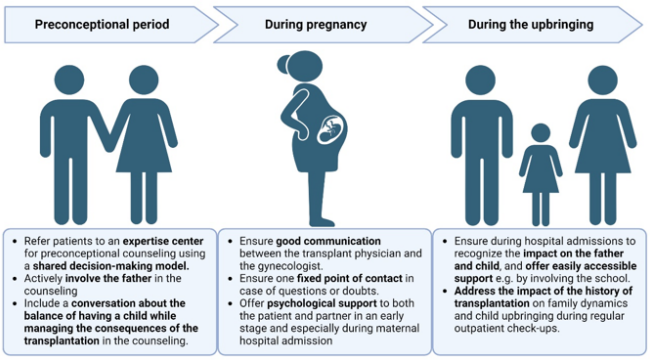
Background: To optimize care for families with a transplanted mother, it is important to understand perspectives of all family members. This study explored how both parents experienced the preconception and pregnancy period and how parents and their child(ren) experienced upbringing after transplantation, comparing families with a maternal kidney (KT) or liver (LT) transplantation.

Methods: This qualitative, single-center study used semi-structured online interviews and medical records from two groups with a post-transplantation pregnancy: a long-term group (children born ≥16 years ago, both parents and offspring interviewed) and a short-term group (children born 1-10 years ago, only parents interviewed). Interviews were transcribed and analyzed using inductive coding, thematic analysis and research triangulation.

Results: Twenty-eight interviews were conducted with 16 mothers (8 KT, 8 LT), 9 fathers and 4 children. During the preconception and pregnancy period parents emphasized the importance of consistent information, good communication and consideration of the emotional impact. Most families reported few daily limitations and considered themselves "like any other family". Some mothers experienced transplant-related impairments, and especially maternal hospital admissions caused anxiety in the children. Children reported more emotional struggles than parents realized. Fathers expressed more concerns than mothers. KT and LT families experiences were largely similar.

Conclusions: This first study on the perspectives of entire post-transplantation families reports favorable outcomes and gives important insights in how we can further optimize the care for post-transplantation families (Figure 1). Our findings suggest the need for improved communication and psychosocial support before and during pregnancy, ensuring that both parents feel supported and informed. During upbringing, some children struggled more than parents perceived and may have needed additional support.

Figure 1 : Suggestions for optimizing the care for post-transplantation families



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PP_246 MATURITY ONSET DIABETES OF THE YOUNG: AN UNDERAPPRECIATED CAUSE OF DIABETES IN ETHNICALLY DIVERSE WAITLIST CANDIDATES

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Background: Maturity Onset Diabetes of the Young (MODY) comprises 13 monogenic disorders which impair insulin secretion and affects 1-2% of all patients with diabetes. Diagnosis carries significant benefit for patients and affected family members, owing to implications for glycaemic strategies (including pancreas transplantation eligibility) and cascade testing. It may also be an important consideration in the setting of living donation. This study sought to investigate the prevalence of active waitlist (kidney and simultaneous pancreas-kidney) patients with possible unidentified MODY, who would be eligible for genetic testing in the UK.

Methods: 988 waitlist candidates at a large, ethnically diverse single centre were included. Electronic patient records were used to identify waitlisted patients eligible for genetic screening, according to NHS England National Genomic Test Directory testing criteria. This included the use of the Exeter diabetes MODY Calculator tool, which provides a MODY probability score.

Results: 369 (39.8%) patients with diabetes were identified, 342 (92.7%) and 27 (7.3%) on the kidney and pancreas waitlist respectively. 21 (5.7%) patients reached the threshold for MODY genetic testing: 19 (5.5%) and 2 (7.4%) on the kidney and pancreas waitlist. Only 1 (4.8%) patient had a confirmed MODY diagnosis. C-peptide and autoantibody tests were missing for another 9 patients, who would have otherwise qualified. Key differences between patients eligible for MODY screening and their counterparts are shown in Table 1.

Conclusions: Our findings suggest that the contribution of MODY towards advanced CKD may be greater than previously thought. It also provides valuable evidence towards prevalence in a largely non-white cohort. A diagnosis of MODY may have implications for the management of transplant candidates and potential donors, and should be considered where risk factors exist.

	MODY genetic testing eligible n = 21	MODY genetic testing ineligible n = 348
Age at diabetes diagnosis (years) (mean ± SD)	24.2 +/- 7.2	41.6 +/- 13.6
BMI (kg/m^2) (mean ± SD)	25.9 +/- 3.8	28.6 +/- 6.5
Non-white	100% (n = 21)	81.0% (n = 282)
Parent with diabetes	100% (n = 21)	40.5% (n = 141)
Insulin use	47.6% (n = 10)	53.7% (n = 187)

Table 1.

PP_247 THE IMPACT OF PULSE PRESSURE ON DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: Pulse pressure (PP) is a hemodynamic indicator associated with arterial stiffness. However, its role in kidney transplant remains unclear, especially in the context of living donor kidney transplantation (LDKT) versus deceased donor kidney transplantation (DDKT). This study aims to investigate the impact of PP and according to donor type in kidney transplant recipients.

Methods: Total 2,504 kidney transplant patients were analyzed between 2014 and 2022 from the Korea Organ Transplantation Registry database. PP was derived from systolic and diastolic blood pressure at 1-year post-transplantation. Patients were stratified into four groups based on PP and donor type: LDKT with normal/high PP, and DDKT with normal/high PP. Primary outcomes were graft loss and mortality over an 8-year follow-up.

Results: Only high PP with DDKT group represented markedly higher graft loss (HR 2.260, 95% CI 1.183-4.317, p=0.014) and mortality (HR 2.202, 95% CI 1.098-4.417, p=0.026). Conversely, other groups showed no notable differences in graft loss or mortality. Moreover, high PP with DDKT group maintained consistently lower estimated glomerular filtration rates throughout the 5-year follow-up period. Also, DDKT group exhibited significantly higher PP compared to the LDKT group at 1-year post-transplantation, with a higher prevalence of high PP (>60 mmHg) in DDKT.

Conclusions: In DDKT, elevated PP is associated with inferior graft survival and increased mortality rates, whereas LDKT recipients show a lesser susceptibility to the effects of PP. When considering higher prevalence and impact of elevated PP in DDKT, it essentially should be considered a crucial risk factor in DDKT.

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PP_248 IMPACT OF LIPID LOWERING THERAPIES ON HEART TRANSPLANT RECIPIENTS: A SINGLE CENTRE EXPERIENCE

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[1]Azienda Ospedale Università Padova; Cardiac Surgery Unit; Department of Cardio-Thoracic-Vascular Sciences and Public Health, [2]Padova University Hospital; Cardiac Surgery; Department of Cardio- Thoracic Vascular Sciences and Public Health, [3]Padova University Hospital; Cardiac Surgery; Department of Cardiac, Thoracic and Vascular Sciences and Public Health, [4]Padua University Hospital; Cardiac Surgery; Department of Cardiac Thoracic Vascular Sciences and Public Health, [5]Hospital University of Padova; University Hospital of Padova; Department of Cardio-Thoracic-Vascular Sciences and Public Health, [6]Padova University Hospital; Cardiac Surgery; Department of Cardio-Thoracic-Vascular Sciences and Public Health, [7]Cardiac Surgery Unit; Padova University Hospital; Department of Cardio-Thoracic-Vascular Sciences and Public Health, [8]University of Padova; Padova University Hospital; Department of Cardio-Thoracic-Vascular Sciences and Public Health

Background: Statin therapy up-titration is hindered in heart-transplant (HTx) recipients due to concern for pharmacological interactions and side effects. Alternative lipid lowering therapies (LLT) are now available for patients who are poorly tolerant to statins or those with significant dyslipidaemia despite maximal dose statin treatment and dietary advice. Elevated lipoprotein (a) [Lp (a) is an independent causal risk factor for cardiovascular disease, but its association with HTx outcomes has not been firmly established. The aim of the study was to analyse the lipid status of HTx patients following the recent adoption of novel LLT and investigate the possible correlation of Lp (a) levels and cardiac allograft vasculopathy (CAV).

Methods: A retrospective observational cohort study including adult patients who underwent HTx between 2012-2023, under follow up in a tertiary centre. Lipid profile, prevalence of statin and other lipid lowering drugs prescription were assessed at 2024 follow up and compared to same data measured previously in 2020/2021. Lp (a) was included in lipid profile in 2024.We also evaluated the presence of moderate and severe cardiac allograft vasculopathy (ISHLT CAV 2-3) detected by either coronary angiography or coronary computer tomography angiography.

Results: Two hundred thirty patients were included. Patients' characteristics and lipid status are shown in Table 1. While the proportion of statin therapy prescription did not significantly change with follow up, the prescription of ezetimibe increased, and PCSK9 inhibitors and bempedoic acid were adopted. LDL levels for paired values were significantly lower at the 2024 follow up compared to the previous assessment (p=0.003). Serum Lp (a) concentrations [median 39 (14.00-139.25) nmol/l] were available in 154 participants. 19 patients displayed evidence of CAV 2-3. Mean Lp (a) levels did not differ between patients with CAV 0-1 and patients with CAV 2-3 [37 (13-147.4) vs 42.5 (18-70.5); p=0.736]. The single independent predictor of CAV 2-3 in this cohort was ischemic cardiomyopathy prior to HTx (p=0.036, OR 5.115).

Conclusions: Increased adoption of non-statin LLT was associated with achievement of LDL levels suggested by ISHLT guidelines for general HTx population. The role of Lp (a) levels in HTx outcomes merits further study.

Table 1. Patients' clinical data, lipid status and lipid lowering treatments

Patient characteristics		
Age (years)	57 (47-63)	
Gender (male)	170 (74%)	
LVEF (%)	62 (57-67)	
GFR (ml/min/1,73 m²)	50,5 (37,00-64,25)	
CKD grade ≥ 4	33 (14%)	
Dialytic therapy	11 (4,8%)	
Pre-transplant history		
Dyslipidaemia	83 (36%)	
Hypertension	88 (33%)	
Type 2 Diabetes mellitus	37 (16%)	
Obesity	23 (10%)	
Smoking	76 (33%)	
Ischemic cardiomiopathy	79 (34%)	
Post-transplant history		
Ciclosporin/tacrolimus	206 (91%)/20 (8.8%)	
MMF/everolimus/azathioprine	145 (64%)/52 (23%)/9(4%)	
Corticosteroids *	41 (18%)	
Cellular rejection ≥ ISHLT 3 *	6 (2.7%)	
Humoral rejection ≥pAMR2 *	4 (1.8%)	
CAV 2-3	19 (8.3%)	
Time to CAV 2-3 (years)	3 (1-4.5)	
Lipid lowering therapy	**2020/2021**	**2024**
Statins	124 (64%)	155 (68%)
Ezetimibe	15 (7.7%)	68 (30%)
PCSK9i	0	6 (2.7%)
Bempedoic acid	0	3 (1.3%)
Omega 3 PUFA	34 (17%)	49 (22%)
Lipid status		
Total cholesterol	184 (167-211)	176 (134-194.5)
LDL (mg/dl)	110 (93-134)	95 (73-116)
TG (mg/dl)	112 (73.50-169.00)	113 (85-157.5)
Lp (a) (nmol/l)		39 (14-139.25)

Legend: *=>1 year after heart transplantation, LVEF= left ventricle ejection fraction, GFR= glomerular filtration, CKD= chronic kidney disease, CAV= cardiac allograft vasculopathy, PCSK9i= PCSK9 inhibitors, PUFA= polyunsaturated fatty acids

PP_249 GLOMERULITIS AND INTERSTITIAL FIBROSIS IN KIDNEY TRANSPLANTS ARE ASSOCIATED WITH CARDIOVASCULAR RISK

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Background: Graft rejection has been linked to cardiovascular risk in epidemiological studies in kidney transplantation, which may result from the pathophysiological link between renal inflammation and cardiovascular events. However, data on the association between histological lesions observed in graft biopsies and cardiovascular risk are lacking.

Methods: We included kidney transplant recipients who underwent kidney allograft biopsy between 1 and 12 months post-transplant, from 2008 to 2022, using data from the ASTRE database and the local database of Strasbourg University Hospital. Our objective was to describe, using a Cox model, the association of renal histological lesions according to the 2022 Banff classification with the occurrence of major cardiovascular events (MACE).

Results: We included 3,153 patients who underwent kidney allograft biopsy within the first year post-transplant, of whom 9.1% (N=287) experienced a MACE, with a median occurrence of 1 year. In univariate analysis, interstitial infiltrates (i), tubulitis (t), glomerulitis (g), interstitial fibrosis (ci), and chronic vascular lesions (cv) were associated with the occurrence of cardiovascular events. In multivariate analysis, after adjusting for recipient age, donor type, renal function at the time of biopsy, cardiovascular history and risk factors, and pre-transplant dialysis duration, three histological lesions were associated with MACE: g (Hazard ratio 1.59, 95% Confidence Interval 1.26-2.00), ci (HR 1.63, CI 1.18-2.24) and cv (HR 1.19, CI 1.00-1.42). Univariate analysis of the Strasbourg cohort (N=479) showed that microcirculation inflammation without DSA (HR 2.33, 95% CI 1.15–4.71) and BK virus nephropathy (HR 2.57, 95% CI 1.30–5.08) were the most strongly associated with MACE.

Conclusions: Glomerulitis, interstitial fibrosis, and chronic vascular lesions are independently associated with an increased cardiovascular risk when identified in kidney graft biopsies during the first year post-transplantation. This raises the question of a potential relationship within the framework of cardiorenal interactions. However, certain confounding factors must be considered, including long-term decline in renal function and adjustments to immunosuppressive therapy.

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PP_250 COMPARATIVE ANALYSIS OF NGS AND DDPCR FOR DD-CFDNA QUANTIFICATION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Donor-derived cell-free DNA (dd-cfDNA) has been demonstrated to reflect graft injury, aid in risk stratification, evaluate responses to anti-rejection therapy, and assist in the timing of re-biopsies post transplantation. Despite substantial evidence supporting its utility, widespread clinical adoption in Europe has been hindered by uncertainties regarding optimal testing strategies and the associated costs. While various dd-cfDNA assays are available, comparative data across these assays remain limited.

Methods: In this analysis, dd-cfDNA was quantified in a cohort of 96 kidney transplant recipients with indication biopsies using two commercially available assays. Both assays use predefined bi-allelic single nucleotide polymorphisms (SNPs). Assay1 (AlloSeq, CareDx) tests 202 SNPs on a next generation sequencing platform, whereas Assay2 (GraftAssure, Oncocyte) determines 48 SNPs with last generation droplet digital PCR (ddPCR). The lower limit of quantification according to the manufacturers is 0.23% (Assay1) and 0.04% (Assay2).

Results: Overall, there was no difference between the two assays (*P*=0.35), with consistent results across all BANFF-defined biopsy categories. The regression showed no deviation from the line of identity [Assay2 = 1.0xAssay1 (CI: 0.95–1.13) -0.01 (-0.04–0.012)] with a Pearson's r of 0.96. Using pre-defined cut-offs of 0.57%[1] and 0.5%, the agreement was 95% and 93%, respectively. Notably, dd-cfDNA levels were highest in patients with antibody-mediated rejection, with both assays yielding comparable results (Assay1: mean 1.85 ± SD 1.33 vs. Assay2: mean 1.90 ± SD 1.33; *P*=0.98).

Conclusions: This is the first direct comparison of two different commercially available test kits, based on NGS or ddPCR. The results demonstrate equivalency between dd-cfDNA levels measured by the two different test kits. The comparable performance of these two assays underscores their reliability in dd-cfDNA quantification and supports their integration into routine transplant care, with this comparative analysis serving as a step towards a broader clinical implementation.

Benning L et al. Donor-Derived Cell-Free DNA (dd-cfDNA) in Kidney Transplant Recipients With Indication Biopsy-Results of a Prospective Single-Center Trial. Transpl Int. 2023, 36:11899.

PP_251 BKPYV-SPECIFIC CD8 HYPORESPONSIVENESS IS ASSOCIATED WITH THE INHIBITORY RECEPTOR NKG2A IN BKPYVAN

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Background: BK virus (BKPyV) reactivation is a major complication in kidney transplantation affecting #40% of kidney transplant recipients (KTR) and is associated with graft loss. BKPyV-specific CD8 T lymphocytes (BKPyV-LT-CD8) play a crucial role in BKPyV control. BKPyV-LT-CD8 exhaustion is associated with the development of BKPyVAN.

Methods: To investigate this specific alteration of BKPyV-LT-CD8, we have compared them to the functionality of matched EBV-LT-CD8. Then we carried out a transcriptomic study on a cohort of 17 KTR comparing BKPyV-LT-CD8 with EBV-LT-CD8 from peripheral blood.

Results: Compared with EBV-LT-CD8, BKPyV-LT-CD8 exhibited lower functionalities in patients with BKPyVAN. We identified that these cells are overexpressing NKG2A transcripts compared with EBV-LT-CD8 cells, a membrane receptor expressed by NK lymphocytes and some LT-CD8. In an in-silico transcriptomics study (public data GSE47199) of renal biopsies (stable vs BKPyVAN), we also showed the overexpression of NKG2A in BKPyVAN. We confirmed transcriptomic data by immunohistochemistry and showed infiltration of LT CD8+ NKG2A+ cells in BKPyVAN biopsies. NKG2A+cells ($p<0.0087$) as well as NKG2A+ CD8 cells ($p<0.0043$) were more frequently observed in BKPyVAN than in control kidneys. In addition, we characterized the expression of HLA-E, the ligand of NKG2A which inhibits the cytotoxic functions of NK and CD8-LT cells. HLA-E was more frequently observed on BKPyVAN biopsies compared with normal kidneys ($p<0.044$).

Conclusions: Our results showed that NKG2A is overexpressed in circulating BKPyV-LT-CD8 and NKG2A/HLA-E are detected in renal biopsy of patients with BKPyVAN suggesting an important role of the pathway in the development of BKPyVAN.

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PP_252 AORTIC ANEURYSMS AND AORTIC ECSTASIA IN LIVER TRANSPLANT RECIPIENTS

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Background: Cardiovascular diseases are a major cause of morbidity and mortality among liver transplant recipients (LTx recipients), but the burden of aortic aneurysms (AA) is unknown. This study aimed to determine the prevalence of AA and the mean aortic diameter in LTx recipients and population controls using contrast-enhanced standard CT. Furthermore, we aimed to identify associated risk factors.

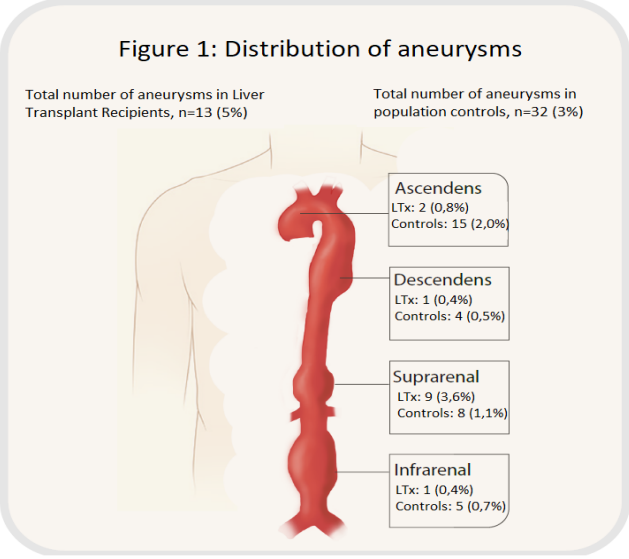
Methods: In this cross-sectional study, participants from the Danish Comorbidity in Liver Transplant Recipients (DACOLT) study and matched controls from the Copenhagen General Population Study (CGPS) underwent gold standard contrast-enhanced CT-scans of the thorax and abdomen. Aortic aneurysms, aortic diameter and aortic wall thickness were measured. Logistic and linear regression models adjusted for age, sex, traditional and transplantation-specific risk factors were analyzed.

Results: We included 253 LTx recipients and 759 matched population controls, clinical characteristics are shown in Table 1. The overall prevalence of AA was 5% in LTx recipients and 3% in controls (P = 0.38). For distribution of aneurysms, see Figure 1. Living with a transplanted liver was borderline associated with higher odds of overall AA (adjusted odds ratio (aOR) 2.12; P = 0.06), and associated with suprarenal AA (aOR 5.77, 95% CI 1.90–18.28; P < 0.01). Furthermore, living with a transplanted liver was associated with aortic ectasia (aOR 1.67, 95% CI 1.03–2.65; P = 0.03) and with greater aortic wall thickness (0.2 mm; 95% CI 0.1–0.2; P < 0.01). Risk factors associated with AA in LTx recipients included hypertension (aOR 2.13, 95% CI 1.03–4.54; P = 0.04) and re-transplantation (aOR 11.45 (95% CI 2.25¬–61.35; P < 0.01).

Conclusions: LTx recipients had higher odds of suprarenal AA and aortic ectasia than population controls. Thus, increased awareness of AA in LTx recipients may be needed and longitudinal studies should clarify risk factors for aortic pathology progression in LTx recipients.

Table and Figures:

Clinical characteristics	LTx recipients (N=253)	Controls (N=759)
Age, median (IQR)	54 (43–63)	54 (45–63)
Male sex, % (n)	59.3 (150)	69.3 (526)
BMI, median IQR)	26.7 (24.1–29.7)	25.3 (23.3–27.8)
Smoking, pack years, median (IQR)	0 (0–5)	0 (0–12)
Never smoker	147 (60)	383 (51)
Current smoker	25 (10)	96 (13)
Previous smoker	74 (30)	280 (37)
Hypertension, % (n)	24 (60)	45 (338)
DM, % (n)	19 (48)	1 (9)
Dyslipidemia, % (n)	47 (110)	61 (462)
Transplant related data	**LTx recipients (N=253)**	
Time since transplantation, years, median (IQR)	10.1 (6–16)	
Cause of transplantation, % (n)		
Autoimmune liver disease	51 (130)	
Alcoholic and cryptogenic cirrhosis	16 (41)	
Cancer (hepatocellular carcinoma)	3 (9)	
Fulminant hepatic failure	7 (18)	
Metabolic liver disease	4 (10)	
Hepatitis B or C	2 (5)	
Calcineurin inhibitor, % (n)		
Tacrolimus	81 (206)	



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Infectious diseases, malignancies & long term challenges

PP_255 LONG-TERM SURVIVAL AND RECURRENCE IN HCC VS. NON-HCC LIVER TRANSPLANT: A TWO DECADE ANALYSIS

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Background: we aim to compare the long-term survival outcomes of patients who have received liver transplants as a result of primary hepatocellular carcinoma (HCC).

Methods: A retrospective registry analysis of SRTR database was done for liver transplants that were performed in the United States from January 2000 to June 2023.

Results: A total of 143717 liver transplant (LT) cases have met both the inclusion and the exclusion criteria and were included in the final analysis. The most common primary diagnosis in the non-HCC cohort were hepatitis C virus (HCV) (14813 cases, 27%), and alcoholic cirrhosis (6631 cases, 12.1%) in the 2001-2010 cohort, and alcoholic cirrhosis (18370 cases, 20.7%), and non-alcoholic steatohepatitis (NASH) (13997 cases,15.8%) in the 2011-2023 cohort. The allograft survival difference became more significant after the 5 years of follow-up with a 10% difference between the two timeframes in both HCC and non-HCC groups. Patients who met and were selected based on Milan's criteria had significantly better outcomes in both cohorts. Five-year allograft and patient survival were also significantly higher in the patients who met Milan's criteria in 2011-2023 cohort, compared to 2001-2010 cohort (74.4% vs. 66.1%, P-value <0.001, and 76% vs. 68.7%, P-value <0.01, respectively). Acute and chronic rejections were significantly higher in the non-HCC groups in both timeframes. It was 6.5% vs. 4.8%, P=0.03 in 2001-2010, and 13.6% vs. 8.2%, P=0.0007 in 2011-2023, for acute rejection and 10.8% vs. 6.7%, P=0.0001 in 2001-2010, and 14.1% vs. 10.3%, P=0.01 in 2011-2023, for chronic rejection.

Conclusions: Short- and long-term outcomes of HCC liver transplant is almost equal to the other causes of liver transplantation in the recent decade, which can significantly overcome the dilemma of doing liver transplant in patients with HCC diagnosis.

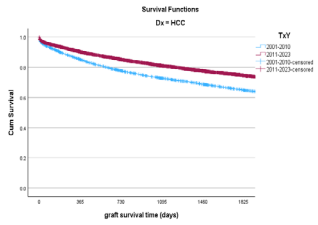

Figure 1. Graft survival rate for HCC patients comparison between the 2000-2010 and 2011-2023 groups (p<0.001)

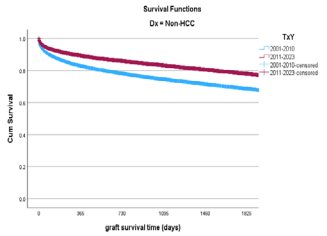

Figure 1. Graft survival rate for non-HCC patients comparison between the 2000-2010 and 2011-2023 groups (p<0.001)

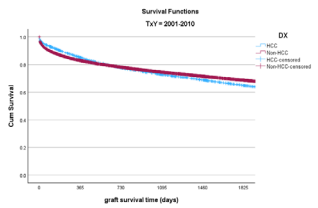

Figure 1. Graft Survival rate comparison between non-HCC and HCC patients in the 2001-2010 group (p<0.001)

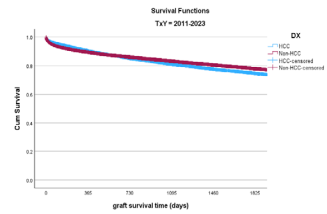

Figure 1. Graft Survival rate comparison between non-HCC and HCC patients in the 2010-2023 group (p<0.001)

PP_256 CARDIO-RENAL PROTECTION OF SGLTI VS. DPP4I IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS

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Background: Diabetes is the most common cause of chronic kidney disease (CKD) globally. The renal and cardio-vascular benefits of the new anti-diabetic agents are not assessed comprehensively. We aimed to evaluate the short term renal and cardio-protective effects of Sodium-Glucose Cotransporter-2 Inhibition (SGLT2i) Vs. Dipeptidyl peptidase-4 Inhibition (DPP4i) among diabetic kidney transplant recipients.

Patients and methods: In this observational trial, 222 diabetic kidney transplants recipients (NODAT or type 2 diabetes) were enrolled and were categorized into two groups. Group 1 (n=99) received SGLT2i while group 2(n=123) received DPP4i as an add on antidiabetic medications. All patients in the two groups were followed up for 12 months.

Results: Most patients in the two groups (1&2) were men (59.6 vs. 61.7%, p=0.73) in their middle age (58.5±11.9 vs. 54.4±12.9, p=0.016) years respectively. The two groups were matched regarding their demographics especially the type of donor, type of immunosuppression (induction or maintenance), number of cardiovascular events before enrollment in the study and the number of patients who were maintained on ACEi or ARB(p>0.05). The minority of patients were smokers (12.9 vs.8.7%), and chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% in the two groups, respectively. Most of the enrolled patients (72.8 vs. 78.6%) underwent hemodialysis pre-transplant. During follow up period, patients in both groups were comparable regarding mean blood pressure, body weight, HbA1C, 24-hour urine protein, and graft function (represented by the mean serum creatinine) at different time intervals and compared to base line values(p>0.05). However, the mean HbA1C was significantly higher in group 1 during the whole follow up period of the study (p<0.05) but it did not drop significantly compared to baseline values (p>0.05). We did not report any macroangiopathic events (cerebral stroke, acute myocardial infection, or peripheral arterial disease) in the two groups during the study.

Conclusion: Both GLT2i and DPP-4 I are comparable regarding renal and cardio-vascular protection among diabetic kidney transplant recipients.

Keywords: DM, renal protection, kidney transplant

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Infectious diseases, malignancies & long term challenges

PP_257 TRANSPLANTATION OF ORGANS FROM DONORS DIAGNOSED WITH AMIOTHROPHIC LATERAL SCLEROSIS

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Background: Patients with ALS (Amiotrophical Lateral Sclerosis) frequently die in circumstances of death which are consistent with organ donation. Because the pathogenesis of ALS is not fully understood and the lack of specific treatment, there have been concerns about the safety of the clinical use of organs obtained from donors diagnosed with this disease. The aim of the present study is to describe the outcomes of recipients of deceased organ donors diagnosed with ALS.

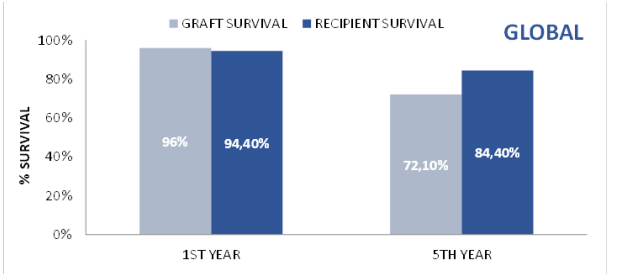
Methods: This is a multicenter countrywide prospective study performed in which one we analyzed the demographic and clinical characteristics of deceased organ donors diagnosed with ALS, and the baseline features and outcomes of recipients of their organs from 1 January 2013 to 31 December 2022. We have used the statistical package IBM® SPSS®Statistics version 25.

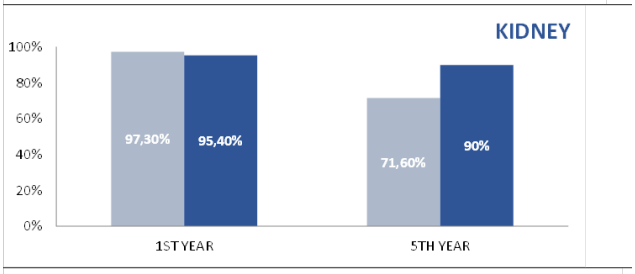
Results: During the study period, 175 actual donors with a diagnosis of ALS were registered in Spain, of whom 167 transitioned to utilized deceased organ donors, with 508 organs transplanted into 455 recipients. Follow-up information was obtained from the 455 recipients(100%). Utilized donors were 167(60%) males, with a mean age of 59(SD=9) years. Most donors (134;80%) died following the decision not to initiate or continue life-supporting therapies that were required for the management of their disease. Other causes of death were MAiD(15;9%), anoxic encephalopathy following a cardiac arrest(12;8%), stroke(2;1%), trauma(2;1%) and death caused by other events(2;1%). Consequently, in the majority of cases(161;96%) death was determined by circulatory criteria, while in 6(4%) death was determined by neurological criteria. Baseline features and outcomes of recipients of organs obtained from donors diagnosed with ALS are detailed in Table and figure1.

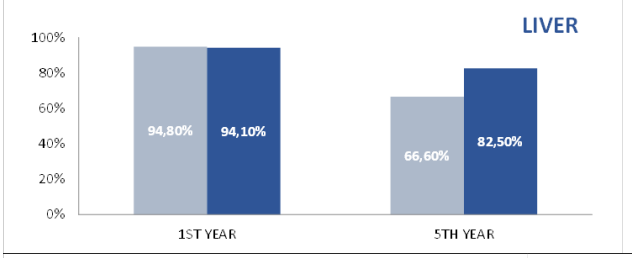
Conclusions: No adverse reaction has been reported derived from the donor condition so, the preliminary results of this Spanish experience seem to confirm the safety in the transplantation of organs from donors with ALS.

Table 1: Baseline demographics and clinical features, and outcomes of recipients of organs obtained from deceased organ donors with a diagnosis of ALS

	KIDNEY N=264	LIVER N=122	HEART N=6	LUNG N=55	PANCREAS-KIDNEY N=6	LIVER-KIDNEY N=2	TOTAL N=455
Age in years, median (IQR)	57(50-66) Media 57 DE 13	60(53-64) Media 57 DE 10	55(50-65) Media 56 DE 8	61(52-65) Media 58 De 10	44(33-53) Media 43 DE 11	Media 61 DE 3	60 Media 57 DE 12
Sex male, n (%)	166 (63%)	85 (70%)	3 (50%)	35 (64%)	1 (17%)	2 (100%)	292 (64%)
History of previous transplant, n (%)	12 (5%)	2 (1%)	0 (0%)	0 (0%)	2 (33%)	0 (0%)	16(4%)
Urgency status, n (%)	0	12 (10%)	2 (33%)	7 (13%)	0	0	21(5%)
Follow-up in months, median (IQR)	26 (IQR 20-31)	24 (IQR 15-31)	14 (IQR 12-27)	24 (IQR 12-33)	24 (IQR 18-30)	17	24 (IQR 17-31)
Graft loss, n (%)	30 (11%)	13 (11%)	0 (0%)	11 (20%)	2 (33%)	0 (0%)	56(12%)
Cause of graft loss							
Primary non-function	13(5%)	3(3%)		1(2%)	1(17%)		18(4%)
Surgical complications	2(1%)	2(2%)		1(2%)	1(17%)		6(1%)
Acute Rejection	4(2%)	-		-			4(0.8%)
Chronic allograft dysfunction	8(3%)	4(3%)		7(13%)			19(4%)
Death with a functioning graft	3(1%)	3(3%)		2(4%)			8(2%)
Unknown	-	1(1%)		-			1
Patient death, n(%)	18 (7%)	17 (14%)	2 (33%)	12 (22%)	0 (0%)	1 (50%)	50 (11%)
Cause of patient death							
Infection	7(3%)	3(3%)	-	2(4%)			12(3%)
Cardiovascular	1(0.4%)	2(2%)	2(33%)	-			5(1%)
Neoplasia	2(0.8%)	4(3%)	-	1(2%)			7(2)
Graft loss	-	1(1%)	-	5(9%)			6(1.3%)
Cerebrovascular	1(0.4%)	-	-	-			1(0.2%)
Other	6(2%)	7(6%)	-	4(7%)		1(50%)	18(4%)
Unknown	1(0.05%)	-	-	-			1(0.02%)
Adverse reaction, n (%)	0	0	0	0	0	0	0







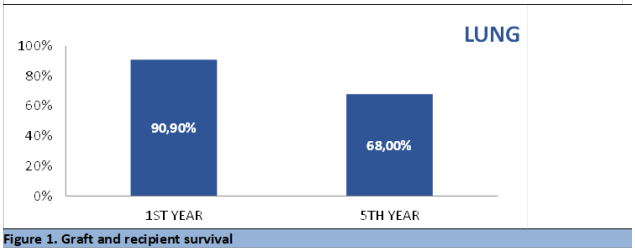


Figure 1. Graft and recipient survival

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Infectious diseases, malignancies & long term challenges

PP_258 HEALTHCARE PROVIDER PREFERENCES FOR TREATMENT OF POST-TRANSPLANT CYTOMEGALOVIRUS INFECTION

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Background: Management of cytomegalovirus infection (CMV) can be challenging in the solid organ transplant (SOT) patient population. Understanding how the complex convergence of patient, drug, and viral factors impact decision-making and treatment preferences of healthcare providers (HCPs) offers opportunities to improve patient outcomes. This study aimed to assess HCP preferences for antiviral attributes when treating CMV in SOT recipients, using a discrete choice experiment (DCE) design.

Methods: A web-based DCE was conducted to assess HCP preferences for CMV treatment attributes in SOT recipients. Attribute selection was informed by a literature review and qualitative interviews with HCPs (**Table 1**). A DCE survey was deployed to 301 HCPs, and data collected formed the basis of the quantitative report. Two complicated hypothetical SOT patients with CMV were presented to HCPs to illustrate CMV treatment scenarios. HCPs were then given 11 pairwise choice sets and asked to select their preferred treatment option (with varying attributes) based on the previously presented patient case. HCPs who were SOT specialists completed this task twice, as there were 2 different patient cases. A random-parameter logit model was used to estimate mean preference weights for every level of each attribute.

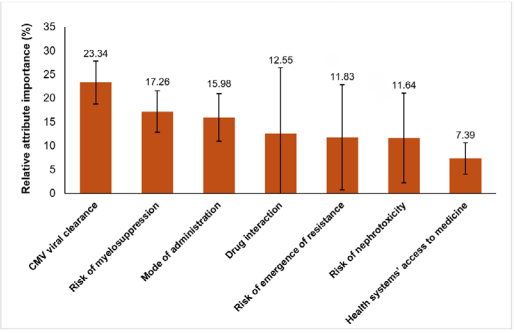
Results: The DCE was completed by 211/301 HCPs (90 SOT specialists, 90 infectious-disease specialists, and 31 pharmacists). HCP preferences for attribute levels were ordered as expected, preferring better attribute levels over worse levels. The only exception was a higher preference for medium barrier to resistance over high barrier to resistance; however, these coefficients were not statistically significant. "CMV viral clearance" (relative attribute importance [RAI]=23%) was most important relative to all other attributes, followed by "risk of myelosuppression" (RAI=17%), and "mode of administration" (RAI=16%) (**Figure 1**). The least important attribute was "health systems' access to medicine", referring to formulary versus non-formulary availability and approval (RAI=7%).

Conclusions: The most important attributes to HCPs for treatment of CMV in SOT recipients from this DCE were effective CMV viral clearance, risk of myelosuppression, and mode of administration.

Table 1. Illustrative DCE task

Attributes	Treatment A	Treatment B
Mode of administration	Oral	IV – no home infusion
Health systems' access to medicine	On inpatient formulary or available at a general pharmacy	Non-formulary inpatient, requires a specialty pharmacy
Risk of myelosuppression	Approximately 52%	Approximately 12%
Risk of nephrotoxicity	Approximately 15%	Approximately 30%
CMV viral clearance	Approximately 24%	Approximately 75%
Risk of emergence of resistance	Medium barrier to resistance	Low barrier to resistance
Drug interactions	No significant drug interactions	Requires dose adjustment for renal function
Which treatment would you choose?		

Figure 1. Relative attribute importance for CMV treatment for SOT recipients, with 95% confidence intervals



PP_259 A LONG-TERM ANALYSIS OF PANCREAS TRANSPLANTATION OUTCOMES IN THE USA OVER THE PAST TWO DECADE

Mahmoudreza Moein[1], Reza Saidi[1]

[1]Suny Upstate Medical University; Surgery/Transplantation Services

Background: The most common types of pancreas transplants performed in the United States are simultaneous kidney-pancreas transplants (SKP), pancreas-after-kidney transplants (PAK), and pancreas transplants alone (PTA). A longitudinal, two-decade analysis of the outcomes of these procedures in the United States can provide a clearer understanding of their benefits for patients.

Methods: We performed a retrospective registry analysis utilizing the OPTN/UNOS database for different types of pancreas transplants performed in the United States from January 2001 to December 2020 to assess transplant outcomes.

Results: 21,561 patients were included in the analysis after the study exclusions. The cohort consisted of simultaneous kidney-pancreas transplants (SKP, n=16,359; 75.9%), pancreas-after-kidney transplants (PAK, n=2,951; 13.7%), and pancreas transplants alone (PTA, n=2,251; 10.4%). All transplants were performed between 2011 and the end of 2020. Baseline characteristics were compared across the groups, with no significant differences observed, except for hospital length of stay following transplantation. PTA recipients had a longer average hospital stay (18 days) compared to SKP (12 days) and PAK recipients (9 days). The overall 5-year allograft survival rates were 74.8% for the SKP group, 58.8% for PAK, and 54.4% for PTA. To provide a more detailed analysis, the study cohort was divided into two time frames: 2000–2010 and 2011–2020. Table 1 and Figure 1 illustrate the allograft survival rates for each type of pancreas transplantation across these periods. A significant improvement in allograft survival was observed for PAK transplants during 2011–2020, increasing from 56.9% in 2000–2010 to 66.4% in 2011–2020.The overall 5-year patient survival rates were more comparable among the groups, with the SKP group demonstrating slightly better outcomes (Figure 2).

Conclusions: The study highlights the effectiveness of pancreas transplantation, with SKP emerging as the optimal choice for many patients. However, the improved outcomes of PAK and PTA over the years, provide viable alternatives to reduce waiting times, address donor-recipient imbalances, expand the donor pool, and improve quality of life.

Parameter	SKP	PAK	PTA
Pancreas transplant year			
2001-2010	72%	56.9%	52.7%
2011-2020	78.6%	66.4%	58.4%

Table 1.

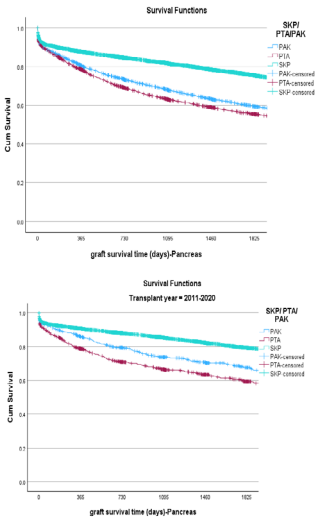


Figure 1.

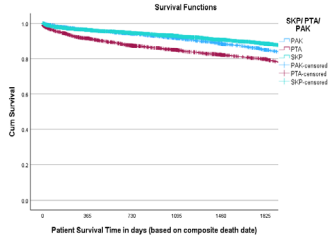


Figure 2.

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Infectious diseases, malignancies & long term challenges

PP_260 LUNG RE-TRANSPLANTATION: A SINGLE CENTER DUTCH EXPERIENCE

Prathi Nishanth[1], C. Tji Gan[2], Anna Van Gemert[3], Erik A.M. Verschuuren[4], tjerk Hylkema[1], Eline A. van der Ploeg[1], Caroline Van De Wauwer[5], Michiel Erasmus[6], Willie Steenhuis[1]

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Background: Lung transplantation (LTx) is a well-known and accepted treatment option provided for patients with end-stage lung disease. The development of chronic lung allograft dysfunction (CLAD) restricts long-term survival in LTx patients, and in these cases a re-transplantation (re-LTX) may be considered. International registry data shows that the long-term survival of re-LTx patients is impaired when compared to the survival of primary LTx patients. Since the long-term survival of Dutch LTx patients are superior to international registry data, we aim to investigate the long-term survival of re-LTx patients at the largest Dutch lung transplant center.

Methods: The study includes patients > 18 years who received a re-LTx at the University Medical Center Groningen (UMCG), The Netherlands from 1990-2023. The demographics and patient characteristics were summarized, and survival was assessed by a Kaplan-Meier curve with GraphPad prims 10.1.0.

Results: During 1990-2023, a total of 896 LTx were performed at the UMCG. In this group, 20 patients (2.2%) received a re-LTx for CLAD: 14 bilateral, 5 unilateral and 1 heart-lung transplantation. The initial diagnoses were pulmonary fibrosis n = 1, cystic fibrosis n = 5, pulmonary arterial hypertension n = 4, emphysema n = 7, and other n = 3. The median age for re-LTx was 41 [25-48] years. Furthermore, the time between the 1st and 2nd transplantation was 4.0 [1.1-7.7] years. The one-year survival rate was 85%, and the median survival was 4.5 years with no difference between unilateral or bilateral transplantations.

Conclusions: Re-LTx is an uncommon procedure and is predominantly performed in younger patients. The early outcomes of a re-LTx are good, however, the long-term survival of patients is significantly worse than the 11-year median survival of Dutch primary LTx patients. The results found are comparable to the international registry data, and further research is warranted to identify the cause of the poor survival rates in re-LTx.

PP_261 ADHERENCE AND HEALTH-RELATED QUALITY OF LIFE AFTER LUNG TRANSPLANTATION

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Background: Non-adherence (NA) to immunosuppressive treatment after lung transplantation is not uncommon and is often associated with poor outcome. At our Out-patient Clinic screening for NA at follow-up visits started in 2013. Health-related quality of life (HRQoL) has also been screened for. The use of instruments for screening in clinical settings are unusual. This is a retrospective longitudinal overview of the prevalence of NA and HRQoL during 2013-2022.

Methods: Adult lung-transplanted individuals (LuTx) were screened at 1, 2 and 3 year follow-up visits post lung transplantation for NA and HRQoL. HRQoL was also screened for pre transplantation. For screening of NA, the questionnaire the Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS) was used. The BAASIS measures adherence over the past 4 weeks and with 4 dimensions (taking, dosing, timing and skipping). HRQoL was screened for using the standardized instrument EQ-5D, which also has a reference from a Swedish background population. The analysis of EQ-5D was limited to only include the visual analogue scale (VAS) i.e. HRQoL 0-100%, where 0 is the worst and 100 the best.

Results: 217 patients were included, 103 woman and 114 men. The mean age was 54 years (range 18-71). 194 patients received double lung transplantation and 23 received single lung transplantation. The mortality was none the first year, 21 persons the second and 40 the third. The results of 1-3 year follow-up of NA is shown in Table 1. HRQoL (VAS), was pre transplant mean 34 %, 1 year post op 72 %, 2 year 73% and 3 year 71 %.

Conclusions: HRQoL increased post transplantation and stayed at the same level up to 3 years. Screening should be an integrated part of follow-up visits. Self-reported NA was low in our population compared to international studies. However, the proportion increased over time. The results confirm that regular and longitudinal screening of NA in LuTx is vital in clinical settings.

	BAASIS NA in total %, (n)	Taking %	Dosing	Timing %	Skipping	More than 1 NA problem %
1 year, n= 216	12 %, (26)	62 %	0	54 %	0	19 %
2 year, n=161	14 %, (22)	73 %	0	50 %	0	23 %
3 year, n=130	21 %, (29)	48 %	0	66 %	0	14 %

Table 1. Non-Adherence /year.

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PP_262 PROPOSAL FOR A NOVEL CARDIOVASCULAR RISK STRATIFICATION TOOL IN KIDNEY TRANSPLANTATION

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Background: Cardiovascular (CV) disease represents a major cause of morbidity and mortality after kidney transplantation (KT). Currently, there are no reliable risk-stratification tools for the prediction of major acute cardiovascular events (MACE) in KT recipients.

Methods: We retrospectively analyzed data from 498 consecutive KT patients with a follow up ≥1 year. Based on the occurrence of post-transplant MACE, these recipients were sorted into MACE (n=28) and non-MACE (n=470) groups. Baseline characteristics of the two groups were compared. Recipients were also stratified using five CV risk scores originally designed for the general population (Framingham, Hard Framingham, SCORE, INDANA, and Project Heart). Time-dependent risks were estimated with Cox regressions and receiver operating characteristic (ROC) curves whereas time-dependent variables were assessed with Kaplan-Meier method and log-rank test.

Results: At univariate analysis, recipient age (P=0,010), body mass index (P=0,022), uric acid (P=0,017), C-reactive protein (CRP; P=0,016), and diabetes mellitus (P=0,007) as recorded at the time of KT were associated with post-transplant MACE. Multivariate analysis (-2ln likelihood: 76,524; $\chi2(2)$ = 49,425; P<0,001) showed that CRP (P<0,001) and INDANA score (P=0,004) at transplant were the best predictors of post-transplant MACE. Accordingly, we developed a composite score (C-INDANA) using baseline CRP and INDANA, following the equation 0,316 * CRP + 19,123 * INDANA (the coefficients resulted from the regression coefficients β). The equation was applied to our study population. Resulting values ranged from 0,029 to 11,910. Based on recipient operating characteristic curve coordinates, the 80th percentile was chosen as discriminatory criterion to stratify KT recipients per the cumulative incidence of MACE (P=0,002), patient survival (P=0,005), and graft survival (P=0,057).

Conclusions: C-INDANA score can stratify KT patients for the risk of MACE and mortality. Therefore, it could represent an easy-to-use screening tool for the selection of patients requiring a more aggressive CV surveillance after transplant.

PP_263 A NOVEL UK DONOR SCREENING AND THE IMPACT OF DONOR-DERVIED HUMAN HERPES VIRUS TYPE 8 IN SOLID ORGAN TRANSPLANTATION

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Background: Infection rates with Herpes virus type 8 (HHV-8) vary significantly between geographical areas and populations, with low incidence of disease in solid organ transplant (SOT) recipients. Kaposi's sarcoma (KS) is often associated with reactivation of pre-existing infection, but in graft-acquired infection, severe disease such as visceral KS, Multicentric Castleman Disease (MCD) and Kaposi Sarcoma Inflammatory Cytokine Syndrome (KICS) can occur within months from transplantation.

Methods: Several cases of fatal donor-derived HHV-8 infection were investigated in the UK, leading to an expert committee review, and a recommendation to commence serological screening in deceased organ donors. Post-donation testing uses lytic and latent indirect immunofluorescence assays on plasma; reactive samples are tested for viral DNA by polymerase chain reaction (PCR). Antibody reactive donor result triggers recipient follow up for early identification of infection and disease manifestation.

Results: Between May 2023-December 2024, 2595 donors were tested. In the absence of a confirmatory gold standard, the antibody reactivity rate was 6.63%, with 3.77% being inconclusive, 1.97% low reactive and 1.89% positive; the latter is in keeping with the expected seroprevalence in our donor population. PCR was performed in all 172 reactive samples, 9 (0.35%) had detectable HHV-8 DNA. 347 recipients commenced follow up, with *de novo* infection detected in 16; notably, all transmissions were solely linked to the 9 donors with detectable viral DNA. Out of 5 newly infected kidney recipients, one developed KS and is on treatment, one died (unrelated cause). Amongst 8 liver recipients, 1 is under follow up, 2 remain asymptomatic and 5 developed KS, MCD or KICS and died. 2 kidney-pancreas and 1 lung recipient remain asymptomatic. (Table 1)

Conclusions: Determinants of transmission via the transplanted graft, and of disease development in recipients are yet to be defined. Donor screening and recipient follow up has been very challenging but awareness of HHV-8 infection in the context of SOT has been raised; multidisciplinary efforts will hopefully bring experience in monitoring and managing patients, with the aim to improve outcomes. Our next steps are being planned, using the information gained since start of screening.

Table 1: Outcomes of recipients of organs from HHV-8 positive donors

DONOR			RECIPIENT										
Lytic antibody	Latent antibody	Virus DNA	HEART	R LUNG	L LUNG	RIGHT KIDNEY	LEFT KIDNEY	SPK	PANCREAS	WHOLE LIVER	R LIVER LOBE	L LAT SEGMENT	BOWEL
Indeterminate	Not detected	Detected				Day +213	Day +375				RIP Day +204	Day +435	
Detected	Detected	Detected				Day +257	RIP Day +154 (unrelated cause)			Day +423			
Detected	Detected	Detected				On treatment	Day +315			RIP Day +189			
Detected	Not detected	Detected				Day +210		Day +265		RIP Day +321			
Detected	Detected	Detected	Day +140	Day +148			Day +170	Day +201		RIP Day +222			
Detected	Not detected	Detected				Graft removed							
Detected	Detected	Detected				Day +131	Day +116			Day +153 (to be confirmed)			
Detected	Detected	Detected				No information available	No information available			RIP Day +68			
Detected	Indeterminate	Detected				Day +67	Day +21			Day +51			

KEY
No evidence of primary infection
Evidence of primary infection, no disease so far
Information not available
Evidence of transmission and disease

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Infectious diseases, malignancies & long term challenges

PP_264 CYTOMEGALOVIRUS INFECTION AND EPICARDIAL ADIPOSE TISSUE IN LIVER TRANSPLANT RECIPIENTS

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Background: Epicardial adipose tissue (EAT) volume is associated with cardiovascular disease (CVD) in the general population. Liver transplant recipients are at high risk of cytomegalovirus (CMV) infection after transplantation and have increased risk of CVD compared to the general population. We aimed to investigate if CMV infection was associated with EAT volume in liver transplant recipients.

Methods: From the Danish Comorbidity in Liver Transplant Recipients (DACOLT) Study, a nationwide prospective cohort study, we included liver transplant recipients who underwent contrast-enhanced cardiac computed tomography from which EAT volume was measured. CMV test results were collected from the national microbiology database. Using linear regressions, we investigated the relationship between EAT divided by body surface area (EAT/BSA) and CMV.

Results: We included 166 participants, of whom 54 had CMV DNAemia and 20 had CMV disease after transplantation. CMV DNAemia (-8.30 [95% confidence interval (CI): -14.9 to -1.69] ml/m^2, *P*=0.02) and CMV disease (-10.9 [95%CI: -20.6 to -1.09] ml/m^2, *P*=0.03) were associated with lower EAT/BSA after adjusting for age, sex, time since transplantation, smoking, use of corticosteroids, dyslipidemia, and diabetes mellitus.

Conclusions: CMV DNAemia and CMV disease after transplantation were associated with lower EAT/BSA in liver transplant recipients. The mechanism behind this association is still unknown, but intensified CVD surveillance in recipients without CMV infection should be explored.

Table 1 Cytomegalovirus and epicardial adipose tissue after liver transplantation *(N = 166)*

	β (95% CI)	P	Adjusted β_1 (95% CI)	P	Adjusted β_2 (95% CI)	P
CMV DNAemia	-7.49 (-14.07 to -0.91)	**0.03**	-8.17 (-14.3 to -2.01)	**0.01**	-8.3 (-14.9 to -1.69)	**0.02**
Peak CMV DNAemia, per doubling[1]	-0.02 (-1.67 to 1.62)	0.98	-0.61 (-2.2 to 0.98)	0.46	-1.4 (-3.71 to 0.9)	0.24
Positive recipient CMV serostatus	3.48 (-3.15 to 10.1)	0.31	2.69 (-3.56 to 8.9)	0.40	2.3 (-4.48 to 9.09)	0.51
CMV disease	-9.35 (-18.9 to 0.15)	0.06	-10.7 (-19.7 to -1.72)	**0.02**	-10.9 (-20.6 to -1.09)	**0.03**

Linear regression analyses of association between CMV-related variables and epicardial adipose tissue volume divided by body surface area (mL/m^2). P ≤ 0.05 shown in bold. β_1 adjusted for age and sex. β_2 adjusted for age, sex, time since liver transplantation, smoking, use of corticosteroids at baseline, dyslipidemia, and diabetes mellitus. **CMV**, cytomegalovirus. **CI**, confidence intervals. [1]Only positive samples analyzed at Copenhagen University Hospital – Rigshospitalet, n = 46

Figure 1 Epicardial adipose tissue volume assessment with contrast-enhanced cardiac CT

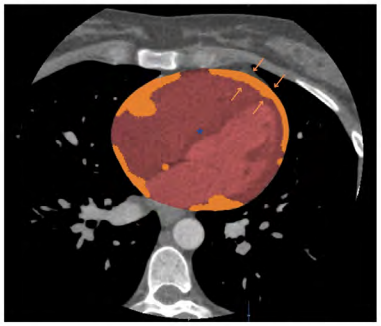

Figure shows an axial image at the mid-ventricular level. Red area marks tissue within the pericardial sac. Orange area and arrows mark epicardial adipose tissue defined as voxels with radiodensities ranging from -190 to -70 Hounsfield Units within the pericardium. Blue asterisk * marks the myocardium. **CT**, computerized tomography

PP_265 NOVEL REPAIR OF TRANSPLANT LATERAL HERNIAS ACHIEVES RECURRENCE COMPARABLE TO NON-TRANSPLANT HERNIAS

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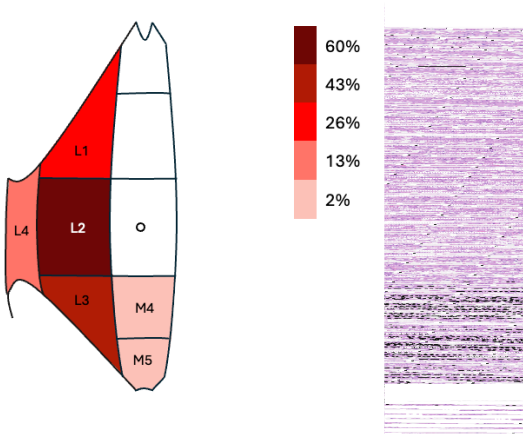
[1]Manchester University NHS Foundation Trust; Transplant ; Manchester Centre for Transplantation, [2]Manchester Foundation Trust; Renal & Pancreas Transplant, [3]Manchester Royal Infirmary, Manchester University NHS Foundation Trust; Dept of Renal & Pancreas Transplantation, [4]Manchester Royal Infirmary; Manchester Royal Infirmary; Dept of Renal & Pancreas Transplantation

Background: Lateral incisional hernia (LIH) repair comes with additional challenges compared to midline repairs and has a reported recurrence rate of 7%. Transplant recipients bring added technical and clinical complexity to LIH repair resulting in a 16% recurrence rate. There is a paucity of evidence for optimal techniques in LIH repair. We describe our centre's novel technique for LIH repair in renal transplant recipients and report outcomes from a series of 47 repairs following renal transplantation.

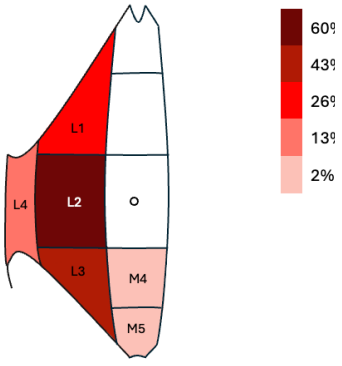
Methods: We performed descriptive statistical analysis of a prospective database of all LIH repairs following transplantation through a lateral incision maintained between May 2016 and June 2024. We report our novel combination of surgical techniques, utilising hybrid mesh systems intended for placement in the transversalis fascial plane, without fixation, in renal transplant recipients.

Results: 47 hernias were repaired in 45 patients. The median BMI was 29.3kg/m^2 (IQR: 26.8-31.2) and average age 58 years (IQR: 48-67). Median defect size was 120cm^2 (IQR: 61-227). The median follow-up was 68 months (IQR: 27-87) and yielded a recurrence rate of 9%. The rates of surgical complication, particularly wound complications, were lower than expected, however, there were two mortalities resulting from medical complications postoperatively, neither of which were related to the surgical technique.

Conclusions: This study represents the third largest series of lateral incisional hernia repairs post-renal transplantation, with the longest follow-up reported to date. The large sample size and extended follow-up demonstrate feasibility of our technique across various defect sizes and locations in transplant recipients and shows recurrence rates comparable to non-transplant repairs. The significantly longer follow-up in this series suggests potential superiority of the recurrence rates reported in the existing literature. Further research, including interventional studies and standardised reporting is needed to optimise techniques and further advance the field.



Patient, hernia and follow-up data. BMI (body mass index), VHWG (ventral hernia working group).



A non-lateralised schematic heat map demonstrating the locations of hernias. Hernias which extended through multiple regions were included in each.

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PP_266 OBESITY AND FAT DISTRIBUTION IN LIVER TRANSPLANT PATIENTS: LONG-TERM TRENDS AND IMPACT ON RECOVERY

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Background: Obesity is increasingly prevalent among patients with end-stage liver disease (ESLD) awaiting liver transplantation (LT), reflecting global trends. Post-LT, weight gain and obesity remain significant concerns. In ESLD patients, ascites renders BMI unreliable for assessing adiposity. The ratio of visceral adipose tissue (VAT) to subcutaneous adipose tissue (SAT) critically affect outcomes, with VAT associated with poorer cardiovascular and survival outcomes. Limited data exist on how LT affects fat compartments. This study examines long-term changes in obesity and fat distribution after LT and their associations with survival and length of hospital/ICU stay.

Methods: A retrospective cohort study analyzed 81 ESLD patients undergoing LT (2009–2015) with available CT/MRI scans at the L3 vertebral level. SAT and VAT were assessed pre-LT (at waitlist activation) and post-LT, with follow-up up to 10 years. Linear mixed models assessed changes in BMI, SAT, VAT, and VAT/SAT ratio. Associations of pre-LT SAT, VAT, and VAT/SAT ratio with patient survival and ICU/hospital stay were examined via survival analysis and Spearman correlations.

Results: Mean age at LT was 55 ± 12 years; 53% were male. Pre-LT, 53% of the patients had a BMI>25. BMI decreased immediately post-LT, returned to baseline within 2 years, and increased thereafter (Figure 1). SAT rose steadily over 10 years (Figure 2A), while VAT initially decreased post-LT, increased over 4–5 years, and then gradually declined (Figure 2B). VAT/SAT ratio increased over 10 years, with the rate of increase slowing after ~4.5 years (Figure 2C). Pre-LT VAT/SAT ratio was significantly associated with longer hospital (Rho = 0.32, p = 0.019) and ICU stays (Rho = 0.3, p = 0.03) (Figure 3A-B). Pre-LT VAT was also linked to longer ICU stay (Rho = 0.41, p = 0.002) (Figure 4). No significant associations were found with reduced survival.

Conclusions: Obesity is highly prevalent in LT patients, with notable changes in body composition post-LT. The associations of pre-LT VAT and VAT/SAT ratios with longer ICU/hospital stays suggest that fat distribution plays an important role in post-LT recovery. Future research should aim to develop targeted interventions and elucidating the evolution, reversibility, and influence of body composition on post-LT recovery.

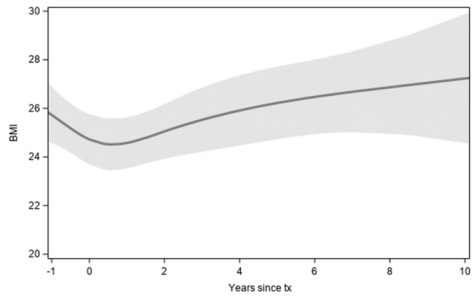
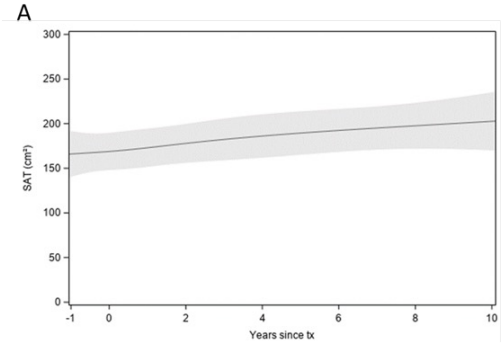


Figure 1. Evolution of BMI after LT



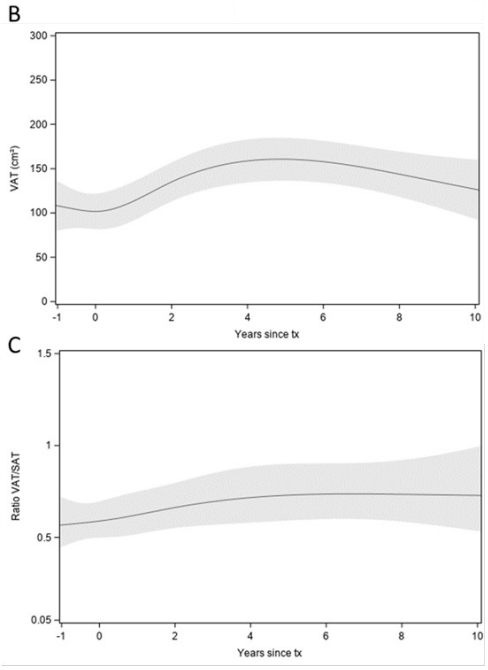


Figure 2.Changes in (A) SAT, (B) VAT, and (C) VAT/SAT ratio after LT

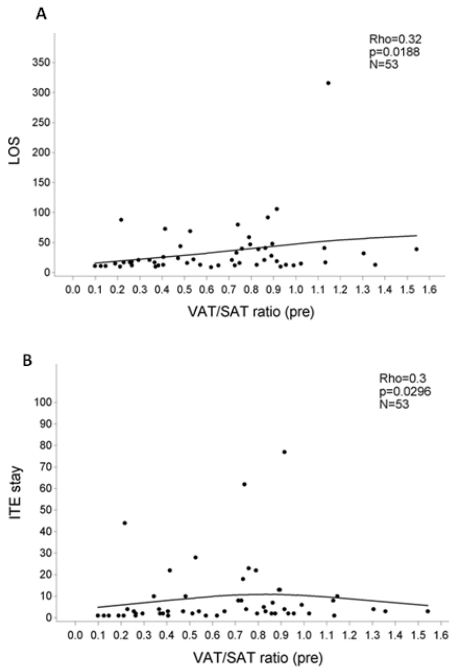


Figure 3.Association of pre-transplant VAT/SAT ratio with (A) length od hospital stay (LOS) and (B) ICU stay

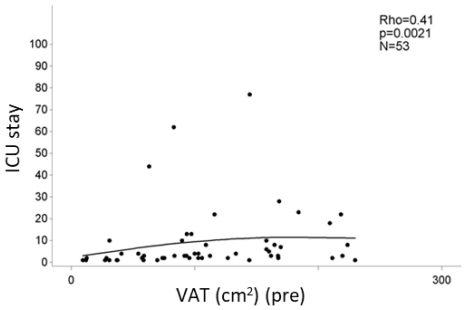


Figure 4.Association between pre-transplant VAT and length of ICU stay

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Infectious diseases, malignancies & long term challenges

PP_267 RISK OF FRACTURES IN TRANSPLANTED KIDNEY PATIENTS A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Background: Fractures in renal postransplantation represent one of the complications that increase morbidity and mortality in patients. The risk factors for fracture after transplant remain uncertain. Aim: To determine the risk factors for transplantation of nonvertebral fractures in renal transplant recipients

Methods: The data of clinical histories of 737 renal transplanted patients since 2009-2015 were analyzed, where the risk factors of fractures were evaluated. They were determined as general factors: age, sex; and specific factors: etiology of chronic kidney disease (CKD), dialysis time, dialysis modality, donor characteristics: age, sex, type of donor, living or cadaveric (LD, DC), different immunosuppression treatments, rejections, treatment with steroid pulses, use of bisphosphonates and biochemical parameters like intact parathormone (PTHI), Pro -Vitamin D (25OHD) and Creatininemia Exclusion criteria: patients <18 years, retransplantation or dual transplants and follow up less than 1 year

Results: 44 patients presented 50 non-vertebral fractures. 62% of the fractures were presented in the first 3 years of the transplant. In the multivariate model it was observed that the general risk factors associated with fracture risk were the advanced age of the receptor (aHR per year increases 1.03, 95% CI: 1.00-1.05] and the female sex (aHR = 1.60, 95% CI: 0.85-2.99), while the specific risk factors were dialysis time (1.07 IC95%: 1.02-1.12), the higher age of the donor (1.03 IC95: 1,00-1,05) and the deficit of 25OHD (3.17 IC95: 1.57-6.41)

Conclusions: This study allowed to evaluate predictive factors of non-vertebral fracture in our patients with kidney transplantation.

PP_268 POSTTRANSPLANT MALIGNANCY AMONG RENAL TRANSPLANT RECIPIENTS FOR 50 YEARS AT A JAPANESE SINGLE CENTER

Shuji Nobori[1]

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Background: Malignancy after transplantation is one of important problems for long-term follow-up in organ transplantation because overall incidence of malignancy is higher than in the general population. A number of studies have observed increased cancer incidence rates among renal transplant recipients.

Methods: We retrospectively analyzed 1179 renal transplant recipients in Kyoto Prefectural University of Medicine between 1970 and 2022 to evaluate the incidence of malignancies.

Results: A total of 96(8.14%) kidney recipients out of 1179 developed 100 malignancies. The malignancies of our series included 22 gastro-intestinal tract cancers, 18 skin cancers, 11 breast cancers,9 liver cancers, 8 renal cell carcinomas, 6 leukemia, 6 lung cancers, 5 thyroid cancers,4 tongue cancers, 2 pancreas cancers, one uterus cancer, and 8 others include 7 lymphoma and one Kaposi's sarcoma (KS). Sites of malignancies occurring within three years following transplantation were breast, stomach, uterus, liver, leukemia, adult T cell lymphoma(ATL), Kaposi Sarcoma and posttransplant lymphoproliferative disorder(PTLD). The cumulative incidence of malignancies of all 1179 renal recipients was 4.8% at 10years, 14.9% at 20years and 24.3% at 30 years, respectively. Univariate analysis showed that age at the time of transplantation (>50yo., OR=7.005,p<0.01), diabetic nephropathy (OR=6.638, p<0.01), ABO-incompatible transplant(OR=5.758, p<0.01) and use of mycophenolate mofetil(OR=5.126, p<0.01) were significant risk factors to develop malignancies within 5 years. Among them, age at the time of transplantation (OR=4.8575, p<0.05) and diabetic nephropathy(OR=4.6911,p<0.05) were independent risk factors by multivariate analysis.

Conclusions: With CNI induction, the early incidence rate increased, chiefly for virus-related cancers as malignant lymphoma and Kaposi`s sarcoma, but the long-term incidence rate decreased. In the long-term follow-up, it is crucial to pay special attention to those who have risk factors to develop them.

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Infectious diseases, malignancies & long term challenges

PP_269 PERFORMANCE OF THE IBOX IN AFRICAN AMERICAN KIDNEY TRANSPLANT RECIPIENTS: A MULTICENTER STUDY

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[1]Tenon Hospital; Nephrology, [2]Paris Transplant Group; Paris Institute for Transplantation and Organ Regeneration (Pitor), Paris, France; Paris Institute for Transplantation and Organ Regeneration (Pitor), Paris, France, [3]Paris Institute for Transplantation and Organ Regeneration (Pitor), [4]Necker Hospital; Necker Hospital; -, [5]Paris Institute for Transplantation and Organ Regeneration, [6]University of Wisconsin Madison, [7]Emory University School of Medicine, [8]New York University; Nyu Grossman School of Medicine, [9]Northwestern University Feinberg School of Medicine, [10]Virginia Commonwealth University, [11]Albert Einstein College of Medicine, Montefiore Medical Center,; Kidney Transplantation Program; Renal Division, [12]Cedars Sinai Transplant Center; Cedars-Sinai Medical Center; Comprehensive Transplant Center, [13]University OF Minnesota; Surgery, [14]University of Nebraska, [15]Nyu Langone Grossman School of Medicine; Surgery; Population Health, [16]Cedars-Sinai Medical Center, [17]University of Illinois Chicago, [18]Necker Hospital

Background: The iBox is a validated prognostication system that predicts graft loss in kidney transplant recipients (KTRs), but its performance in the specific population of African American recipients has not been fully studied.

Methods: We conducted a multicenter study on 2,778 KTRs from six North American cohorts, including 679 (24.4%) African American KTRs, to assess the impact of race on the iBox's performance in predicting graft loss. Performance metrics and plots were assessed in the whole study population, and in subgroups defined by race ("African American recipients" vs. "non-African American recipients"). Heterogeneity of performances between subgroups was assessed using an interaction term between iBox score values and the grouping variable (race), in a Cox proportional hazards regression model predicting the outcome and stratified by study center. A Z-test for independent samples was used to test for the statistical significance of differences observed between group for performance metrics

Results: Performance metrics for the prediction of graft loss at 5 years post-evaluation were similar for both African American and non-African American KTRs, in terms of overall fit (Brier score of 0.085 [95%CI: 0.066-0.104] and 0.069 [95%CI: 0.058-0.081], respectively; p=0.243) and discrimination (C-index: 0.817 [95%CI: 0.779-0.854] and 0.838 [95%CI: 0.814-0.863], respectively; p=0.358). No significant interaction between iBox score values and race was found in multivariate analysis stratified by center (p=0.950 for the interaction term). Results were consistent for the prediction of 3 or 7-year graft loss; and regardless of the equation used to estimate glomerular filtration rate (Kidney Recipient Specific [KRS], CKD-EPI, or MDRD).

Conclusions: The iBox prognostication system accurately predicts graft loss up to 7 years post-evaluation in African American KTRs and confirms its relevance as a surrogate end point in this population.

PP_270 TRAJECTORIES OF FATIGUE AMONG KIDNEY TRANSPLANT RECIPIENTS PRIOR TO AND POST-TRANSPLANTATION

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Background: Fatigue is common in kidney transplant recipients (KTRs). Yet, little is known on how fatigue evolves after transplantation (Tx) in KTRs. Therefore, this study aimed to identify distinct fatigue trajectories from before to 24 months after Tx, to explore covariables associated with these trajectories, and to assess their relation with health-related quality of life (HRQoL) and rehospitalization.

Methods: Longitudinal data of the TransplantLines Biobank and Cohort Study were used. Fatigue was assessed using the 8-item Checklist Individual Strength Revised prior to and at 6, 12, and 24 months post-Tx. Fatigue trajectories were identified by Latent Class Growth Analysis. HRQoL was assessed by the Short Form-12 at 12 and 24 months post-Tx. Rehospitalization was defined as the total days readmitted within the first post-Tx year.

Results: In total, 500 KTRs were included (36.6% female, age 55±13 years). Four trajectories were identified: persistent low fatigue (9.0%), resolved mild fatigue (24.8%), severe fatigue that improved to mild fatigue (43.0%), and persistent severe fatigue (23.2%). Univariate logistic regression showed that, compared to KTRs in the trajectory of persistent low fatigue, KTRs within the resolved mild fatigue trajectory more often had a living donor, depressive symptoms, and less personal control. KTRs within both the trajectories of severe fatigue that improved to mild fatigue and persistent severe fatigue had poorer sleep quality, more symptoms of depression and anxiety, less personal control, and used more often the coping styles palliative reactions, avoidance, passive reactions and expression of emotions. KTRs within the persistent severe fatigue trajectory reported significantly lower HRQoL at 12 and 24 months post-Tx, and were rehospitalized more days within the first post-Tx year compared to the other trajectories.

Conclusions: A significant subset of KTRs experienced persistent severe fatigue post-Tx, accompanied by reduced HRQoL and more rehospitalization days. Personal variables show a strong association with fatigue trajectories and may be targets for interventions.

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PP_271 CMV PROPHYLAXIS VS. PRE-EMPTIVE THERAPY AFTER LIVER TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY OF 610 CASES.

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Background: The literature is conflicting whether prophylaxis with valgancyclovir (VG, high or lower doses), or regular liquid biopsies and early treatment (pre-emptive strategy) is more effective for cytomegalovirus (CMV) disease prophylaxis. We aimed to compare the effectivity of the two methods after liver transplantation in our practice.

Methods: Data from 610 liver transplantations were retrospectively analyzed (2013-2023). Based on donor's and recipient's CMV serostatus, patients were categorized into high- (D+/R-), moderate- (D+/R+, D-/R+), or low-risk (D-/R-) group. Patients either received prophylaxis with low-dose oral valganciclovir (VG, 450mg/day) from day 14 after transplant for 100 days, or pre-emptive therapy. The regimen was selected according to hepatologist's and patient's preference; prophylaxis was more frequently preferred in the presence of risk factors (serostatus, treated acut rejection, induction therapy). CMV replication was monitored with the antigenemia method (2013-2019), or polymerase chain reaction (PCR, from 2020 onwards).

Results: High-risk patients (77) received mostly prophylaxis; however, even this was not sufficient to prevent CMV infection (PCR: 79% infection rate, antigenemia: 51%, p>0.2). In moderate risk group (507 patients) prophylaxis, even only with low-dose, decreased the risk by 2-6 times (PCR - prophylaxis: 7.4%, pre-emptive: 42%, p<0.0001; antigenemia - prophylaxis: 12.5%, pre-emptive: 24.9%, p=0.1) - although other risk factors (treated rejection or induction therapy) were more frequent in this group (51% vs. 15%). Leukopenia (<3G/L) as an adverse effect of prophylaxis was detected in 14%. No infection occurred among low-risk patients.

Conclusions: In the moderate-risk group, where most patients belong low-dose VG prophylaxis is more effective than pre-emptive therapy in preventing CMV infection with an acceptable risk of leukopenia. Low-dose VG prophylaxis is insufficient in the high-risk group, thus standard dose of VG (900 mg/day) is encouraged in these patients. For low-risk patients, regular CMV monitoring and pre-emptive therapy proved to be sufficient.

PP_273 PREGNANCY AFTER KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Background: Reproductive function of women with end-stage chronic kidney disease improves after kidney transplantation (KT). But pregnancy after KT presents challenges, including increased risks of obstetric complications for both mother and fetus. This study aimed to assess pregnancy outcomes in women following KT.

Methods: Retrospective single center study of women with KT and pregnancy from 2015-2023. Demographic data, immunosuppressive therapy, complications during pregnancy and delivery, and renal graft function were recorded.

Results: Data from 15 pregnancies in 10 women were reviewed. Mean age at transplantation was 28.6 years, median time from transplantation to pregnancy was 65 months [19-150], while mean age at the onset of pregnancy was 34.7 years. Four pregnancies resulted in early miscarriage and one in a spontaneous abortion at 17 weeks. Finally, there were 10 livebirth deliveries and among them, one successful twin pregnancy. Half (50%) of pregnancies were achieved via assisted reproduction. Mean creatinine and 24-h urine protein at pregnancy onset were 1.2mg/dl and 142mg respectively. All patients except one, who was highly sensitized, had low immunological risk and were on stable maintenance immunosuppression, which consisted of a calcineurin inhibitor (tacrolimus 90%/cyclosporine10%), azathioprine and methylprednisolone. The levels of immunosuppressive drugs changed significantly during pregnancy, while frequent monitoring and continuous dose increases of CNIs was implemented. The most common complication during pregnancy was hypertension, which affected 5(50%) of women, while no episode of preeclampsia occurred. A caesarean section was performed in 9 out of 10 (90%) of the cases. Seven out of 10 (70%) of the deliveries were premature (<37 weeks). Among them, three (3/7) were very preterm (≤32weeks). The average birth weight was 2230±579g without occurrence of major complications. Renal function remained stable throughout pregnancy, and no acute rejection occurred.

Conclusions: Most pregnancies in women with KT have a good outcome, with an increased risk of preterm and caesarean deliveries. Close monitoring of kidney function, immunosuppression, and collaboration with obstetricians are critical for optimizing outcomes in these pregnancies.

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PP_274 NAVIGATING BONE HEALTH IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER STUDY

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Background: Quantitative bone disorders are common in kidney transplant patients (KTxps), especially during the 1st year post-transplantation. This study reports preliminary data on the prevalence and progression of bone anomalies in a single-center cohort.

Methods: We retrospectively analyzed 469 KTxps (M=271, mean age 49±11 years) transplanted between 2004 and 2023. Baseline (T0) and 12-month (T12) data were collected, including dual-energy X-ray absorptiometry (DEXA) results. Bone mineral density (BMD) was measured at femoral (F-BMD) and vertebral (V-BMD) sites, with T and Z-scores calculated. Patients with T-scores of -1>T>-2.5 were classified as osteopenic (OPN) and T-scores <-2.5 as osteoporotic (OPS). A >5% decrease in BMD was considered significant worsening (BMDW).

Results: Glomerulonephritis and autosomal dominant polycystic kidney disease were the most common underlying conditions (21% each). Deceased donor transplants accounted for 82%, and 68% of patients underwent hemodialysis pre-transplant. At T12, most patients were on tacrolimus and mycophenolate; steroids were used in 10% (mean cumulative dose 2887±926 mg). Vitamin D supplementation was present in 33%, but mean levels remained low (17±4 ng/dL). F-BMD remained stable, as did V-BMD. OPN and OPS were prevalent at T0 (F-OPN 57%, V-OPN 38%; F-OPS 17%, V-OPS 26%). Significant F-BMDW occurred in 14% and V-BMDW in 16%, associated with older age (p=0.05), higher BMI (p=0.01), and greater urinary protein excretion (p=0.01). Patients with higher initial BMD were more likely to experience BMDW. Multivariate analysis identified initial BMD, age, and urinary protein excretion as key factors for BMDW. In multivariate analysis apart T0 BMD (F-BMDW p=0.005 and V-BMDW p<0.001), age at transplant (p=0.05) and Prot U at T1 (p=0.02) resulted the most impacting modifiable factors in determining respectively F-BMDW and V-BMDW.

Conclusions: Quantitative bone anomalies are prevalent in KTxps from the start of transplantation. Despite vitamin D supplementation, levels remained low, highlighting a potential area for intervention. Significant BMDW in a subset emphasizes the need for addressing modifiable factors such as age and proteinuria. Long-term monitoring of BMD is crucial to optimize bone health and guide personalized interventions.

PP_275 TRANSPLANTATION FOR INCIDENTAL COMBINED HEPATOCELLULAR CHOLANGIOCARCINOMA: PROPENSITY SCORE ANALYSIS

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Background: Combined hepatocellular-cholangiocarcinoma (cHCC–CC) is a tumor with a challenging differential diagnosis from HCC. Some patients who undergo LT for a supposed HCC are eventually diagnosed with cHCC-CC. The purpose of this study is to assess the outcomes of patients whose final pathology revealed cHCC-CC after they received LT for HCC.

Methods: From 2004 to 2021 we retrospectively analyzed all patients who underwent LT for cHCC-CC in our Center. Outcomes after LT were compared to HCC recipients. We performed a case match analysis pairing patients at the same propensity score without reinsertion matching for number of nodules, size and aFP-level. Next, we examined the recipients' overall survival, disease-free survival and associated prognostic variables.

Results: cHCC-CCs were discovered in 27 patients that underwent LT during the research period. At five years, there were notable variations in overall survival (p=0,011). Both OS and DFS results showed a significant difference following PS matching. The overall survival was 85.41% vs 91.89%, 69.6% vs 74.34% and 49.8% vs 68.44% at 1, 3 and 5 years, in cHCC and HCC respectively [p=0,0098]. Tumor biology was a negative predictive factor at the multivariate Cox regression analysis for disease recurrence (HR 2.40, p=0,031

Conclusions: Based on our analysis, cHCC-CC had a worse oncological ou tcome compared to HCC. Nonetheless, the survival rate of cHCC-CC recipients reaches nearly 50% at 5-years , therefore this primary liver cancer could also be approached from a "Transplant Oncology" perspective. For these reasons, new studies are required for optimized the management of cHCC-CC patients.

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PP_277 THE ROLE OF MTOR INHIBITORS IN COVID-19 OUTCOMES AMONG HEART TRANSPLANT RECIPIENTS

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Background: Organ transplant recipients are at increased risk of severe infections, with SARS-CoV-2 presenting a particular threat to those undergoing immunosuppressive therapy. Some immunosuppressive agents, such as mTOR inhibitors (sirolimus, everolimus), may have immunomodulatory effects in the context of COVID-19. This study explores the role of mTOR in heart transplant recipients (HTx) during COVID-19 infection.

Methods: We conducted a retrospective analysis of a large cohort of HTx from a single center, assessing the impact of COVID-19 infection from the onset of the pandemic to March 2024. The study compared outcomes between pts. receiving mTOR and those on non-mTOR regimens. Additionally, an analysis was conducted on pts. in the group receiving mTOR, depending on whether they were also undergoing calcineurin inhibitors (CNI) therapy.

Results: Among 556 heart transplant recipients, 88 (15.8%) were on mTORs, 66 (11.9%) were on a combination of mTOR and CNI, and 22 (3.96%) were on a CNI-free regimen. The mean age of mTOR patients was 60.5 years (IQR: 47–67.5) and non-mTOR patients was 57.5 (43-65.5); P = 0.07. COVID-19 incidence was 33% (29/88) in the mTOR group and 34.18% (160/468) in the non-mTOR group (P = 0.82). Hospitalization rates were 3.4% (3/88) in the mTOR group versus 6.41% (30/468) in the non-mTOR group (P = 0.4), among them there were 2 hospitalizations in CNI-free regimen group (P=0.68) and 1 hospitalization in mTOR+CNI group (P = 0.13). COVID-19-related mortality rates were 3.41% (3/88) in the mTOR+CNI group versus 3.2% (15/468) in the non-mTOR group (P = 0.4). There were no deaths related to COVID-19 in the mTOR CNI-free pts. The risk of COVID-19-related mortality was as follows: for the entire mTOR group compared to patients without mTORs, HR= 0.69 (95% CI: 0.197–2.39; p=0.55), for mTOR recipients with CNI vs the remaining patients, HR= 1.98 (95% CI: 0.568–6.926; p=0.28). For recipients on CNI-free regimen no COVID-19-related deaths were observed, making Cox regression analysis unfeasible.

Conclusions: No significant differences in COVID-19 outcomes were observed between mTOR and non-mTOR regimens. The lack of deaths in the CNI-free group is notable but requires cautious interpretation due to the small sample size. The underlying mechanisms of this observation warrant further investigation.

PP_278 WORKFORCE REINTEGRATION AFTER LIVER TRANSPLANT: EVALUATION OF RISK FACTORS FOR UNEMPLOYMENT

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Background: The reintegration of liver transplant (LT) recipients into the workforce is a crucial goal, yet specific guidelines for this process are lacking. The BRIC-2022-ID25 project investigates the impact of liver disease and transplantation on work ability by examining correlations between clinical, social, and occupational factors before and after LT, aiming to enhance professional reintegration.

Methods: In collaboration with the occupational medicine department, we enrolled patients (pts) who underwent LT at our center between 2018-2023, aged 18 to 68 years, who were not retired prior to LT. Participants completed the WHODAS 2.0 (World Health Organization Disability Assessment Schedule) and Work Ability Index (WAI) questionnaires, with results merged with clinical and occupational data from both pre- and post-LT follow-ups. Interim analyses were performed on pts interviewed between January and June 2024.

Results: A total of 281 pts participated; 83% had cirrhosis (42% with hepatocellular carcinoma - HCC), and 11% were diagnosed with hepatic/hepatorenal polycystosis. The mean age at interview was 55 years (range 24-68), with 65% males and an average of 44 months between LT and the interview. Notably, 55% had a middle-school education. Post-LT, 39% were unemployed, with 64% indicating health issues as a barrier to their job search. Significant correlations were found between unemployment and factors such as age ≥65 years (p=0.04), having a caregiver outside the household (p=0.01), middle-school education (p=0.03), and a longer waiting list time (p=0.02). A low self-assessment of work ability (WAS) correlated with being over 50 years old (p=0.03), smoking (p=0.01), and lower education levels (p=0.04). The total WAI score was lower in non-Italian pts (p=0.01) and in those with polycystosis. Poorer disability scores (WHODAS) were associated with non-Italian nationality (p=0.01), alcohol use disorder (p=0.04), and longer hospital stays after LT (p=0.03).

Conclusions: Our study revealed a 39% unemployment rate following LT, with health status affecting 64% of cases. Factors such as caregiving responsibilities, education level, nationality, age, and complications significantly impact work ability. Enhanced efforts are needed to ensure equitable employment opportunities for transplant pts.

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PP_279 BIOPSY-BASED TRANSCRIPT DIAGNOSTICS IMPROVES PROGNOSTICATION ALONG THE AMR CONTINUUM

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Background: Clinical utility of biopsy-based transcript diagnostics with respect to risk stratification and prognostication for graft outcome used in addition to histology along the AMR continuum of Banff 2022 has not been investigated.

Methods: We examined 297 kidney allgraft biopsies by histology and the Molecular Microscope Diagnostic System (MMDx) from 2021 to 2023. Histologic findings were grouped into probable AMR (n=52), DSA-negative C4d-negative MVI (n=42), AMR (n=71), and no AMR (n=132). Groups were further divided into those with (n=86) and without molecular signs of AMR (n=211). Outcome was assessed using a combined endpoint of allograft loss, eGFR < 15 ml/min and eGFR decline of >30%.

Results: We followed kidney allograft biopsy cases for a median of 27 months (IQR 18; 38). Molecular AMR was found in 56% of AMR, 69% of DSA-negative MVI, 13% of probable AMR, and 6% with no AMR. At 1, 3, and 5 years after biopsy, molecular AMR cases had higher rates of the combined endpoint than no molecular AMR (25% vs. 4%, 28% vs. 8%, 54% vs. 11%; p=0.0003). This difference was reproducible in all histologic groups. Rejection archetype R3 (p<0.0001), R5 (p=0.048) and R6 (p<0.0001) showed significantly higher rates of combined endpoint than no molecular AMR. Creatinine (p=0.003), proteinuria (p=0.019), R3 (p=0.001) and R6 archetype score (p=0.005) and IFTA classifier score (p=0.052) remained independent predictors of outcome in a multivariate analysis.

Conclusions: Molecular AMR is associated with higher rates of kidney allograft loss and eGFR decline along the AMR continuum defined by Banff 2022.

PP_280 GRAFT OUTCOMES IN KIDNEY TRANSPLANTS FROM MARGINAL DONORS: A MULTICENTER RETROSPECTIVE STUDY

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Background: In Japan, kidney donations are scarce compared to other countries, with living donor transplants as the primary form of transplantation. To address the shortage of donors, kidney transplants from marginal donors, who do not meet standard criteria, are also performed. This study compares the transplant outcomes between marginal and non-marginal donors.

Methods: The study included 643 cases of living-donor kidney transplant recipients registered with the Michinoku Renal Transplant Network (MRTN), a network established by transplant facilities across four prefectures in northern Tohoku (Aomori, Akita, Iwate, and Yamagata) between 1998 and 2021. Patients were divided into two groups (standard donor and marginal donor) based on marginal donor criteria, which included (1) advanced age (70 years or older), (2) renal dysfunction (eGFR ≤ 80), (3) hypertension, and (4) diabetes. Background factors were assessed, and the Gray test was used to compare graft survival durations.

Results: The study found 62 elderly donors (10%), 285 donors with renal dysfunction (45%), 154 donors with hypertension (24%), and 44 donors with diabetes (6%). In evaluating background factors for each group, graft survival time was significantly shorter in elderly marginal donors (p = 0.03). No significant differences were observed with other marginal factors. The Gray test also confirmed a significant difference in graft survival duration for elderly marginal donors (p = 0.004).

Conclusions: The findings suggest that, within marginal donor criteria, advanced age (70 years or older) may be associated with a shortened graft survival period.

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PP_281 SODIUM BICARBONATE TREATMENT AND VOLUME RETENTION IN KIDNEY TRANSPLANT RECIPIENTS WITH METABOLIC ACIDOSIS

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Background: Metabolic acidosis is a frequent complication after kidney transplantation and often treated with sodium bicarbonate. However, in non-transplant CKD, concerns exist about possible volume retention due to sodium loading. As this adverse effect after transplantation is poorly studied, the aim of this research was to investigate the effect on volume retention parameters.

Methods: We performed an exploratory analysis of data from the Preserve-Transplant Study, a randomized, single-blinded, placebo-controlled trial, primarily designed to assess the effect of sodium bicarbonate on allograft function. Participants (n=242) were randomized 1:1 at 3 university hospitals in Switzerland (Zurich, Berne, Geneva) to receive 1.5 to 4.5 g/d sodium bicarbonate or placebo over 24 months. We investigated changes in body weight, renin, aldosterone, nighttime systolic blood pressure (SBP) dipping, antihypertensive medication use and sodium balance throughout the study period applying descriptive statistics and mixed effects regression models.

Results: Sodium bicarbonate treatment was associated with weight (kg) gain (between-group difference (BGD): 1.21, 95% CI from -0.14 to 2.56; p = 0.08), reductions in logarithmized plasma renin (mU/l) (BGD: -0.13, 95% CI from -0.34 to 0.08; p = 0.23) and plasma aldosterone (ng/l) (BGD: -0.17, 95% CI from -0.29 to -0.04; p = 0.008). Subgroup analyses by treatment dosage, eGFR, serum bicarbonate level, and concomitant antihypertensive medication showed no evidence for differential treatment effects. Sodium bicarbonate was associated with a higher chance of nighttime SBP dipping (odds ratio: 2.28, 95% CI from 0.88 to 5.87; p = 0.089). Antihypertensive drugs remained similar in both groups. We observed elevated serum sodium levels (mmol/l) (BGD: 0.55, 95% CI from 0.13 to 0.97; p = 0.01) and increased logarithmized sodium excretion (mmol/24h) (BGD: 0.17, 95% CI from 0.08 to 0.26; p=0.0003) in the sodium bicarbonate group.

Conclusions: Sodium bicarbonate treatment of metabolic acidosis after kidney transplantation was associated with weight gain, reductions in plasma renin and aldosterone and a higher chance of nighttime SBP dipping. These findings emphasize the need for further confirmatory research to clarify risks and benefits and thereby direct treatment decisions.

PP_282 THE ROLE OF CYTOMEGALOVIRUS AND CORTICOSTEROIDS ON PNEUMOCYSTIS PNEUMONIA IN TRANSPLANT RECIPIENTS

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Background: *Pneumocystis jirovecii* pneumonia (PCP) is a significant opportunistic infection in solid organ transplant (SOT) recipients. However, the impact of cytomegalovirus (CMV) co-infection and adjunctive corticosteroid therapy on clinical outcomes remain controversial.

Methods: We retrospectively studied SOT recipients diagnosed with PCP from April 2018 to March 2024. Patient demographics, clinical characteristics, morbidity and mortality were analyzed. Morbidity and mortality were further evaluated based on the presence of pulmonary CMV co-infection and the use of adjunctive corticosteroid therapy.

Results: Of 112 SOT recipients with PCP (median age: 60 years [Interquartile range (IQR), 52-66], 57% male), kidney (49%) and liver (38%) transplants were most common. Late-onset PCP (>1year post-transplant) was observed in 77 patients (68.7%), with a median onset of 20.3 months (IQR 10.7-92.5). CMV co-infection was identified in 30.4% of cases and was associated with significantly increased morbidity, including prolonged hospital stays (85 vs. 22 days, p<0.001), higher ICU admission rates (76% vs. 38%, p<0.001), and increased mechanical ventilation requirement (74% vs. 36%, p<0.001) though no significant difference in 30-day and 90-day mortality was observed. In moderate-to-severe PCP cases (n=77), adjunctive corticosteroid therapy did not demonstrate significant benefits in hospital length of stay (39 vs. 37 days, p=0.67), ICU admission rates (67% vs. 70%, p=0.78), need for mechanical ventilation (54% vs. 70%, p=0.18), or mortality at 30 days (8.3% vs. 21%, p=0.32) and 90 days (17% vs. 28%, p=0.27)

Conclusions: CMV co-infection was associated with significantly increased morbidity but not mortality, whereas adjunctive corticosteroid therapy showed no significant benefit for either morbidity or mortality in moderate-to-severe cases. These findings suggest the need for targeted strategies to mitigate the impact of CMV co-infection and re-evaluation of steroid use in SOT recipients with moderate-to-severe PCP.

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PP_283 CLINICAL SIGNIFICANCE OF 5-YEAR PROTOCOL BIOPSY IN KIDNEY TRANSPLANTATION

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Background: Although surveillance biopsy within one year after kidney transplantation (Tx) has been proposed to lead to early detection of graft dysfunction, such as subclinical rejection, the value of medium or long term protocol allograft biopsy has scarcely been discussed.

Methods: This study included 65 adult kidney transplant recipients, ≥ 18 years of age, who underwent Tx at our center between April 2008 and December 2018 and 5-year protocol biopsy from 4 to 6 years after kidney Tx. Light microscopy findings were assessed in accordance to the Banff classification. Immunofluorescence staining using antibodies for IgG, IgA, IgM, complement components (C1q, C3, C4, C4d) and fibrinogen was performed in 58 recipients and electron microscopy in 57. The patients studied were followed up until the end of the observation period in December 2024.

Results: The mean estimated glomerular filtration rate (eGFR) of the recipients at the 5-year biopsy was 47.6 ± 12.3 mL/min/1.73 m^2.The prevalence of ≥ 2 positive score for arteriolar hyalinosis (ah ≥ 2) was 23.1%. The prevalences of positive scores ≥ 2 for hyaline arteriolar thickening (aah ≥ 2), tubular atrophy (ct ≥ 2), interstitial fibrosis (ci ≥ 2) and total inflammation (ti ≥ 2) were all 12.3%. The main pathological diagnosis of 5-year biopsy in 10 patients was *normal*, interstitial fibrosis/tubular atrophy (IF/TA) grade I was diagnosed in 41, IF/TA grade II in 6, IgA nephropathy in 4, *borderline* in 3 and chronic active antibody-mediated rejection in 1. Depending on the pathological findings on protocol biopsy, we reduced the dose of immunosuppressants, mainly calcineurin inhibitors, in 30 patients; modified the immunosuppressive regimen, for example, everolimus addition, in 9; or treated with steroid for nephropathy or graft inflammation in 6 recipients. Graft function, namely, the mean eGFR 1 year after the biopsy (48.1 ± 12.5) did not decrease compared with that at the 5-year biopsy (p = 0.486).

Conclusions: These results indicate 5-year protocol kidney biopsy might lead to medical intervention for the purpose of maintaining graft function in medium term after Tx.

PP_284 TORQUE TENO VIRUS DOES NOT AFFECT LONG-TERM OUTCOMES IN LIVER TRANSPLANT RECIPIENTS: A MULTICENTER COHORT STUDY

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Background: Liver transplant recipients have twice the cancer risk of the general population and de novo cancer is a leading cause of mortality after transplantation. Torque Teno Virus (TTV) is a potential marker of immune function, but its association with long-term outcomes remains unexplored.

Methods: This was a Scandinavian, multicenter cohort and biobank study. Plasma samples collected one year after transplantation were analyzed for TTV load to investigate the association with (1) *any* de novo cancer, (2) de novo cancer excluding non-melanoma skin cancer (NMSC), (3) NMSC, and (4) all-cause mortality using Cox regression analyses. The 5-year cumulative incidence of any de novo cancer was calculated using the Aalen-Johansen estimator. TTV load was log10-transformed and categorized into low-, and high-TTV load.

Results: A total of 625 liver transplant recipients were included. During a median follow-up of 4 years, 83 (13%) recipients developed 105 de novo cancers of which 39 were de novo cancers excluding NMSC, 66 were NMSCs, and 47 (8%) recipients died. In the multivariable regression analyses, a high- vs. low-TTV load was not associated with *any* de novo cancer when adjusting for age, sex, time from transplantation to TTV measurement, prior cancer, retransplantation, cirrhosis, HCC, and autoimmune liver disease (adjusted hazard ratio [aHR] 1.03 [95% confidence interval 0.64–1.67]). Similarly, a high-TTV load was not associated with de novo cancer excluding NMSC, NMSC, or all-cause mortality (aHR 1.20 [0.64–2.25], 1.00 [0.50–2.01] and 1.00 [0.53–1.86], respectively). The 5-year cumulative incidence of any de novo cancer in the cohort was 17.2% [13.5–20.9] and was not significantly different between the low and high-TTV group (p = 0.386).

Conclusions: This large multicenter cohort study in liver transplant recipients, found no association between TTV load measured one year after transplantation and de novo cancer or all-cause mortality.

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Infectious diseases, malignancies & long term challenges

PP_287 CYSTINOSIS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: CASE CONTROL STUDY FROM KUWAIT

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Background: Cystinosis is an autosomal recessive liposomal storage multi-system disease characterized by deficient cystinosin that results in cystine accumulation in the lysosomes. It can lead to end-stage kidney disease in most cases before 20 years' age. We aimed to evaluate the outcome of renal transplantation in pediatric renal transplants with cystinosis.

Methods: Data of renal transplant recipients with Cystinosis (n=15) in Hamed Al-Essa organ transplant center were retrospectively evaluated against matched control cohort (n=128). Demographic data in both groups were compared and post-transplant complications and both graft and patients' outcomes were assessed.

Results: Most of cystinosis patients (53.3%) were Kuwaiti males in their second decade of life with their mean age 13.3±3.9 vs. 68% and mean age of 14 ±3.1 years in the control group. The two groups were comparable regarding type of donor, pre-transplant comorbidities (p>0.05). The percentage of cystinosis cases with immediate graft function was significantly higher than the control (p=0.024), and this was reflected by relatively lower basal creatinine but did not rank to significance (>0.05), and they received significantly less induction therapy (p=0.002). The two groups were maintained on a comparable immunosuppressive regimen and we did not find any significant difference between the two groups regarding post-transplant complications like post-transplant diabetes, viral infections, graft function at 1,3,5,10 years, and both graft and patient outcomes were comparable (p>0.05).

Conclusion: Under standard immunosuppression therapy with steroid calcineurin inhibitors, mycophenolate mofetil, renal transplant is safe with good long-term outcome in patient with cystinosis.

PP_288 URINARY METABOLITE PROFILES ASSOCIATED WITH RENAL FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: In a steady state, urinary excretion of metabolites is not necessarily directly related to renal function, but rather to the balance between exposure and breakdown. Therefore, the urinary metabolome provides valuable insights into systemic metabolic pathways. We aimed to investigate urinary metabolite profiles associated with renal function in kidney transplant recipients (KTR).

Methods: Urinary metabolite concentrations were measured using gas chromatography-mass spectrometry (GC-MS) in a cohort of KTR and corrected for dilution effects using creatinine. Principal component analysis with varimax rotation was applied to identify principal components that explain variability in the metabolite data and their relationship to markers of renal function.

Results: Urinary data from 513 KTR (230 females (44.8%), 57 ± 13 years) were included, with an estimated eGFR of 50.3 ± 17.6 mL/min/1.73m². The first principal component (PC1), accounting for 14,7 % of variation in the dataset, represented high loadings of the urinary metabolites 3-hydroxyisobutyric acid, 2-ethylhydracrylic acid, 3-hydroxypropionic acid, 3-hydroxyisovaleric acid, 2-methyl-3-hydroxybutyric acid, 2-hydroxybutyric acid and glycolic acid. PC1 showed a strong positive correlation with renal function markers cystatin C-estimated glomerular filtration rate (eGFR) ($r = 0.50$, $p < 0.001$) and creatinine eGFR ($r = 0.60$, $p < 0.001$), after adjusting for sex, age, and race. Among the individual metabolites, 3-hydroxyisovaleric acid ($r = 0.56$ with cystatin C eGFR and $r = 0.60$ with creatinine eGFR, both $p < 0.001$) and glycolic acid ($r = 0.56$ with cystatin C eGFR and $r = 0.60$ with creatinine eGFR, both $p < 0.001$) were strongest. These strong correlations were unique to PC1 and were not observed for other principal components.

Conclusions: A strong correlation was identified between PC1, representing specific urinary metabolites, and the renal function markers cystatin C-eGFR and creatinine-eGFR. The high loadings of metabolites like 3-hydroxyisovaleric acid and glycolic acid may indicate disruptions in metabolic pathways, including amino acid metabolism, in KTR. These findings provide a foundation for further research into the role of these pathways in kidney diseases and the potential use of these metabolites as biomarkers.

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Infectious diseases, malignancies & long term challenges

PP_291 SINGLE CENTRE TRANSPLANT OUTCOMES OF KIDNEYS FROM HEPATITIS C VIREMIC DECEASED DONORS

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Background: Demand for kidney transplantation is greater than organ availability and hence efforts to increase the deceased donor pool are needed. The development of direct acting antivirals (DAAs) has facilitated the use of kidneys from hepatitis C (HCV) viremic donors. Outcomes when using HCV viremic donor kidneys in the UK are unknown.

Methods: We undertook a single centre, retrospective, observational cohort study of kidney transplants undertaken using HCV viremic donors between 2016-2024. All kidney transplant recipients (KTRs) were screened for the development of HCV viremia post-transplant, and DAAs were started once viremia was detected. We assessed success of HCV treatment and determined graft and patient outcomes at 1 year

Results: 16 kidney transplants were undertaken from HCV seropositive donors and 6 donors were HCV viremic. Median viremic donor age was 47 (IQR 32-53) years, 5 (83.3%) were DCD, and median terminal creatinine was 75 (IQR 55-75) umol/L. Median KTR age was 62 (59-62.75) years, 5 (83.3%%) patients were male, and 5 (83.3%) were on dialysis prior to transplant with median time on dialysis 1281 (IQR 722-1581) days. No recipients of HCV seropositive non-viremic donors developed viremia. All recipients of viremic kidneys developed HCV viremia by day 10 post-transplant and were treated with Glecaprevir/Pibrentasavir. HCV clearance occurred in all patients at a median of 9.5 (IQR 6-13) days. A sustained virological response at 12 weeks (SVR12) was achieved in 100% of the 4 patients who have currently completed follow-up to this timepoint. No patient developed serious adverse effects of therapy. 1-year follow-up has occurred in 4 patients; graft and patient survival are 100% and median creatinine is 107 (IQR 98-108) umol/L.

Conclusions: Transplantation using kidneys from HCV viremic deceased donors is feasible and effective, with excellent short-term outcomes in this single centre study. Longer term outcomes with data from multiple UK centres should be collated.

PP_292 LONG-TERM HEALTH IN OFFSPRING OF FEMALE ORTHOTROPIC LIVER TRANSPLANTATION RECIPIENTS - A PROSPECTIVE DUTCH COHORT STUDY

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Background: Research on long-term health outcomes of offspring born to mothers with a liver transplantation (LiTx) is limited. Existing studies focus on short-term outcomes and have small sample sizes. This is one of the first cohort studies including long-term (age >12 years) outcomes.

Methods: This is a multicenter prospective cohort study (offspring born between 1988 and July 2024). Data were collected using questionnaires and maternal electronic health records. Offspring was identified through the Dutch LiTx centers. Questionnaires covered pregnancy outcomes, infection, medication history, and physical development. The following definitions were used: low birth weight (LBW): <2500g and preterm birth: <37 weeks gestation. For offspring <8 years, developmental milestones were assessed using the Van Wiechen scheme (VWS) and questions about reading, writing and biking. For those ≥8 years, quality of life was evaluated through the Positive Health Questionnaire, which scores six dimensions: quality of life (QoL), participation (P), mental well-being (MW), daily functioning (DF), bodily functions (BF), and meaningfulness (MF). Participants rate each dimension from 0 (very negative) to 100 (very positive). Results are presented with {reference value}.

Results: Out of n=123 eligible participants, n=64 (52%) completed the questionnaire. 19% (n=12) had LBW {10%}. 24% (n=15) were born preterm {8}. Only 73% (n=46) followed reference growth curve {90%}. 89% (n=54) had an healthy age-adjusted body mass index {48%}. Of participants aged <8 (n=31), VWS milestones were reached in 94% (n=29) of cases {81-100%}. For participants aged 3.5-8 years, 100% (n=17) recognized letters, 88% (n=15) wrote letters and 94% (n=16) biked independently. For those ≥8 years (n=33), health dimension scores were: QoL 88, P 87, MW 78, DF 87, BF 84, and MF 81.

Conclusions: Maternal LiTx offspring has increased rates of premature birth and low birth weight, as well as lower rates of reaching the reference growth curve compared to the general population. However, long-term outcomes appear favorable, with higher age-adjusted rates of healthy BMI and developmental milestones attainment than the general population. Also, five of six health dimensions are rated above 80, graded as excellent in literature.

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PP_293 IMPACT OF MISSING DATA IMPUTATION STRATEGIES ON PERFORMANCES OF KIDNEY ALLOGRAFT FAILURE PREDICTION MODELS

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Background: Real-world transplantation datasets are inherently challenged by missing data, yet their handling is frequently overlooked. This is particularly crucial in risk prediction modeling, where inappropriate handling of missing data or suboptimal imputation strategies can significantly compromise model reliability. We aimed to assess the impact of imputation strategies on the development and predictive performance of a prognostic model for kidney allograft failure.

Methods: We used data from the Paris Transplant Group qualified cohort (NCT03474003) of 4,000 French kidney recipients. The regression coefficients and predictive performances of a validated Cox-based prognostication system were used as reference values. We then assigned missing values to the model's predictors ranging from 5% to 50% and imputed them using 7 single imputation (SI) methods (mean, k-nearest neighbors, 5 random forests-based) and 6 multiple imputation (MI) methods (4 MICE-based, 2 gradient boosting-based). We compared imputation errors, regression coefficients, and resulting predictive performances in terms of calibration, discrimination, overall accuracy, and clinical utility.

Results: Gradually increasing the proportion of missing data led to substantial bias in regression coefficients when exceeding 30% (for instance, at 40% missing data, absolute relative bias was 17.8% and 13% for the eGFR coefficient using MI and SI respectively). Overall, regression coefficients based on MI were closer to the reference coefficients. MI showed stable discrimination and accuracy that more closely matched the reference values compared to SI, regardless of the percentage of missing values (c-index range 0.79-0.83, Brier scores range 0.097-0.107). Decision curves showed instability above 30% of missing values, regardless of the imputation method.

Conclusions: This study demonstrates the critical importance of imputation strategies in prediction model development. While multiple imputation tended to maintain the model's predictive accuracy, our findings reveal a clear degradation of model reliability beyond 30% of missing data. These results provide practical guidance for clinical prediction modeling, emphasizing the fundamental relationship between data completeness and prediction quality.

PP_294 EFFECT OF DONOR HYPERTENSION ON GRAFT SURVIVAL IN KIDNEY TRANSPLANTATION (COLLABORATIVE TRANSPLANT STUDY)

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Background: It has been shown that recipient hypertension has a negative impact on graft outcomes after kidney transplantation. Here we explored the effect of donor hypertension on death-censored graft survival (DCGS) in deceased-donor kidney transplants using data of the Collaborative Transplant Study (CTS).

Methods: We analyzed 52,453 adult-donor adult-recipient deceased-donor kidney-only transplants performed in 226 transplant centers from around the world between 2000 and 2022. Kaplan-Meier analysis was used for univariate death-censored graft survival. Multivariable Cox regression was used for one-, three- and five-year DCGS to adjust for additional confounders.

Results: Kaplan-Meier analyses showed significantly better 1-year, 3-year and 5-year DCGS for transplantations of donors without hypertension (93.7%, 90.1% and 86.8%, respectively) compared to donors with hypertension (89.9%, 84.8% and 79.9%, respectively). Multivariable Cox regression analyses confirmed these results after adjusting for transplant number, transplant period, recipient and donor sex, recipient and donor age, geographical region, antihypertensive drugs, HLA-A+B+DR mismatches, induction therapy, CMV serostatus and cold ischemia time. As illustrated in Figure 1, multivariable Cox regression indicated increased hazard ratios for graft loss of 1.28, 1.24 and 1.25, respectively. We found no statistically significant interactions between confounders and donor hypertension, demonstrating donor hypertension as a risk factor that is independent from other confounders.

Conclusions: Our analyses showed that not only recipient but also donor hypertension has a detrimental effect on death-censored graft survival in kidney transplant patients. On-going work is carried out to evaluate how this risk factor affects the recipient blood pressure. This patient group should be closely monitored and receive appropriate treatment.

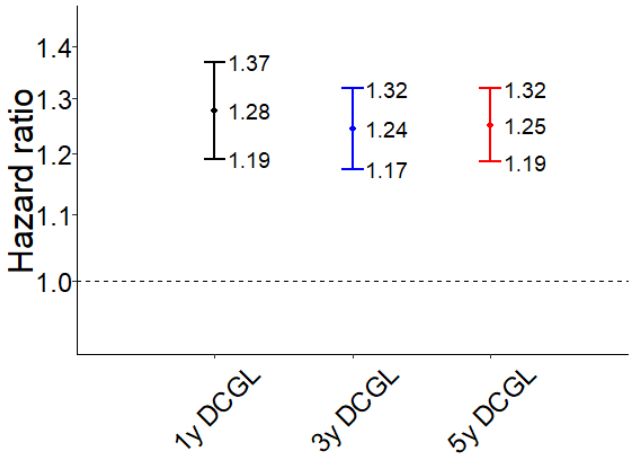

Figure 1. Hazard ratio for 1-year, 3-year and 5-year death-censored graft loss (DCGL) with 95% confidence intervals obtained from multivariable Cox regression analyses for donors with hypertension.

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Confounder	DHY: No N=26,316	DHY: Yes N=26,137	P-value	Unknown
Donor age			<0.001	-
Mean (SD)	46 (15)	59 (11)		
Number of HLA-A+B +DR mismatches			<0.001	753
0–1	5,237 (20%)	3,552 (14%)		
2–4	17,817 (69%)	17,346 (67%)		
5–6	2,876 (11%)	4,872 (19%)		
Transplant Period			<0.001	-
2000–2007	11,229 (43%)	8,623 (33%)		
2008–2015	9,091 (35%)	11,357 (43%)		
2016–2022	5,996 (23%)	6,157 (24%)		
Cold ischemia time			<0.001	5,281
Mean (SD)	18 (7.5)	16 (7.0)		
Transplant Number			<0.001	-
First transplant	22,514 (86%)	23,009 (88%)		
Retransplant	3,802 (14%)	3,128 (12%)		
CMV Serostatus			<0.001	10,954
R– D–	2,423 (12%)	2,366 (11%)		
R– D+	2,830 (14%)	3,594 (16%)		
R+ D–	4,492 (23%)	4,371 (20%)		
R+ D+	9,928 (50%)	11,495 (53%)		

Table 1. Demographics of deceased donor kidney-only transplants performed between 2000 and 2022 (DHN: Donors without hypertension, DHY: Donors with hypertension).

PP_295 HOW AGGRESSIVE IS TOO AGGRESSIVE: NAVIGATING REFLUX AND REJECTION AFTER LUNG TRANSPLANTATION

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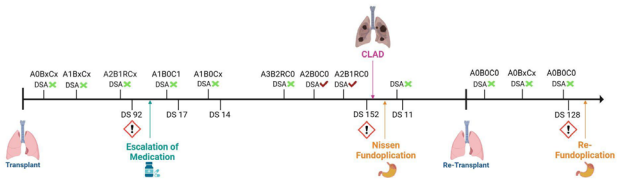
Background: Gastroesophageal reflux (GER) is a common challenge after lung transplant (Tx), linked to inferior outcomes. This case highlights the pitfalls of management of GER in a rejection-prone Tx recipient.

Case report: A 21-year old female was indicated for Tx due to end-stage cystic fibrosis. Patient was immunologically uncomplicated and received bilateral Tx, followed by an uneventful perioperative period. At 9 months post-Tx, the patient experienced A2 grade acute cellular rejection (ACR) without clear etiology. The rejection did not respond to initial anti-rejection treatment, raising suspicion of GER as the underlying cause, confirmed via pH-metry. This prompted escalation of anti-reflux therapy along with further anti-rejection treatment, resulting in a clinical response. Two years later, the patient presented a significant drop in lung function. Biopsy showed ACR grade A3, followed by *de novo* donor specific antibodies. Despite therapy, the patient developed rapidly progressive chronic lung allograft dysfunction (CLAD). Repeated pH-metry confirmed worsening GER and led to a Nissen fundoplication. Following pHmetry afterward was negative. A year after fundoplication, re-Tx was performed due to end-stade CLAD. Post re-Tx course was favourable, with no rejection complications. However, surveillance pH-metry showed persistent GER despite status after fundoplication. Given the patient's history of rejection associated with GER, a second Nissen fundoplication was performed as a preventive measure. Following this intervention, the patient remains rejection-free. Interestingly, no bile acids in bronchoalveolar lavage or GER symptoms were present through the entire course. Figure.

Conclusions: This case highlights a link between GER and rejection, ultimately necessitating re-transplantation. The role of fundoplication as a preventive versus curative strategy warrants further study, emphasizing the need for comprehensive GER management guidelines in lung transplant patients.

Figure: Timeline of patient's post-transplant course. Above the timeline are depicted performed biopsies and donor-specific antibodies (DSA), below DeMeester Scores (DS) of performed pH-metries.



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Infectious diseases, malignancies & long term challenges

PP_296 RISK FACTORS AND OUTCOMES OF METABOLIC COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS: A LONG-TERM STUDY IN THAILAND

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Background: Metabolic complications post-kidney transplantation, including post-transplant diabetes mellitus (PTDM), dyslipidemia, and obesity, significantly impact graft survival, cardiovascular diseases and mortality in kidney transplant recipients (KTRs). This study aims to identify risk factors for these complications and their impact on clinical outcomes among Thai KTRs

Methods: A retrospective analysis was conducted at Siriraj Hospital, analyzing 1001 kidney transplant recipients between 2000 and 2022. Patients with pretransplant diabetes mellitus were excluded. Risk factors and clinical outcomes, including graft loss, cardiovascular complications, and all-cause mortality related to metabolic complications were identified.

Results: In 1001 KTRs, 15% (N=150) developed PTDM. The mean age of patients was 41.7 ± 10.6 years, with 54.8% being male. Among them, 93.3%, 36.6%, and 1.6% had hypertension, dyslipidemia, and coronary artery disease as underlying diseases, respectively. The median time follow-up was 106 ± 70.7 months. The significant risk factors for diagnosed PTDM were high pre-transplant body mass index (BMI) (OR 4.48, 95% CI 1.45-5.81, P < 0.001), pretransplant hypertension (OR 3.48, 95%CI 1.06-11.45, P=0.04), and dyslipidemia (OR 2.44, 95%CI 1.63-3.64, P<0.001). Moreover, PTDM was strongly associated with newly diagnosed dyslipidemia and obesity after transplantation. Notably, post-transplant BMI ≥25 kg/m2 correlated with increased all-cause mortality and adverse composite outcomes. However, composite metabolic complications did not significantly contribute to graft loss, major adverse cardiovascular events (MACE), or all-cause mortality.

Conclusions: Metabolic complications, including PTDM, newly diagnosed dyslipidemia, and obesity, are prevalent among KTRs. Obesity significantly increases the risk of all-cause mortality and composite outcomes such as MACE, graft loss, and mortality. Therefore, effective weight management after transplantation is crucial for improving long-term outcomes. Statin therapy showed potential in mitigating mortality and cardiovascular outcomes; however, further studies are needed to validate its efficacy.

PP_297 NAVIGATING THE CROSSROADS OF IMMUNOSUPPRESSION AND INFECTION: A CASE OF HER NEUROINFECTION AFTER LUNG TRANSPLANTATION

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Background: Hepatitis E (HEV) represents a potentially lethal infectious complication after lung transplantation (LuTx). We present a rare case of HEV neuroinfection after LuTx.

Case Report: A 57-year-old female with severe COPD underwent uneventful bilateral LuTx. Basiliximab induction was followed by maintenance therapy with tacrolimus, mycophenolate mofetil (MMF), and prednisone. A year after LuTx, the patient developed acute HEV infection and ribavirin therapy (800 mg/day, patient weight: 67 kg) with MMF reduction was initiated. A month later, she presented with vertigo, headache, and diarrhea. At that time, viral load in peripheral blood was almost negative. High viral load of HEV was confirmed via lumbar puncture. MRI of the brain did not demonstrate any abnormalities. Immunosuppressive therapy was adjusted: initially reduced MMF (half-dose) was subsequently discontinued, along with prednisone reduction. Control lumbar puncture in a month showed a continued decline in a viral load, correlating with full neurological resolution. During ribavirin treatment, chronic anemia worsened (hemoglobin 76 g/L). Hemolytic anemia was ruled out (Coombs test negative, normal haptoglobin, and free Hb). However, the patient did not require erythropoietin or additional transfusions. After 3 months of negativity for HEV in serum, ribavirin therapy was stopped. No HEV relapse was observed and liver stiffness assessment revealed no evidence of fibrosis. The patient maintained stable lung function despite transient reduction of maintenance immunosuppression. Figure.

Conclusions: We present a unique case of HEV neuroinfection after LuTx, in which adjustments of immunosuppression and strict infection surveillance were essential to achieving clinical stability. Given the absence of guidelines on managing maintenance immunosuppression and optimizing ribavirin therapy (both duration and dosage) in LuTx recipients, further clinical studies are required.

Figure: Evolution of HEV viral loads in serum and CSF with corresponding medication adjustments and laboratory trends post-LuTx

Time post LuTx	HEV (CSF) IU/ml	HEV (serum) IU/ml	MMF (Dose) mg/day	Ribavirin (Dose) mg/day	Hb g/L	WBC x10⁹
9 months	N/A	N/A	2000	N/A	107	11.1
12 months	N/A	77895115	1000	800	99	9.9
13 months	5748	36	**STOPPED**	800	86	2.3
14 months	3891	**NEGATIVE**	**STOPPED**	800	76	2.9
15 months	N/A	**NEGATIVE**	1000	STOPPED	93	6.3

HEV: Hepatitis E virus, CSF: cerebrospinal fluid, MMF: mycophenolate mofetil, Hb: hemoglobin, WBC: white blood cell count

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PP_298 KIDNEY TRANSPLANT RECIPIENTS NON-RESPONSIVE TO COVID-19 VACCINE DEVELOP SIMILAR ADAPTIVE IMMUNE RESPONSES AFTER BOOSTER

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Background: Kidney transplant recipients (KTRs) remain at risk for developing severe COVID-19, especially KTR with impaired immune responses due to immunosuppressive therapy. Additional vaccine doses improve virus-specific immune responses, but the quality of these immune response upon repeated booster remains unclear. This study compares the quality of antibody and T-cell responses in KTRs who responded to the priming vaccination (detectable antibodies 28 days after two mRNA-1273 doses, initial responder) versus KTRs with detectable antibodies 28 days after additional doses (late responder).

Methods: Age- and sex-matched initial (n=40) and late (n=40) responders were selected from two clinical studies. Serum and PBMCs were analyzed for the presence of functional antibodies and T-cells, including binding and neutralizing antibodies, Fc functions, and cytokine production (IL-21, IFN-γ, T-helper cytokines). T-cell activation and phenotyping were assessed by detection of activation-induced markers (AIM) assay and spectral flow cytometry.

Results: Both groups showed significant increases in binding and neutralizing antibodies 28 days after the last vaccination (p<0.0001), with no differences between initial and late responders. Fc-mediated functions were also similar. T-cell responses were comparable in IFN-γ and AIM+ CD4/CD8 T cell frequencies, but IL-21 production was higher in initial responders (p<0.01). Spectral flow cytometry revealed minor differences in CD8 and γδ T cell phenotypes, with late responders showing higher frequencies of CD8 TEMRA cells and increased CD8 expression on γδ T cells. UMAP analysis identified three AIM+ CD4 T cell clusters: activated memory cells, CD27-CD28+ cells, and Tregs, with activated memory cells more frequent in initial responders.

Conclusions: Functional antibody responses were comparable in both groups. Minor differences in T cell phenotype between groups is likely an indication of the delayed response. Combined, the data suggest that late responders achieve similar protection from severe COVID-19 with additional doses.

PP_299 COMPARISON OF LOCOREGIONAL AND SURGICAL TREAMENT FOR HEPATOCELLULAR RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: The indication for liver transplantation (LTx) for hepatocellular carcinoma (HCC) is increasingly expanding, with the development of criteria that include an ever-increasing number of patients, at the expense of the increase in post- LTx HCC recurrence. Innovations in interventional radiology have led to the development of therapeutic alternatives to the classic surgical resection of HCC. The efficacy and safety of treatments for post- LTx HCC recurrence have been analyzed , comparing patients eligible for the different therapeutic options.

Methods: The literature search was performed on PubMed and Scopus databases without time limit until April 2024. Clinical studies describing survival after HCC recurrence in LTx patients were retrieved for full text evaluation. The included studies were 1174. After elimination of duplicates, case reports, studies without full text availability, and non-English language studies, a total of 15 retrospective studies were selected.

Results: The surgical group had a higher median OS and DFS at 1 year (73% and 60%) compared to the OS and DFS at 1 year (61% and 47%, respectively) of the non-surgical group (p value 0.028). However, the surgical group, compared to the non-surgical group, had a lower number of pre-LTx Milano-out cases (18% vs 42%, p value 0.031), a reduced rate of histologically poorly differentiated HCC (22% vs 61%, p value 0.018), a lower finding of microvascular invasion (21% vs 38%, p value 0.02) and a median alpha- fetoprotein concentration lower pre-LTx (9 ng /ml vs 24.2 ng /ml, p value 0.042).

Conclusions: Based on all included studies, surgery provides the best prognosis, in terms of OS and DFS, for the treatment of post- LTx HCC recurrence . However, most patients, especially those with more critical recurrence patterns, are not considered suitable for the resective option . In oncologically advanced patients, therefore, loco-regional interventional therapies (TACE, TARE, RFA) present clear results in terms of survival. Finally, the pre-LTx characteristics most correlated with the surgical treatment of HCC recurrence have been highlighted.

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PP_302 PROPROTEIN SUBTILISIN KEXIN CONVERTASE INHIBITION AMONG KIDNEY TRANSPLANT RECIPIENTS: KUWAIT EXPERIENCE

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Background: The benefits of reduction in low-density lipoprotein cholesterol by evolocumab (nearly 60%) has not been evaluated properly among kidney transplant recipients. We aimed to assess the effectiveness and safety of evolocumab, a proprotein convertase subtilisin/kexin-9 inhibitor, in changing lipid profile and cardiovascular events among kidney transplants in a randomized controlled study.

Materials and methods: We enrolled 197 kidney transplant recipients with high cardiovascular risk score (>20). Patients who received evolocumab (140 mg sc injection every 2 weeks) comprised group 1 (n = 98) while patients who were maintained on statin therapy alone comprised group 2 (n = 99). We followed patientsin both groups clinically and with necessary laboratory investigations over 24 months.

Results: Demographic characteristics were comparable in the two groups (P > .05). Before enrollment in the study, smokers were significantly more prevalent in group 1, whereas posttransplant diabetes mellitus was more prevalent in group 2 (P = .033). Moreover, the baseline serum creatinine was higher in group 1, whereas immunosuppression was equivalent in both groups (P > .05). We found no significant differences between the 2 groups regarding cardiovascular events. Moreover, both graft and patient outcomes were comparable (P > .05). The higher baseline cholesterol in group 1 (5.5 vs 4.7 mmol/L; P < .001) decreased significantly after 3 months and thereafter (P = .031) compared with the corresponding levels in group 2 (P < .001). We reported 2 cases of acute myocardial infarction and 1 atrial fibrillation in group 2.

Conclusions: Proprotein convertase subtilisin/kexin-9 inhibitors, as an added therapy to statins, are safe and effective in treating hypercholesterolemia after kidney transplant. Evolocumab can minimize cardiovascular events after kidney transplant in patients with high events at baseline. Longer-term trials with larger number of patients are needed to confirm its beneficial effects on cardiovascular complications and patient and graft survival.

PP_303 SELF-REPORTED HEALTH AND QUALITY OF LIFE AMONG SOT RECIPIENTS; INSIGHTS FROM THE VALUE-BASED HEALTHCARE SYSTEM

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Background: Next to survival, Quality of life (QoL) is an important outcome after solid organ transplantation (SOT). We investigated differences in patient self-reported QoL and health before and after transplantation (tx) and compared QoL and self-reported health between SOT recipients of heart, lung, liver and kidneys.

Methods: QoL and health-rating were measured cross-sectionally via our online value-based healthcare system using the PROMIS (Patient Reported Outcome Measurement Information System) Global Health questionnaire in patients before and after SOT between July 2023 and October 2024. The questions (Global01) 'In general, would you say your health is' and (Global02) 'In general, would you say your quality of life is' were scored on a scale ranging from 1 (poor) to 5 (excellent). We assessed QoL prior and 1-10 years after SOT. For kidney tx recipients no measurements prior to tx were available. Descriptive statistics were used, and non-paired between group comparisons were made with ANOVA.

Results: The questionnaire was completed by 158 unique SOT recipients before tx and 1089 after tx. Health-rating and QoL pre- and post-tx across SOT types is presented in table 1. Comparing pre-tx self-reported health and QoL across SOT type, both health-rating and QOL are significantly lower in lung tx recipients than in liver tx recipients (P<0.01). The mean self-reported health-rating increased significantly between pre- and post-tx in all SOT types. QoL increased significantly among lung tx recipients (p<0.001) and heart tx recipients (p=0.01) (based on very small numbers).

Conclusions: An increase in health status is observed in assessed SOT recipients. The largest improvement is observed among lung tx recipients, who also have the lowest pre-tx QoL. More, paired and repeated measurements will be performed as time progresses, and will provide additional insights. For now, the value-based healthcare system already offers valuable insights, and will prove invaluable for future value-based health outcome research.

Health rating						Quality of life					
	Pre		Post		P-value		Pre		Post		P-value
Organ	N	Mean±SD	N	Mean±SD		Organ	N	Mean±SD	N	Mean±SD	
Heart	2	2±1,4	81	3,2±1.1	0.05*	Heart	2	3,0±1,4	79	3,5±1,0	0.01*
Liver	30	2,5±1,1	193	3,0±0,9	0.04	Liver	31	2,7±1,2	195	3,1±0,9	0.17
Lung	126	1,9±0,8	134	2,7±0,9	<0.001	Lung	124	2,1±0,8	139	3,1±0,9	<0.001
Kidney			680	2,9±0.9		Kidney			676	3,2±0.9	

Table 1. Self reported health-rating and QoL across different SOT. No pre-tx data was available for kidney tx recipients. *These P values should be interpreted with caution given the very limited pre-tx values.

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Infectious diseases, malignancies & long term challenges

PP_306 LONG TERM OUTCOMES OF RENAL TRANSPLANTATION IN PATIENTS WITH END STAGE KIDNEY DISEASE DUE TO STONE FORMING CONDITIONS

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Background: The absence of published data on renal transplantation in patients with end stage kidney disease (ESKD) secondary to stone forming conditions is a noticeable gap in the existing literature. The aim of our study is to provide the first insight into long-term renal allograft outcomes in this patient population.

Methods: We performed a retrospective review of patients who underwent renal transplantation surgery in a National Kidney Transplant Service between 1977 and 2022 and identified all those with ESKD secondary to stone forming conditions. The primary outcome variables were allograft survival, death censored allograft survival and overall patient survival. The secondary outcome variable was the incidence of nephrolithiasis in the renal allografts.

Results: Of the 4,959 transplant recipients, 60 recipients (1.21%) had ESKD secondary to stone forming conditions. The mean recipient age was 47 years +/- SD (range 1 - 70). The median follow-up time from time of first transplant until death or censoring was 13.3 years. Allograft survival was 88.6%, 79.5% and 63.1% at 1, 5, and 10 years post renal transplant respectively. Death censored allograft survival was 92.8%, 86.5% and 76.9% at 1, 5, and 10 years post renal transplant respectively. Overall survival was 96.4%, 94.5% and 82.1% at 1, 5, and 10 years post renal transplant respectively. Only one patient required surgical intervention for kidney stones, and no incidental nephrolithiasis was identified in the renal allografts of the 18 patients who underwent CT imaging.

Conclusions: There were no statistically significant differences in graft-specific survival (P=0.917), death censored graft survival (P=0.497) or overall survival rates (P=0.925) between recipients with ESKD secondary to stone forming conditions and recipients with ESKD due to other causes in a matched patient cohort. ESKD due to stone forming conditions is not a risk factor for de novo stones in a renal allograft.

PP_307 CMV INFECTION IN SEROPOSITIVE KIDNEY TRANSPLANT RECIPIENTS WITH DIVERSE IMMUNOLOGICAL RISKS UNDER PREEMPTIVE STRATEGY

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Background: Cytomegalovirus (CMV) infection remains the most prevalent viral infection in kidney transplant recipients. Despite effective preventive strategies, the use of desensitization therapies and potent immunosuppressive agents in patients with high immunological risks underscores the ongoing significance of CMV as a major concern. This study aims to establish the incidence and outcomes of CMV infection in patients with diverse immunological risks.

Methods: We evaluated 614 CMV seropositive adult patients who underwent kidney transplantation between 2010 and 2020. CMV was managed in a preemptive setting and patients were screened using quantitative CMV PCR tests. CMV infection was defined as detectable CMV DNAemia based on PCR testing.

Results: 231 patients (37.6%) underwent immunologically incompatible transplantation, including 75 ABO- and 156 HLA-incompatible transplants. During the median follow-up of 60 months, 354 patients (57.7%) experienced CMV infection. Multivariable analysis identified older recipient age, deceased donor, rituximab, and anti-thymocyte globulin as independent risk factors for CMV infection, while the use of mammalian target of rapamycin inhibitor was identified as protective. Multivariable Cox regression analysis confirmed that CMV infection was independently associated with increased risks of death-censored graft loss (adjusted hazard ratio [aHR], 2.05; 95% confidence interval [CI], 1.17-3.59) and all-cause mortality (aHR, 3.40; 95% CI, 1.60-7.23).

Conclusions: CMV infection negatively impacts graft and patient outcomes in seropositive recipients managed under preemptive strategies. These findings emphasize the need for enhanced CMV prevention strategies in recipients with high immunological risks.

	Multivariable[a]	
Variables	**aOR (95% CI)**	**p-value**
Recipient age	1.015 (1.000, 1.029)	0.044
Use of Rituximab	1.717 (1.113, 2.649)	0.015
Use of Anti-thymoglobulin		
No use	reference	
Low cumulative dose (≤ 6.0mg/kg)	2.712 (1.776, 4.144)	<0.001
High cumulative dose (> 6.0mg/kg)	10.595 (5.804, 19.340)	<0.001
Deceased donor	1.683 (1.081, 2.619)	0.021
Use of mTOR inhibitor	0.277 (0.126, 0.612)	0.001

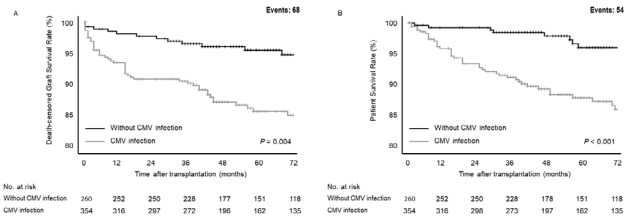

Table. Risk factors for CMV infection

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PP_308 DE NOVO MALIGNANCIES IN KIDNEY TRANSPLANTED PATIENTS- A CASE SERIES PRESENTATION

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Background: Kidney transplant patients(KTP) face a higher risk of developing malignancies compared to general population and dialysis patients, with a 2 to 5-fold increased risk. It is considered primarily due to the use of immunosuppressive agents in order to preserve the graft function. These drugs weaken the immune system, making it less effective at identifying and destroying pre/cancerous cells. Malignancies account for a significant portion of mortality in KTP, contributing from 9% to 16% of deaths.

Methods: Over a period of 14 years(2010-24), 241 patients underwent kidney transplantation (KTx) in a single center. Fifteen of those developed some type of cancer. We reviewed retrospectively the clinical features and the outcomes of these KTP from their medical charts.

Results: During the follow-up, there were 15 cancer cases, 10(66.6 %) males, with cumulative incidence of de novo malignancies 6.22%. The mean time for cancer onset after KTx was 8.13± 3.3 years. The mean age of cancer onset in KTP was 51.93±11.04 years, ranging from 34-78 years. Twelve (80%) patients received anti-thymocyte globulin (ATG), and 20% were on basiliximab, as an induction therapy, while 53,3% had a maintenance therapy with tacrolimus+-mycophenolate mofetil and prednisolone. Death occurred in six (40%) KTP with de novo malignancies. The most common initial malignancy was skin cancer (40%), followed by two cases, each of: some type of hematologic malignancy, breast cancer and renal cell carcinoma- one originating from the renal graft, and singe cases of testicular seminoma, anaplastic oligodendroglioma and adenocarcinoma of papilla of Vater. The baseline characteristics of the KTP with de novo malignancies are summarized in table 1.

Conclusions: Since malignancies are claimed an important cause of death in KTP and have a higher risk of developing cancer than the general population, it's an imperative to define as save as possible immunosuppressive regimen and tailor it, in accordance to the evaluated risk for malignancies. Also a proper screening at specific intervals and individual risk approach should be enabled for their follow-up. We anticipate that cancers detected in an early stage will be treated in a shorter and more efficient time, patient and graft survival will increase, and the financial burden of the health care system reduced.

Table 1. Kidney transplant patient's demographic and clinic characteristics.

Case No	Gender	Type of Tx LKD/ CAD	Age of Tx	Age of Ca onset	Time of Ca onset after Tx (years)	Immunosup. Treatment Induction / Maintenance	Type of tumor	Treatment	Evolution
1	M	CAD	55	59	4.5	ATG / CyA, MMF, CS	NHL	Surgery/ chemotherapy	Remission/ Alive
2	F	LKD	31	39	8	ATG/ CyA, MMF, CS	Melanoma malignum	Surgery/ chemotherapy	Metastasis/ Death
3	M	LKD	67	78	11	ATG/ CyA, MMF, CS	Carcinoma cutis auriculae	Surgery/ No follow up	MS/ Death
4	M	LKD	45	52	7	Basiliximab/ CyA, MMF, CS	RCC	Surgery	Remission/ Alive
5	M	LKD	47	53	6	ATG/ TAC, MMF, CS	Skin Basal-cell carcinoma	Sugery	Folow up/ Alive
6	M	LKD	37	50	13	Basiliximab/ TAC, AZA, CS	Skin Basal-cell carcinoma	Surgery	Remission/ Alive
7	F	CAD	42	45	3	ATG/ TAC, MMF, CS	Breast Cancer St. IIIa	Surgery/ Radio and hormonal therapy	Ongoing Treatment/ Alive
8	M	LKD	25	34	9	Basiliximab/ TAC, MMF, CS	Seminoma testis	Surgery/ Chemoth.	Remission/ Alive
9	M	LKD	48	54	5.5	ATG/ TAC, MMF, CS	Skin basal-cell carcinoma	Surgery	Remission/ Alive
10	M	LKD	41	46	5	ATG TAC, MMF, CS	Plasmablastic plasmocytoma	None	Death onset at the time of dg.
11	M	LKD	44	57	13	ATG/ CyA, MMF, CS	RCC/ Invasive urothelial Ca.	Surgery	Alive
12	F	LKD	35	46	8	ATG/ CyA, MMF, CS	NMSC	Surgery/ Follow up	Alive
13	F	LKD	50	58	8	ATG/ TAC, MMF, CS	Adenoca. Papilla of Vater	Surgery	Death
14	F	LKD	35	42	7	ATG/ TAC, MMF, CS	Invasive Breast Cancer/MS.	Surgery/ Radio and hormonal therapy	Death
15	M	CAD	52	66	14	ATG/ CyA, MMF, CS	Anaplastic Oligodenro-glioma	Surgery	Death

M - male; F - female; Tx - Transplantaion; LKD - Living kidney donor; CAD - Cadaveric donor; Ca - cancer; ATG - antithymocyte globulin; CyA - cyclosporine A; MMF - micophenolat mofetil, CS - corticosteroids; TAC - tacrolimus, NHL - Non Hodgkin lymphoma; MS- metastasis; ; NMSC- Non- melanoma skin cancer

PP_309 SWITCHING TENOFOVIR DISOPROXIL FUMARATE TO TENOFOVIR ALFENAMIDE IN LIVER TRANSPLANT RECIPIENTS WITH CHRONIC HEPATITIS B

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Background: Chronic hepatitis B virus (HBV) continues to pose a significant global health threat, even with the existence of vaccination programs and effective antiviral medications. Progression to cirrhosis and related complications is also influenced by age, gender, level of fibrosis upon diagnosis, and presence of viral co-infections. Untreated chronic hepatitis B (CHB) in adults can lead to cirrhosis in 8% to 20% of cases within five years. Antiviral treatment aims to reduce the health complications and deaths associated with CHB. Tenofovir alafenamide (TAF) is the latest agent approved for treating chronic hepatitis B virus (HBV). The study aims to assess the patient's renal function after switching from TDF to TAF, evaluate the HBV disease burden, assess new or recurrent hepatocellular carcinoma (HCC), and determine the incidence of any type of rejection.

Methodology: This is a single-center, retrospective study assessing switching from TDF to TAF in post-liver transplant patients. Patients > 18 years old who were on TDF and subsequently switched to and remained on TAF for at least 4 weeks were included. The primary outcome is to evaluate the mean change in serum creatinine levels at 3, 6, 9, and 12 months. The secondary outcomes were to evaluate for HBV disease burden (measuring HBV DNA), the incidence of new or recurrent HCC, and the incidence of any rejection during the first year after switching. (RAC# 2241207)

Results: A total of 25 patients were enrolled in the study from January 2021 to June 2024. The majority of the patients were male (76%) and had a living liver transplant (80%). The results suggest an estimated 0.016 mmol/L decline in serum creatinine per day following switching from TDF to TAF. This decline is not statistically significantly (p = 0.303), and the confidence interval for the daily change in serum creatinine is (-0.046, 0.015). Furthermore, within the first year following the switch, none of the patients exhibited a recurrence of HBV or HCC, nor did they experience any form of rejection.

Conclusion: In adult liver transplant patients, switching from TDF to TAF is associated with a slight decrease in serum creatinine levels. More prospective head-to-head studies with larger sample size are needed to determine how well these treatments compare to each other in adult liver transplant patients.

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PP_310 PREDICTIVE ROLE OF VISCERAL FAT AREA IN STABLE RENAL TRANSPLANT RECIPIENTS: MORTALITY AND CARDIO-RENAL IMPLICATIONS

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Background: Cardiovascular (CV) morbidity and all-cause mortality are highly prevalent in renal transplant recipients (RTRs). The obesity parameters measured prior to kidney transplantation (Ktx) or in the early period after Ktx were predictive for survival and CV events in RTRs. There is no data regarding the predictive role the visceral fat area (VFA) in late period after Ktx. The objective of the study was to evaluate the predictive value of VFA, in relation to various clinical outcomes in stable RTRs

Methods: At baseline, VFA was measured with InBody 170 (InBody, Eschborn, Germany) during a routine visit in RTRs. The follow-up was 54 months. The primary endpoints of the study were all-cause mortality and CV events (stroke, myocardial infarction, peripheral artery thrombosis). Secondary endpoints encompassed graft loss or deterioration in renal function (at least 30% increase in blood creatinine concentration). VFA receiver operating characteristics (ROC) curve analyses were employed to assess the prognostic capabilities. Predictive cut-off values were established using the Youden method. Kaplan-Meier curves were employed to scrutinize the likelihood of a patient's survival based on VFM value falling below or exceeding the determined cut-off values.

Results: 335 stable RTRs with a median age of 52.7 years, (62.5% male) transplanted between 1994 and 2018, were enrolled. The mean creatinine level, estimated glomerular filtration rate value, and transplantation vintage were 1.47mg/dl, 50.5ml/min/1.73m^2, and 73 months, respectively. The median VFA was 93,2cm^2 153 patients (44.5%) were obese according to a VFA value >100 cm^2 Cut-off values for all-cause mortality, CV events were for both 83.5cm2, respectively and 68.4cm^2 for renal outcomes. Spearman's analysis showed a significant correlation of VFA with total cholesterol (r=0.12), systolic blood pressure (r=0.21), diastolic blood pressure (r=0.21), and with glycated hemoglobin (r=0.41). Figure 1 shows the likelihood of patient survival, CV and renal outcomes based on VFA values falling below or exceeding the cut-off values during the follow-up.

Conclusions: VFA value has a significant predictive ability for mortality. There was no influence of VFA on CV and renal outcomes. It is necessary to perform further analysis in terms of KTRs survival and obesity.

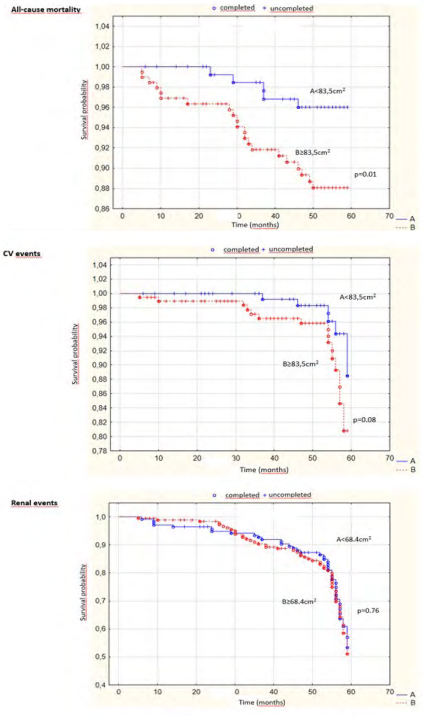

Figure 1 The predictive role of VFA in terms of all-cause mortality, CV and renal events.

PP_312 SELF-REPORTED IMMUNOSUPPRESSION MEDICATION ADHERENCE PREDICTS EGFR AT 12 MONTHS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Adherence to immunosuppression medication has been shown to be an important determinant of graft outcomes in kidney transplant recipients (KTRs). Moreover, medication non-adherence is common in KTRs, with rates estimated between 36 and 55%. This study explored the association between self-reported adherence and eGFR at 12 months follow-up.

Methods: KTRs completed the Medication Adherence Report Scale (MARS-5) when attending their outpatient appointment between September 2022 and October 2023. Patients were classed as non-adherent if they scored ≤ 24. eGFR at 12 months was extracted from electronic medical records. A hierarchical multiple linear regression was conducted to determine the impact of adherence on 12-month eGFR.

Results: N=292 KTR completed the questionnaires. Mean 12-month eGFR was 46.1 mL/min (SD=23.06) in the total sample, 49.91 mL/min (SD=23.32) in the adherent group (N=122) and 43.28 mL/min (SD=22.53) in the non-adherent (N=170). Patients classed as non-adherent at baseline had a significantly lower eGFR at 12 months, after controlling for age, ethnicity, donor type and time since transplantation (B=-6.91, SE=2.58, β =−.148, t=-2.68, *p*=.008).

Conclusions: Adherence to immunosuppression medication significantly impacts eGFR at 12 months, independent of demographic and clinical factors. These findings show the contribution of medication adherence to clinical outcomes in KTRs. Future research should aim to identify modifiable factors influencing adherence, informing the development of targeted, evidence-based interventions to support medication adherence and optimise graft outcomes.

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PP_313 CHRONIC KIDNEY DISEASE AFTER VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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Background: Chronic kidney disease (CKD) is a significant complication in nonrenal transplant recipients (NRT), including vascularized composite allotransplantation (VCA) recipients who require lifelong immunosuppression. This study investigated renal function in an international cohort of VCA patients from 17 centers over a follow-up period of 1-10 years (median: 8 years).

Methods: The study included 70 patients: 59 recipients of upper extremity allotransplantation (UET: 38 bilateral, 14 right and 7 left cases), 10 recipients of face and 1 of penis transplantation. Demographic data, immunosuppressive regimens, and serum creatinine values were collected pre- and post-transplantation to calculate eGFR using CKD-EPI 2021. Key outcomes included a ≥50% eGFR decline at consecutive follow-up points, eGFR <29 ml/min, and end-stage kidney disease (ESKD: dialysis or kidney transplantation).

Results: Pre-transplantation, the median eGFR was 105.36 ml/min (71.09–155.39), with 83% of patients at CKD stage 1 and 17% at stage 2. By 3 months post-transplant, eGFR decreased significantly (median: 78.42 ml/min, p=0.001) but remained stable thereafter. Despite higher tacrolimus levels at 3 months, no correlation was found between its levels and eGFR at any time. Over the follow-up, 17.1% of patients experienced a ≥50% eGFR decline, 6.3% progressed to CKD stage 4, and 4.5% developed ESKD. All ESKD cases occurred in UET recipients. The current study's limited sample size, comprising only 3 cases of end-stage kidney disease (ESKD) and 4 cases of CKD stage 4, unequivocally hindered our ability to demonstrate a significant correlation in a multivariate mixed model between the incidence of ESKD or a decline in eGFR of at least 50% and any risk factors.

Conclusions: Renal function decline is evident in VCA recipients, but the incidence of severe outcomes, including ESKD, is lower compared to NRT recipients. While calcineurin inhibitors, particularly tacrolimus, are known to be nephrotoxic, this study could not establish a direct correlation between tacrolimus exposure and renal decline due to limited sample size and therapeutic regimen changes. Strategies to minimize calcineurin inhibitor exposure, especially early post-transplant, are recommended for preserving long-term renal function.

PP_315 INTERACTION OF FRAILTY AND CORONARY DISEASE: RESULTS FROM THE KIDNEY TRANSPLANTATION IN OLDER PEOPLE STUDY

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Background: Frailty increases the risk of adverse clinical outcomes in patients with coronary artery disease (CAD) in the general population. Whilst there has been increasing recognition of the impact of frailty in patients undergoing kidney transplantation, the utility of cardiac screening remains a contentious issue. The aim of this study is to assess the interaction between frailty and CAD, and report on the associated outcomes in the context of transplantation.

Methods: A sub-analysis of the Kidney Transplantation of Older People Study (KTOP) was undertaken. KTOP is a single centre, prospective, longitudinal observational study of waitlist patients >60 years. Frailty was assessed at the time of recruitment by the Edmonton Frail Scale. All patients underwent cardiac screening prior to waitlist activation. Median follow up post recruitment was 4.4 (3.7-5.0) years.

Results: 115 participants who underwent transplantation were analysed, 38 (33.0%) were frail/vulnerable to frailty and 53 (46.0%) had pre-existing CAD. Pre-existing CAD was associated with increasing age, gender and diabetes, but not frailty (**Table 1**). 32 (60.4%) participants with CAD had undergone a coronary artery intervention (CABG/PCI). There were 14 (12.2%) ACS (acute coronary events) post-transplant, 5 occurring in the first month post-transplant. Participants with CAD were at increased risk of a post-transplant ACS (p=0.018), but there was no association between frailty and ACS (p=0.69). In participants with CAD, there was a was a trend for those who were frail to have inferior patient outcomes in the first-year post-transplant; death with a functioning graft (p=0.05) and overall patient survival (p=0.12). Two participants with ACS, and 9 overall, died in the first-year post-transplant, no death was primarily attributed to CAD.

Conclusion: Pre-existing CAD and frailty are common in older transplant recipients. The possible impact of frailty on outcomes in waitlist patients with pre-existing CAD is an important novel finding which requires a dedicated, adequately powered study to investigate further.

		NO CAD N=62 (%)	CAD N=53 (%)	p value
Frailty Status	No Frail/Vulnerable	41 (66.1) 21 (33.9)	36 (67.9) 17 (32.1)	0.84
Age (years)		63 (61-66)	65 (62-68)	0.031
Male		33 (53.2)	39 (73.9)	0.025
Ethnicity (Caucasian)		15 (24.2)	12 (22.6)	0.11
Diabetes		26 (41.9)	35 (66.0)	0.01
Charleson Co-morbidity Index		5 (4-6)	7 (5-8)	<0.001
Time at ESKD at recruitment (days)		735 (254-1479)	771 (535-1313)	0.93

Table 1. Demographics of KTOP participants with and without CAD

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Infectious diseases, malignancies & long term challenges

PP_316 SAFETY OF LIVING RIGHT LIVER DONOR AGED 45 AND OVER: RISKS AND OUTCOMES FOR DONORS AND RECIPIENTS

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Background: The increasing age of liver donors reflects a growing need to address donor shortages. However, the safety and viability of grafts from old aged donors remain unclear. This study aimed to compared donor and recipient outcomes in living donor liver transplantation (LDLT) using right lobe (RL) grafts from older donors (≥45 years, OD) versus younger donors (<45 years, YD).

Methods: LDLT outcomes using RL grafts from the OD group were compared to those from the YD group, both before and after propensity score matching (PSM).

Results: A total of 4,415 RL donors were analyzed, including the OD group (N=4,177) and the YD group (N=238), along with their corresponding recipients (N=4,415). Donor morbidity, including overall, major (Clavien-Dindo ≥3a), biliary, and vascular complications, were not showed in the OD group compared with YD groups. However, recipients of OD RL grafts showed significantly higher incidence of biliary stricture (9.2% vs. 6.2%; p=0.035), 1-year graft failure (5.5% vs. 1.1%; p=0.001), and reduced long-term graft survival (p=0.004) compared to the YD group. These outcomes were consistent after PSM. Multivariate analysis identified OD grafts as a significant risk factor for 90-day biliary stricture and 1-year graft failure. No donor mortality occurred, and all donors fully recovered to their baseline activity levels.

Conclusions: LDLT using RL grafts from donors aged ≥45 years increased the risk of biliary stricture and early graft failure in recipients, while donor safety was not compromised. Careful recipient selection and donor-recipient matching are critical when considering older donors.

PP_317 THE RENAL IMPACT OF NUCLEOS(T)IDE ANALOGUES IN LIVER TRANSPLANTATION PATIENTS

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Background: Liver transplantation is indicated for complications of chronic hepatitis B (CHB) infection, including full-blown liver failure, decompensated cirrhosis, and hepatocellular carcinoma. Potent nucleos(t)ide analogs (NAs) such as entecavir (ETV), tenofovir disoproxil fumarate (TDF), or tenofovir alafenamide (TAF) are considered the first line treatment for CHBs. However renal dysfunction is a major safety concern for patients with CHB during long-term NAs. We aimed to explore the association between the potent NAs treatment and the risk of renal dysfunction for patients with CHB post liver transplantation.

Methods: This retrospective study enrolled 165 patients with CHB received liver transplantation and treated with ETV (n=146) and TDF/TAF (n=19) in Taipei Veterans General Hospital between January 2011 and March 2022. In a 3-year follow-up, the primary outcome was renal dysfunction, which was defined as estimated glomerular filtration rate decreased >30%, or a chronic kidney disease stage worsen ≥ 2 stages compared to baseline.

Results: There were no significant differences in the risk of renal dysfunction between use of TDF/TAF or ETV (HR 0.68; 95%CI 0.31-1.47, P=0.324). A multivariate analysis showed concomitant use of diuretic was a risk factor for renal dysfunction (HR 2.11; 95%CI, 1.33-3.35, P=0.0015).

Conclusions: There were no significant differences in the risk of renal dysfunction between CHB patients after liver transplantation treated with ETV or TDF/TAF.

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PP_319 CAUSES AND FACTOR ASSOCIATED WITH EARLY GRAFT LOSS IN KIDNEY TRANSPLANT RECIPIENT

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Background: Advances in immunosuppressive protocols, surgical techniques, and careful selection of recipients have led to excellent short-term outcomes for kidney transplant recipients. Despite this, there have been only modest improvements in long-term graft survival, with many patients eventually requiring retransplantation or returning to dialysis, which is associated with poor outcomes. This study aims to investigate the factors contributing to early graft loss in kidney transplant recipients by comparing characteristics between graft survival and early graft failure groups.

Methods: We included patients who underwent kidney-only transplantation at a single UK center from 2012 to 2019. Prospective demographic and clinical data were collected. We compared variables between patients with graft failure (return to dialysis or re-transplantation) within 1-5 years post-transplant and those with functioning grafts at 5 years, excluding those who died with a functioning graft.

Results: A total of 591 patients were analyzed, comprising 531 with graft survival and 60 with graft failure within 1-5 years. No significant differences in recipient age, sex, ethnicity, or native kidney disease cause were found. Notably, recipients with graft survival had a trend toward more pre-emptive transplantations and shorter pre-transplant dialysis times. Delayed graft function was more prevalent among patients with graft failure, who also had higher creatinine levels at 1-year post-transplant. Increased intra-patient tacrolimus variability and higher rates of rejection (T-cell and antibody-mediated) were observed in the graft failure group. The leading cause of allograft failure was rejection, accounting for 40% of cases, followed by unresolved AKI, infections, chronic injury, and recurrent disease.

Conclusions: Rejection is the primary cause of early graft failure within 1-5 years post-transplant. The findings emphasize the importance of addressing medication adherence and improving treatments for rejection occurring after the first post-transplant year.

Fig 1: Analytic flow of patients

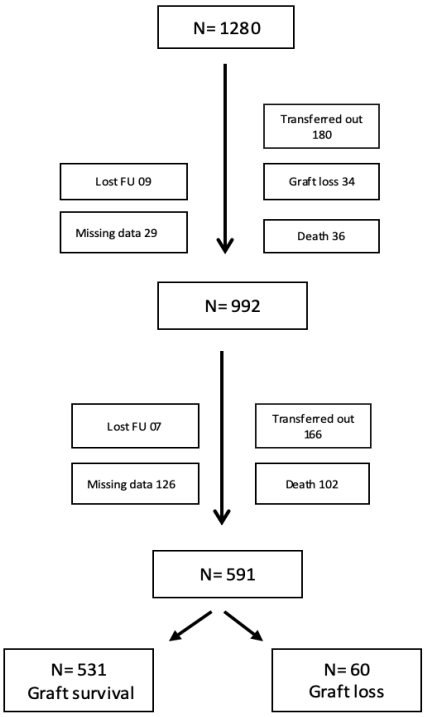

Table 1: Variables in patients with graft survival to 5 years and patients with graft failure group at 1-5 years post-transplant

Baseline characteristics	Graft survival (Control group)	Graft loss at 1–5year post transplant	P value
Median (IQR) or N (%)	**N=531 (89.8%)**	**N=60 (10.1%)**	
RECEPIENT DETAILS:			
Age at transplant	50(18-78)	47(20-78)	0.554
Gender -Male -Female	 342(64.9%) 185(35.1%)	 37(57.8%) 27(42.2%)	0.265
Ethnicity -White -Asian -Black	 233(44.2%) 155(29.4%) 139(26.4%)	 27(42.2%) 14(21.9%) 23(35.9%)	0.213
Cause of native kidney disease DM Non-DM	 103(19.5%) 424(80.5%)	 15(23.4%) 49(76.6%)	0.462
BMI	25.5(16-41.1)	25.65(15.6-39.7)	0.810
Dialysis before transplant -HD -PD - Pre-emptive Tx	 274(52.0%) 106(20.1%) 147(27.9%)	 40(62.5%) 15(23.4%) 9(14.1%)	0.060
Time on dialysis (days)	815 (3-5958)	1137(73-3026)	0.069
cRF% <1 1-84 >85	 312(59.2%) 156(29.6%) 59(11.2%)	 36(56.3) 19(29.7%) 9(14.1%)	0.782
No. of grafts 1 2 3 4	 455(86.3%) 60(11.4%) 9(1.7%) 3(0.6%)	 56(88.9%) 7(11.1%) 0(0.0%) 0(0.0%)	0.431

Table 2: Incidence of causes of graft loss after one year of kidney transplantation

Characteristics	Graft survival (Control group)	Graft loss at 1–5year post transplant	P value
Median (IQR) or N (%)	**N=531 (89.8%)**	**N=60 (10.1%)**	
DONOR DETAILS:			
Donor type -Live donor -DBD -DCD	 155(29.4%) 228(43.3%) 144(27.3%)	 13(20.3%) 29(45.3%) 22(34.4%)	0.256
Cause of death in deceased donor -Trauma -Cardiovascular -Other	 50(13.7%) 292(79.8%) 24(6.6%)	 5(9.8%) 42(82.4%) 4(7.8%)	0.708
ECD	58(11.0%)	9(14.1%)	0.529
HLA Mismatch 0 1 2 3 4 5 6	 39(7.4%) 26(4.9%) 106(20.1%) 197(37.4%) 114(21.6%) 30(5.7%) 15(2.8%)	 4(6.3%) 3(4.7%) 16(25.0%) 20(31.3%) 16(25.0%) 3(4.7%) 2(3.1%)	0.941
Characteristics	**Graft survival (Control group)**	**Graft loss at 1–5year post transplant**	**P value**
Median (IQR) or N (%)	**N=531 (89.8%)**	**N=60 (10.1%)**	

Causes of early graft loss	N- 60
Rejection: -TCMR -ABMR + Transplant glomerulopathy -TCMR+ACMR	24 (40%) 11 09 04
Infections: 1. BK nephropathy 2. Pyelonephritis	10 (16.6%) 03 07
IFTA	06 (10%)
Recurrent GN	07 (11.6%)
Unresolved AKI/ATN	12 (20%)
Unknown	1 (1.6%)

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PP_320 CONSTRUCTION AND IDENTIFICATION OF AN ALLOGENEIC SELECTIVE GENE KNOCKOUT MOUSE MODEL FOR CHRONIC ALLOGRAFT NEPHROPATHY

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Background: To construct and characterize a model of chronic rejection of transplanted kidney in allogeneic selective knockout mice.

Methods: Male 6- to 8-week-old Balb/c^{H2d} and C57BL/6^{H2b} mice, with mismatched major histocompatibility complexes, were purchased and divided into two groups: Chronic allograft nephropathy group(Balb/c^{H2d}→C57BL/6^{H2b} CAN, n=30) and syngeneic renal transplantation (C57BL/6^{H2b}→C57BL/6^{H2b} , SYN, n=20). In stage one, the CAN group received TAC (1mg/kg·d) for 1w, 2w, or 4w, with samples collected at 4w post-transplantation. Stage two identified 2w as the optimal TAC treatment time, with subgroups based on different post-transplant time points (4w, 8w, 12w, 16w). Stage three involved macrophage Rictor gene knockout mice to assess its impact on immune response. Pathological, immunohistochemical staining, and Banff scores were performed, along with creatinine and urea nitrogen measurements.

Results: In the CAN group, the TAC-1w group showed severe rejection and tissue necrosis in the renal grafts, while the TAC-2w group exhibited more interstitial fibrosis than the TAC-4w group. Fibrosis, tubular atrophy, and vascular lesions in the CAN group were significantly greater than in the SYN group, but did not worsen after 8w. After renal transplantation, creatinine were higher in the CAN group than in the SYN group. At the same time, serum urea nitrogen were higher in the CAN group than in the SYN group. Immunofluorescence staining showed that macrophage infiltration in the 4w-CAN group's transplanted kidney was highest, and gradually decreased with time progression. At 4w after kidney transplantation, Rictor expression in macrophages was low, and selective Rictor knockout led to increased fibrosis compared to the non-knockdown group.

Conclusions: In this study, we successfully constructed a model of chronic transplant kidney rejection in allogeneic wild-type and selective knockout mice with Balb/c^{H2d} as donor and C57BL/6^{H2b} as recipient by using an immunosuppressive regimen of TAC (1mg/kg·d) for 2w post-transplantation.

PP_321 POST-TRANSPLANT OUTCOMES BY MENTAL ILLNESS

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Background: Severe or persistent mental illness (SPMI) may impact kidney transplant outcomes, yet evidence is limited. This study investigates the association between pre-existing SPMI and key post-transplant outcomes: acute rejection, graft failure, and mortality.

Methods: We conducted a population-based retrospective cohort study using data from the Australian and New Zealand Dialysis and Transplant Registry linked to administrative health data from New South Wales (NSW, the largest state in Australia with population over 8 million). The study included NSW residents who received their first kidney transplant between 2005 and 2020. WE defined pre-existing SPMI based on hospitalizations and non-admitted mental health service contacts (primary diagnosis of psychosis or multiple mental health service contacts over more than two years). Time to acute rejection, graft failure, and death were analysed using Kaplan-Meier plots and Cox regression, adjusted for age, sex, and ethnicity, with random effects to account for clustering by transplant hospital.

Results to date: Among 2,941 recipients, 496 (17%) had pre-existing SPMI. Compared with no mental illness, those with SPMI had similar rates of acute rejection (HR 1.00, 95% CI 0.72–1.40, p = 0.9), and mortality (HR 0.77, 95% CI 0.57–1.04, p = 0.2), However, those with SPMI were more likely to experience graft failure (HR 1.59, 95% CI 1.04–2.44, p = 0.08).

Conclusions: Pre-existing SPMI is associated with an increased risk of graft failure but not with acute rejection or mortality in kidney transplant recipients. These findings highlight the need for tailored post-transplant care for patients with SPMI to improve outcomes.

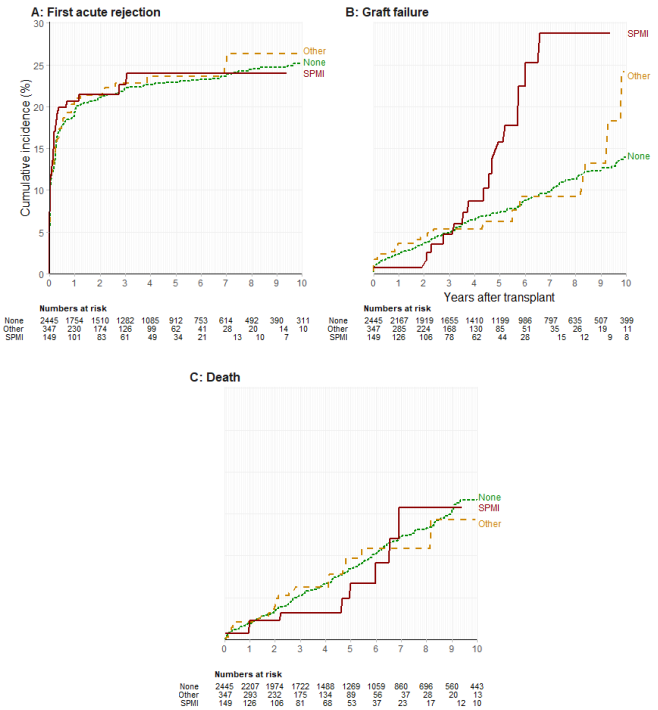

Figure 1: Cumulative incidence plots

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PP_323 TUBERCULOSIS IN KIDNEY TRANSPLANT RECIPIENTS: A 16-YEAR EXPERIENCE IN A TUNISIAN CENTER

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Background: Tuberculosis remains prevalent in our country and poses significant challenges in kidney transplant recipients due to atypical presentations, drug interactions, and potential impacts on graft and patient survival. This study evaluates the prevalence, clinical features, diagnosis, management, and complications of tuberculosis in kidney transplant recipients.

Methods: A retrospective study was conducted on kidney transplant recipients at Sahloul University Hospital, Sousse, from January 2007 to December 2023.

Results: Among 325 recipients, 5 cases of tuberculosis (1.53%) were identified. Patients, aged 32.8 years on average, included 3 males and 2 females. All received living donor grafts and immunosuppressive therapy. Tuberculosis occurred within the first year post-transplant in 2 cases and at 19, 45, and 132 months in others. Symptoms included prolonged fever (4 cases), general deterioration (2 cases), diarrhea (1 case), and leukopenia (3 cases). Pulmonary tuberculosis with extrapulmonary involvement was seen in 3 patients, while 2 had isolated extrapulmonary forms. Treatment included RHZE followed by rifampicin and isoniazid for 12–20 months. No severe complications, graft rejection, or mortality occurred.

Conclusions: Though rare, tuberculosis in kidney transplant recipients remains challenging. Early diagnosis and effective management ensured favorable outcomes, preserving graft and patient survival.

PP_324 STRONG-HD-VIE - PREVALENCE OF STRONGYLOIDES STERCORALIS INFECTION IN HEMODIALYSIS PATIENTS IN VIENNA, AUSTRIA

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Background: *Strongyloides stercoralis (S. stercoralis)* infection is widespread in tropical regions and rare in Europe. However, globalization, migration and global warming are contributing to an increase in cases in Central Europe. Individuals undergoing high-dose corticosteroid treatment, such as kidney transplant (KTX) recipients, are at risk of the potentially lethal hyperinfection syndrome if they harbor latent *S. stercoralis* infection. This syndrome is characterized by autoinfection with *S. stercoralis*, hyperinflammation, severe sepsis, and possibly death. Hyperinfection syndrome can be prevented by a short course of ivermectin treatment. This raises the question of whether KTX candidates should undergo screening for *S. stercoralis* infection. Thus, we assesed the prevalence of *S. stercoralis* infection in all hemodialysis patients in Vienna, Austria

Methods: Blood samples were collected from all consenting hemodialysis patients (n=720) and analyzed for IgG-antibodies. A questionnaire was used to determine prior soil exposition, medical and travel history, symptoms indicative of helminthic infection, and immunosuppressive therapy. Positive serologies were reanalyzed by the Austrian reference center for parasitosis to confirm the results, three stool samples were taken for examination for worm eggs/larvae.

Results: Of the 720 patients, 90 (12.5%) had a history of organ transplantation (10 multiple KTX, 2 heart transplants, 3 liver transplants). *S. stercoralis* - IgGs were detected in 69 patients (9.5%), including 9 with prior KTX. Among IgG-positive patients, gastrointestinal symptoms were reported in 14.4% (n=10), and pruritus in 18.5% (n=13). 74.2% (n=52) had a travel history to endemic areas, 50% (n=35) owned pets and 32.8% (n=23) reported soil contact. However, there were no statistically significant differences in these variables between IgG-positive and IgG-negative patients (p>0.05).

Conclusions: With globalization, migration, and climate change facilitating the spread of helminth infections, the prevalence of *S. stercoralis* in Austria is increasing. As one in ten dialysis patients tested positive for *S. stercoralis*, pre-KTX screening should be considered.

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PP_326 DEFINITION AND CLINICAL IMPACT OF DELAYED GRAFT FUNCTION AFTER PANCREAS TRANSPLANTATION

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Background: Delayed graft function after pancreas transplantation (pDGF) still lacks a homogenous definition. Consequently, its clinical impact is poorly characterized.

Methods: 151 consecutive pancreas transplants (PTx) were performed at the Medical University of Innsbruck between January 2011 and December 2021. 142 were evaluated after excluding those with early graft loss.

Results: pDGF was defined as a mean insulin requirement of ≥ 2.5 UI/day in the first 10 post- transplantation days. 52 recipients (36.6%) developed pDGF. By multivariate analysis, pDGF was associated with donor age (OR 1.05; p=0.010) and the continuous postoperative administration of unfractionated heparin (OR 2.52; p=0.025). pDGF lead to longer hospital stay (23 vs 20 days, p=0.049), intensive care unit stay (5 vs 3 days, p<0.003) and impaired glycemia at day 10 postoperative (146.0 vs 126.4 mg/dl, p<0.001). Also, pDGF was associated with pancreas graft failure at 5 years (p=0.047) in the univariable analysis, while in the multivariable, this trend was not statistically significant (p=0.076). In the multivariable analysis, pDGF showed a strong trend towards worse graft survival without reaching statistical significance (HR:2.33, p=0.069).

Conclusions: pDGF represents a common condition, depending both on donor and recipient conditions. Its clinical impact concerns the postoperative stay and the graft survival.

PP_328 VACCINATION COVERAGE FOR WAITING LIST OR SOLID ORGAN TRANSPLANT PATIENTS

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Background: People who have received or will receive a solid organ transplant are at higher risk of contracting an infectious disease due to their compromised immunity. For transplant recipients, it's important to be vaccinated against the main current infectious diseases. We aimed to link the information of Catalan transplant and waiting list registries with vaccination data of Catalonia's shared clinical record.

Methods: Data of all alive patients included in the transplanted or waiting list population-based registries was used. Information about the doses of vaccines administered in Catalonia and recorded in the shared clinical record was available from 1990 and contains more than 150 million doses. Data linkage was made on 15/11/2024 and describes the vaccination coverage of patients with a functioning kidney (n=8,039), heart (n=654), liver (n=2,598), lung transplant (n=532) or on waiting list (n=1,528). Nominal lists of patients were also generated to provide centers with information about the doses their patients received. Information of vaccination against COVID-19, Herpes Zoster, Pneumococcal, Influenza, Hepatitis B, RSV, HPV and tetanus was obtained. A patient is considered vaccinated when at least one dose has been administered, regardless of the date. Regarding flu, the date of dose should be after the start of the last campaign, and for COVID-19 the last vaccination dose should be less than a year ago.

Results: Figure 1 describes the percentage of vaccination coverage against the different infections and type of transplant. This information was described at center level and shared with hospitals. Nominal lists of patients with information related to doses received of each vaccine were also available.

Conclusions: The information obtained has allowed us to know the vaccination coverage of transplant or waiting list patients, improve the logistics of vaccination campaigns by prioritizing the patients to be vaccinated, and know the vaccine hesitancy. For the oldest vaccines, such as tetanus, the information available in the clinical record is not complete, although there is an intention to improve it by incorporating deferred immunization data. The next data linkage is planned for June 2024 and will show the evolution of the coverage.

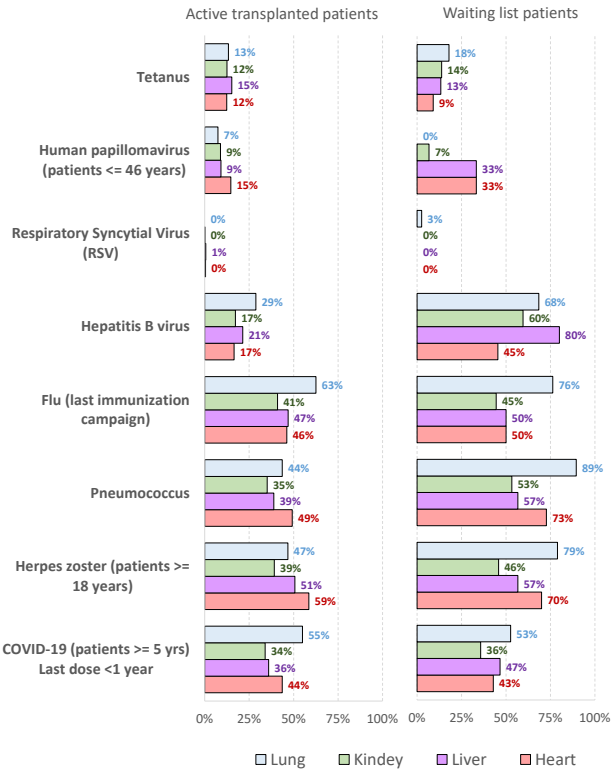

Figure 1. Immunization coverage by vaccine and organ

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PP_329 UNVEILING DONOR-ORIGINATED BKPYV VIREMIA IN KIDNEY TRANSPLANT RECIPIENTS

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Background: BK Polyomavirus (BKPyV) is of notable concern in kidney transplant recipients, as it can lead to BKPyV DNAemia and progress to BKPyV-associated nephropathy (BKPyVAN). BKPyVAN can cause significant damage to the transplanted kidney, potentially resulting in graft loss. Currently, there is no effective treatment for BKPyV infection, underscoring the critical need for preventive strategies. There is emerging evidence that donor-derived BKPyV plays a role in the development of BKPyV DNAemia. To further explore this hypothesis, we conducted a retrospective, multi-center cohort study to evaluate the risk of developing BKPyV DNAemia in kidney recipient pairs from the same deceased donor.

Methods: At Leiden University Medical Center, we identified all recipients of deceased kidney donors between 2011 and 2021 who developed BKPyV DNAemia within the first year post-transplantation. An equal number of recipients who did not develop BKPyV DNAemia within the first year were randomly selected as a control group. The contralateral kidney recipients were identified through the Dutch Transplantation Foundation, and relevant data were obtained with assistance from the respective transplant centers. Cox regression analysis was used to assess whether recipients from the same donor had an increased risk of developing BKPyV DNAemia if the LUMC recipient had experienced BKPyV DNAemia, compared to recipient pairs where the LUMC recipient did not develop BKPyV DNAemia.

Results: A total of 265 postmortem kidney transplant recipients at the LUMC were included, of whom 128 developed BKPyV DNAemia within the first year. Data from 81 contralateral kidney recipients, transplanted across 4 centers were analyzed. The incidence of BKPyV DNAemia was significantly higher among recipients whose contralateral kidney recipient also developed BKPyV DNAemia compared to those whose contralateral recipient did not (28.6% [10/35] vs. 10.9% [5/46], p = 0.042). The corresponding hazard ratio was 3.05 (95% CI: 1.04–8.94, p = 0.042)

Conclusions: This study highlights a significantly increased risk of BKPyV DNAemia in recipients of deceased kidney donors when the contralateral recipient develops BKPyV DNAemia. These findings underscore the critical influence of donor-related factors in BKPyV transmission in kidney transplantation.

PP_331 RETROSPECTIVE REVIEW OF KIDNEY TRANSPLANTS IN SMALL PAEDIATRIC PATIENTS AT REDCROSS WAR MEMORIAL CHILDREN'S HOSPITAL

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Background: For children with kidney failure (KF), kidney transplant is the choice of treatment. Advances in surgical techniques, immunosuppressive therapies and treatments for diseases that previously limited organ recovery for transplantation have allowed a successful outcome in this special group of patients. A high incidence of vascular thrombosis and primary graft failure are responsible for the poor outcome. The same is also true for very young recipients, this is related to vascular thrombosis, technical complications and acute cellular and vascular rejection. We wanted to assess outcomes of kidney transplantation in small children <18 years (weight less that 20 kg).

Methods: Retrospective descriptive study of all kidney transplant for the last 20 years (2002-2022) performed at Red Cross War Memorial Children's Hospital

Results: There were 52 transplants performed during the study, 2 were part of a combined liver and kidney transplant due too primary hyperoxaluria. Sixty nine percent were males and thirty percent females. Four patients had a re-transplant, three for chronic rejection and one for graft loss resulting from venous thrombosis. The median age at transplant was 5 years with a median donor age of 13 years. The weight at transplant was at a median of 14.50 kg. Surgical related complications were at 15.4% (8/52). Two patients experienced graft failure from renal vein occlusion. Urinary tract related infections were experienced in 44% (23/52). Early primary disease recurrence was experienced in 2 (3.8%) of the grafts due to FSGS and HUS/TTP. Fourteen patients have demised. One year patient survival 89.5% (43/48) and 5-year patient survival 77% (37/48). Overall graft survival reported was 1 year graft survival 44/52 (84.6%) and 5 year graft survival 30/52 (57.6%).

Conclusions: The study demonstrates that kidney transplantation in small children under 18 years at Red Cross War Memorial Children's Hospital yields reasonable patient and graft survival rates, despite significant challenges. While surgical complications and disease recurrence were relatively low, long-term graft survival remains an area for improvement. These findings highlight the need for enhanced strategies to optimize outcomes and manage complications in paediatric kidney transplant recipients.

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PP_332 INTRAVENOUS IMMUNOGLOBULIN FOR BK VIRUS IN KIDNEY TRANSPLANTATION: A UK-WIDE RETROSPECTIVE CASE SERIES

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[1]Leeds Teaching Hospitals NHS Trust, [2]St James Hospital; Leeds Teaching Hospitals Trust; Gledhow Wing Inpatient Pharmacy, [3]NHS Greater Glasgow and Clyde, [4]University Hospital of Wales, [5]Lancashire Teaching Hospitals NHS Foundation Trust, [6]Manchester University Foundation Trust; Center for Transplantation, [7]Manchester University NHS Foundation Trust, [8]NHS Fife, [9]NHS Lothian, [10]Royal Free Hospital; Royal Free London; Renal Medicine, [11]Royal Free London NHS Foundation Trust, [12]Nottingham University Hospitals NHS Trust, [13]York and Scarborough Teaching Hospitals NHS Foundation Trust, [14]Hull University Teaching Hospitals NHS Trust

Background: BK polyoma virus (BKPyV) nephropathy causes premature allograft failure. Evidence for use of intravenous immunoglobulin (IVIG) for BKPyV infection in kidney transplant recipients is limited. This retrospective case series describes the UK experience of IVIG use in BKPyV

Methods: Cases were identified via the NHS IVIG database (Medical Data Solutions and Services - MDSAS) where IVIG approvals are recorded. Centres retrospectively compiled anonymised data for relevant patients and contributed data for patients meeting inclusion criteria not identified through the initial search

Results: 25 patients (21 adult, inc. 1 SPK & 1 SIK, and 2 paediatric) from 11 UK centres received IVIG for BKPyV from 2013-2024. Lymphocyte-depleting induction used in 32% patients. Median time to BKPyV 104 days (range 28-1736). At diagnosis, 52% patients were receiving triple immunosuppression and 32% calcineurin inhibitor and anti-proliferative. All underwent immunosuppression reduction following BKPyV detection. Median time from BKPyV to IVIG administration 124 days (range 32-611). Following treatment, 32% patients cleared BK. There were 2 deaths and 7 allograft failures (28%) in the 6 months following IVIG. BK nephropathy contributed to 6/7 (86%) allograft failures. Adult patients with preserved allograft function who completed 6 months follow up had overall unchanged function with pre-treatment creatinine mean 187.1±68.8µmol/L and 6 months creatinine 205.9±95.5µmol/L (p=0.92). There was no difference in eGFR at diagnosis vs. at IVIG treatment, or at 3/6 months after IVIG (Fig. 1a). Including grafts that failed as eGFR=5ml/min shows ongoing deterioration despite IVIG (Fig. 1b, p=0.04)

Conclusions: This multi-centre case series demonstrates no clear benefit of IVIG as an adjunctive therapy for BKPyV. Most patients failed to clear BKPyV and no improvement in graft function was seen. This data does not support IVIG use as a treatment for BK virus in kidney transplant patients. Further work to define the place of IVIG in BKPyV therapy is needed.

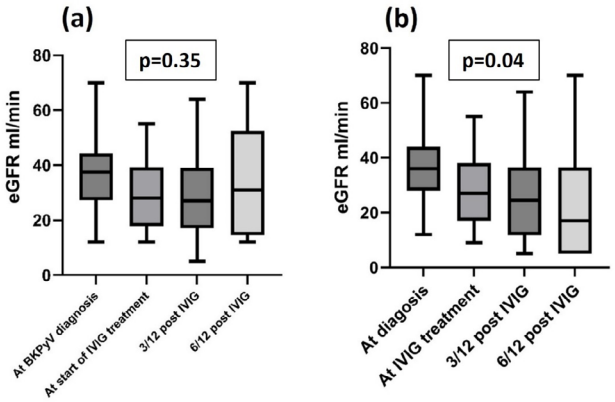

Figure 1: Renal function to 6 months post IVIG treatment for BK virus in adult kidney transplant patients; (a) excluding failed grafts; (b) failed grafts included as eGFR=5ml/min

PP_333 RISK FACTORS FOR DEVELOPMENT OF MALIGNANCIES POST-TRANSPLANTATION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Malignancies constitute a major cause of mortality in kidney transplant recipients and their incidence is increasing globally. We aimed to study the incidence of de novo malignancies and identify the factors associated with cancer development.

Methods: We extracted data on de novo malignancies in patients who received a kidney transplant in “Laiko” Hospital of Athens between 1/1979 and 12/2023. Patients with malignancy were compared with a control group of kidney transplant recipients matched for age, gender and year of transplantation. Demographic and clinical characteristics, data on immunosuppression and cancer type were collected.

Results: Out of 3.098 recipients, we identified 268 (8.6%) patients who developed malignancies in a median time of 8 (IQR 3-16) years after transplantation. 59.3% were male, median age at transplantation was 48 (IQR 39-57) years and median time on renal replacement therapy was 31.5 (IQR 9.5-70) months. 17.2% had histroy of rejection. The majority (66.7%) received a combination of mycophenolate and a calcineurin inhibitor with or without steroids. Most frequent malignancies were lung cancer (13%), post-transplant lymphoproliferative disease (PTLD, 13%) and Kaposi sarcoma (8.2%). On diagnosis, 37% had generalized end-stage disease and 19% aggressive disease with poor prognosis. No significant differences were noticed in comorbidities, primary kidney disease, time on dialysis, sensitization status, rejection and kidney function 1 year post transplant between cancer and control group. Immunosuppression medication (induction, maintenance and anti-rejection) and immunosuppression regimens also did not vary in the two groups. In multivariate analysis, history of rejection (OR 1.75) and glomerulonephritis as primary kidney disease (OR 2.23) were associated with significantly increased risk for malignancy.

Conclusions: Kidney transplant recipients are at high risk of developing malignancies. The risk is rather related with the cumulative burden of immunosuppression than a specific immunosuppressant. Close post-transplant malignancy surveillance is warranted.

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PP_334 PREVALENCE OF URINARY TRACT INFECTION ONE MONTH POST STENT REMOVAL AMONG RENAL TRANSPLANT

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Background: Ureteric stents are commonly used during kidney transplant surgery to prevent early urological complications. These stents are typically removed within a few weeks post-transplantation, during which time patients are at increased risk for urinary tract infections (UTIs). This study aims to identify factors associated with UTI occurrence within 30 days following stent removal in kidney transplant recipients.

Methods: This analysis includes data from an ongoing study of kidney transplant recipients at our center, with plans to include approximately 2000 patients who underwent transplant between 2015 and 2024. For this interim report, we present data on the first 169 patients. Patients were divided into two groups: UTI (n = 36) and Non-UTI (n = 133). Demographic, clinical, and transplant-related variables were assessed to identify significant predictors of UTI.

Results: A cohort of 169 patients was analyzed, with a UTI prevalence of 21.3% post-stent removal. The mean age of the UTI group was significantly higher (51.7 ± 16.5 years) compared to the Non-UTI group (44.6 ± 16.3 years; p = 0.03). While the sex distribution did not reach statistical significance, females exhibited a trend toward higher UTI incidence (53% in UTI vs. 39% in Non-UTI; p = 0.14). Hypertension, diabetes, and glomerulonephritis were not associated with UTI occurrence (p > 0.05). However, pre-transplant ischemic heart disease (IHD) was significantly more common in the UTI group (32%) compared to the Non-UTI group (10%; p = 0.0042). Immunological factors, such as the presence of donor-specific antibodies and HLA mismatches, were not linked to UTI risk (p > 0.05). Notably, 26% of patients who received anti-thymocyte globulin (ATG) induction developed UTIs, compared to only 9% in the Basiliximab group (p = 0.032).

Conclusions: Older age, a history of ischemic heart disease, and ATG induction are significant risk factors for developing a UTI post-stent removal in kidney transplant recipients. These findings highlight the need for targeted prevention strategies for high-risk patients. Further research is needed to explore modifiable risk factors and optimize post-transplant care.

PP_335 INCIDENCE AND LONG-TERM OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS WITH RECURRENT GLOMERULONEPHRITIS

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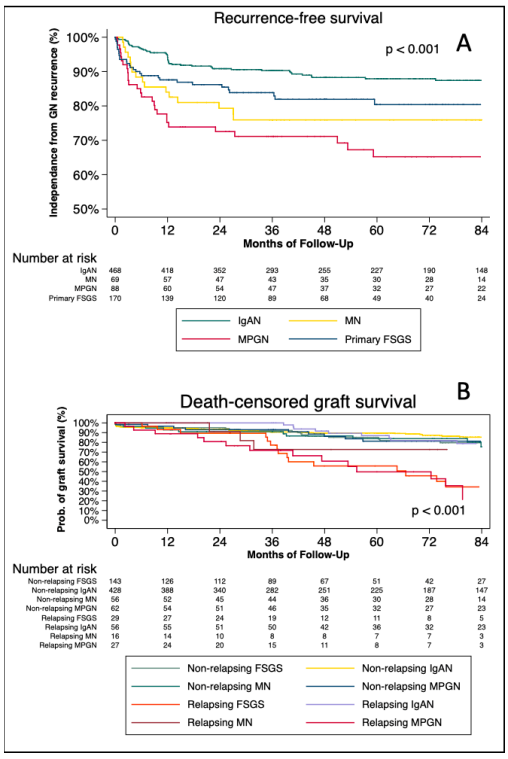
Background: Glomerulonephritis (GN) recurrence after kidney transplantation has been associated with an increased risk of graft loss. However, data addressing its impact on allograft survival are usually derived from selected cases or do not handle immortal time bias. We aimed to investigate, in a multicentric and deeply-phenotyped cohort study, the incidence of GN recurrence and its consequences regarding long-term allograft survival.

Methods: A total of 4986 consecutive patients from 5 centers across Europe and the US were enrolled in a population-based study between 2005 and 2023. Detail on initial kidney disease was provided for all patients. Each allograft biopsy performed during the patient's follow-up was annotated for lesions and diagnoses according to the latest Banff classification at the time of evaluation. Recurrence was defined by the presence on graft biopsy of lesions upon light microscopy or immune deposits in immunofluorescence study that were consistent with the initial disease. Parameters on each biopsy performed such as recurrence or rejection were assessed as time-dependent covariables in a Cox regression model.

Results: Overall, 821 patients were transplanted for a documented native kidney GN at risk of recurrence, comprising 428 (52.13%) IgA nephropathy (IgAN), 180 (21.9%) primary focal segmental glomerulosclerosis (FSGS), 90 (11%) membranoproliferative glomerulonephritis (MPGN), 71 (8.6%) membranous nephropathies (MN). One hundred thirty-four patients (16.3%) had a GN recurrence during follow-up in a median time of 8.0 months (IQR 3.0-19.8), (**Figure panel A**). During the follow-up period, 171 (20.5%) patients experienced death-censored graft-loss. Overall, recurrence was strongly associated with graft loss (HR = 4.68, 95%CI 3.18 – 6.88), even after adjustment for rejection (aHR = 4.38, 95%CI 2.97 – 6.48) with however heterogenous impact on long-term graft survival as regards the initial GN (**Figure panel B**).

Conclusions: In patients at risk of recurrent GN, long-term graft survival was strongly affected by GN recurrence, independently from biopsy proven acute rejection. The impact of recurrence was heterogenous according to each GN category.



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Infectious diseases, malignancies & long term challenges

PP_336 ANTIBODY-MEDIATED REJECTION (AMR) AND RISK OF INFECTION AFTER KIDNEY TRANSPLANTATION: A PROPENSITY MATCHED COHORT STUDY

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Background: Antibody mediated rejection (AMR) is an important cause of graft loss after kidney transplantation. Its management requires the use of immunosuppressive treatments that may enhance the risk of infection. However, the impact of AMR on infectious events remains unclear. This study aims to decipher the infectious burden of patients undergoing AMR compared to those without rejection.

Methods: A prospective cohort study was conducted, including kidney transplant recipients between 2007 and 2020 at two centers in Paris. Patients were categorized based on the first occurrence of AMR (AMR+ group) after transplantation, or the absence of any rejection including T-cell mediated rejection (AMR- group) during their follow-up. Characteristics at the time of transplant and details of each infectious complication that occurred were collected prospectively. Propensity score matching was used to control for confounding factors, and the impact of AMR on the risk of infections was assessed using an Andersen & Gill model.

Results: Among the 1926 transplanted patients, 339 patients were diagnosed with an AMR. A total of 293 patients diagnosed with an AMR (AMR+ group) were matched to 293 without AMR (AMR- group). Within the first five years post-transplant, 782 infectious events occurred in the AMR+ group (684 documented, 224 patients), compared to 658 events among AMR- patients (581 documented, 178 patients). While overall infection rate was similar in the 2 groups prior to rejection (or biopsy without rejection features), it was significantly higher among AMR+ group after rejection compared to AMR- group (HR 1.39 [1.02-1.89], p=0.039), even if the patients were not being treated. Importantly, an increased risk of viral (HR 2.09 [1.46-3.0], p<0.001) and opportunistic infections (HR 1.92 [1.37-2.69], p=0.001), was also observed after AMR whether CMV was included or not.

Conclusions: Overall infection rate is significantly higher in patients who experience AMR after kidney transplantation, whether or not treatment is initiated. Risk of opportunistic infections appears particularly increased, any time after transplantation regardless of the time to AMR occurrence and challenging the traditional timeline for infection risk after transplantation.

PP_337 CONVERSION TO PROLONGED-RELEASE TACROLIMUS ALLEVIATES NEPHROTOXICITY IN PATIENTS AFTER LIVER TRANSPLANTATION

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Background: Chronic tacrolimus (Tac)-induced nephrotoxicity is a complication in the management of patients after liver transplantation (LT). While standard-release Tac is mostly used after LT, Tac can further be administered using MeltDose® technology (LCPT) leading to an extended drug release. The Tac concentration-dose (C/D) ratio is useful for assessing nephrotoxicity-related renal outcomes, as a higher ratio may enhance bioavailability and reduce renal dysfunction. The aim of the study was to investigate the effects of switching from standard-release Tac to LCPT on the C/D ratio and renal function.

Methods: This retrospective study at the University Hospital Münster (August 2010–March 2022) included adult LT recipients with at least 2 years of Tac-based therapy. Patients switched to LCPT formed the LCPT group (n = 63), while those continuing standard-release Tac comprised the control group (n = 107). The conversion day was set as baseline (t0). Clinical data were collected every three months for 24 months, with binary logistic regression used to identify predictors of eGFR improvement.

Results: At t0, both groups had comparable median C/D ratios (p = 0.553). After conversion, the LCPT group showed significantly higher median C/D ratios during the first (p = 0.003) and second (p = 0.004) years. The LCPT group also exhibited an increase in mean eGFR (2.9 ml/min/1.73 m²). In contrast, the control group showed a significant mean eGFR decline at all time points, with a 24-month decrease of -5.4 ml/min/1.73 m² (p < 0.001). In multivariable binary logistic regression, eGFR at t0 (OR 0.985, 95%CI 0.972-0.997) and use of LCPT (OR 3.334 95%CI 1.717-6.475) formulation were predictive factors of eGFR increase.

Conclusions: In comparison to standard-release Tac, LCPT appears to stabilize renal function in liver transplant recipients over a two-year period, potentially offering long-term nephroprotective benefits without compromising graft function.

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PP_338 ACTIVITY AND CHRONICITY INDICES AS PREDICTORS OF KIDNEY TRANSPLANT OUTCOMES IN AMR OR MVI

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Background: Antibody-mediated rejection (AMR) is a major cause of graft loss in kidney trasplant (KT) recipients. Banff classification includes in category 2 active AMR, chronic active AMR and chronic AMR. From 2022 update, isolated microvascular inflammation (MVI) is also incorporated in this category. Considering histologic lesions in kidney biopsies (KB), activity (AI) and chronicity indices (CI) have been developed. Only CI ≥4 has been associated to worse graft survival in AMR, yet the prognostic value of AI and CI in MVI is still unknown. Our aim was to evaluate activity and chronicity indices as prognostic tools of graft loss in AMR and MVI. We also assessed the clinical rejection phenotype combined with the indices as predictors of graft survival.

Methods: Retrospective study of KT recipients (1987-2023) with KB (2013-2023) compatible with category 2, Banff'22 AMR or MVI. We evaluated AI ([glomerulitis (g) + peritubular capillaritis (ptc), arteritis (v)] and CI ([interstitial fibrosis (ci), tubular atrophy (ct), chronic vasculopathy (cv), and 2xchronic glomerulopathy (2cg) scores)]. C4d score was excluded to avoid bias between the two groups. Those cases with increase in serum creatinine >15% and/or >500 mg or duplicated baseline proteinuria, between 3 weeks and 6 months before KB were considered clinical phenotype of rejection. Surveillance biopsies and those performed after donor-specific antibodies (DSA) detection without kidney dysfunction were comprised as subclinical phenotype

Results: One hundred thirty-eight KT recipients with AMR (n=89) or MVI (n=49) in KB were included. Death-censored graft loss at follow-up (36.5 [19.8-70.3] months) was higher in AMR (42.7% vs. 24.5%; p=0.03). AI and CI were similar in both groups. In both AMR and MVI, death-censored graft survival was worse in the group with AI≥4 and in that with CI≥4 (Figure 1). In the multivariate analysis, independent significant associations with graft loss were found for CI (per unit increase), with HR 1.2 [1.08-1.41; p=0.005] and for clinical phenotype, with HR 2.9 [1.36-6.48; p=0.006].

Conclusions: Our findings show that AMR has worse long-term outcome than MVI. Moreover, according to our results, the chronicity index and the clinical phenotype are valuable prognostic tools in AMR.

PP_339 RENAL GRAFT ELASTOGRAPHY: NON-INVASIVE TECHNIQUE FOR DIAGNOSING INFLAMMATORY, VASCULAR AND FIBROTIC CHANGES

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Background: Elastography:non-invasive technique that quantifies tissue stiffness by measuring propagation speed of impulses. Validated for quantification of liver fibrosis replacing serial liver biopsies.

Methods: We present preliminary results from an ongoing prospective study correlating elastography values with findings from renal graft biopsies. A total of 60 kidney transplant recipients (KTR): Cohort 1: De novo (<6 months post-transplant; n=31). Cohort 2: Stable (≥3 years post-transplant; n=29). All participants had an eGFR ≥30 ml/min and proteinuria ≤1.5 g/day. Each patient underwent ultrasound, elastography, and protocol renal biopsy (RB) at t1 (baseline) and t2 (12 months). Elastography was performed using point-shear wave elastography (pSWE) with QElaxto(Esaote). A specific protocol was developed: 10 pSWE measurements on the cortex, 10 on the medulla. For each dataset, calculated the median, (kPa and m/s), interquartile range (IQR), and IQR-to-median ratio for data dispersion. Correlation between elastography values and RB findings (Banff criteria) was analyzed.

Results: Data from 66 procedures were collected. 57 with lower dispersion (IQR/Median <45) were selected. Key findings include: **Global Correlations:**An inverse correlation was observed between medullary pSWE and arteriolar hyalinosis (ah≥1 vs. ah=0) in RB findings (6.5±8 vs. 14±17 kPa; p<0.058).**De novo Cohort (t1):** Inverse correlation between medullary pSWE and inflammation over fibrosis (i-IFTA≥1 vs. i-IFTA=0) (7.7±11.5 vs. 11.4±10 kPa; p<0.066). **Stable Cohort (t1):** Inverse correlation between cortical pSWE and tubulitis presence (t≥1 vs. t=0) (27±11.5 vs. 34±11.6 kPa; p<0.011) and glomerulitis (g≥1 vs. g=0) (28±11 vs. 33±10 kPa; p<0.069). **Arteriolar Thickening:** Significant inverse correlation between cortical pSWE and arteriolar thickening (CV 0-1 vs. CV 2-3: 37±13 vs. 23±4 kPa; p<0.0053; n=17; AUC=0.90) in stable cohort at t1 and t2.**Prediction of FIAT Progression:** In stable cohort at t1, medullary pSWE showed predictive capacity for >10% FIAT progression in RB at t2 (p<0.007; AUC=0.89).

Conclusions: Renal graft elastography could provide non-invasive method for diagnosing and monitoring inflammation and vascular involvement potential as a predictive tool for FIAT progression at 12 months

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PP_340 SOCIO-OCCUPATIONAL ASPECTS IN LIVER-TRANSPLANT CANDIDATES AND RECIPIENTS: A MONOCENTRIC COHORT STUDY

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Background: Cirrhotic liver diseases have made liver transplantation (LT) a life-saving treatment, especially for alcohol-related cirrhosis. Employment significantly contributes to post-transplant outcomes and quality of life, yet socio-professional factors are often overlooked in the pre-transplant period.

Methods: This single-centre cohort study aimed to assess the socio-professional aspects of LT candidates before and after transplantation at Rennes University Hospital. Patients were enrolled during pre-transplant consultations over 18 months (June 2022–December 2023) with one-year follow-up. All LT candidates underwent consultations for infectious risk prevention. Data included demographics, comorbidities, disease severity, socio-professional status, and return-to-work (RTW) outcomes. The prevalence of active candidates, disabled worker status, early occupational health management, and job retention strategies were assessed. Statistical analyses identified factors influencing pre- and post-transplant occupational activity.

Results: Of 245 patients, 141 aged 18–64 years attended consultations. The cohort (65% male, median age 56) was predominantly diagnosed with alcohol-related cirrhosis (43%, median MELD score 18). Inactive patients had higher MELD scores (18 vs 17.5), while active candidates were more often managers or professionals (30% vs 4%). Prevalence of active candidates was 44% [24–40]. Higher education (ORa 2.99 [1.18–7.63]) and remote work (ORa 8.87 [1.27–178.97]) were independently associated with occupational activity. To date, 86 patients were transplanted. RTW prevalence at one year was 31% [22–42]. Among the 27 who returned to work, 44% required workstation adjustments, and 26% changed jobs. Pre-transplant activity (P = 0.007) and occupational health consultations (P < 0.001) were independently associated with RTW, while supplementary insurance (P = 0.004) was inversely associated. RTW patients reported better quality of life (P = 0.013).

Conclusions: This study highlights low occupational activity among LT candidates, underscoring the importance of tailored socio-professional support, occupational rehabilitation, and pre-transplant interventions to improve RTW rates and post-transplant quality of life.

PP_341 RISK FACTORS AND OUTCOMES OF RESISTANT AND PERSISTENT CYTOMEGALOVIRUS INFECTION IN HEART TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) infection is a major cause of morbidity after heart transplantation (HT). Although antiviral strategies based on (val) ganciclovir (VGC) are highly effective to prevent CMV disease, relapsing or persistent infection, drug resistances and drug toxicities may occur frequently and expose patients to major adverse events. In this study we aim to analyze the prevalence, risk factors and outcomes of VGC resistance and persistent (R/P) CMV infection in HT recipients.

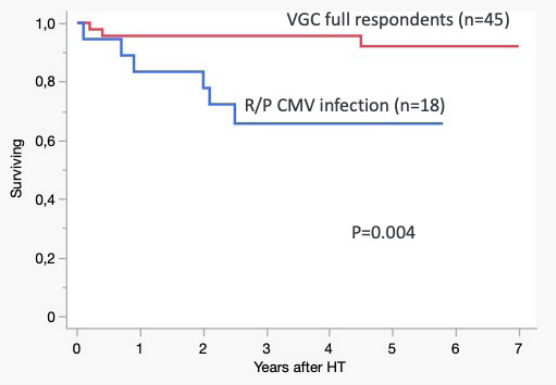
Methods: We reviewed clinical charts of all consecutive patients receiving HT at our center between 2018-22, surviving at least one month and either R+ or D+/R-. All patients were monitored for CMV DNAemia, including those receiving prophylaxis. We defined persistent infection according to guidelines. Rejection occurring after the first year and overall survival were study endpoints.

Results: Of the 90 patients included, CMV DNA was detected in 80(89%) and 63(70%) received anti CMV pre-emptive treatment with VGC at 4.0?0.8 Log IU/ml. Among treated patients, 2 (3%) developed VGC resistance (UL97 mutation) and 16 (25%) showed persistent infection. At infection onset, patients with R/P infection had higher viral load (4.3?0.8 vs. 3.9?0.8 Log IU/ml P=0.04) and lower median lymphocyte count than those full responding to VGC (317(180-496) vs. 477(382-673) counts/mmc; P<0.01). R/P infection was associated with worse patient survival (Figure; P<0.01)

Conclusions: R/P CMV infection Is a frequent condition in HT recipients. Net inmunosuppressive status, as roughly estimated by lymphocyte count, and initial viral load are risk factors for R/P infection, which seem to have a major impact on patient survival. This finding support the need to consider aggressive and personalized CMV treatment in patients with R/P infection.

Source of funding: “DARE – Digital Lifelong Prevention” initiative, PNC0000002

Figure – Survival estimate according to resistant/persistent infection



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PP_342 ELEVATED HEMOGLOBIN LEVELS IN RTRS WITH PCKD VS. OTHER ETIOLOGIES: EXPLORING MECHANISMS AND IMPLICATIONS FOR OUTCOMES

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Background: ADPKD-related end stage renal disease (ESRD) often necessitates transplantation. However, the impact of ADPKD on post-transplant outcomes, specifically hemoglobin levels, remains unknown.

Methods: We retrospectively analyzed 513 KTRs, of whom 81 had ESRD due to ADPKD (20 with pretransplant native nephrectomy and 61 without). Hemoglobin levels were evaluated at multiple time intervals post-transplant.

Results: KTRs with ADPKD vs. KTRs with ESRD due to other causes exhibited significantly higher Hemoglobin levels in repeated measurement analysis. Multivariable analyses confirmed ADPKD as an independent predictor for elevated Hemoglobin levels. In a multivariable logistic regression analysis, the odds for maximum hemoglobin > 15mg/dL at 3–12 months post-transplant were more than twice as high in ADPKD patients vs. all the other KTRs (OR 2.31, 95% CI 1.3-4.13, p <0.001). Pre-transplant native nephrectomy revealed a trend toward lower hemoglobin levels. Elevated hemoglobin levels were linked to improved eGFR at one year post-transplant. Patient survival was enhanced among KTRs with ADPKD compared to other ESRD causes.

Conclusions: KTRs with ADPKD exhibited elevated hemoglobin levels post-transplant, possibly due to prolonged native kidney erythropoietin production. These elevated hemoglobin levels were linked to improved outcomes, including allograft function and patient survival. Future research should further investigate the underlying mechanisms driving favorable ADPKD KTRs outcomes.

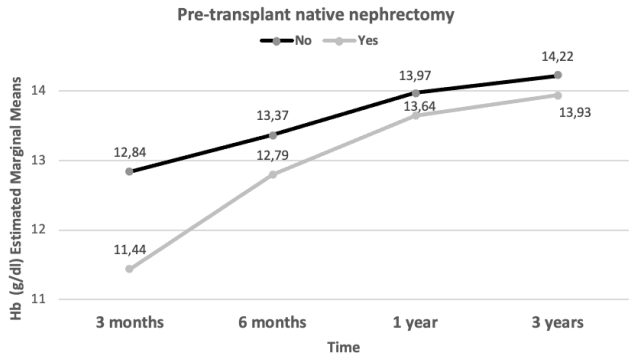

Figure: Repeated measurement analysis for Hb levels post-transplant in RTRs with PCKD who underwent pre-transplant native nephrectomy versus those who did not.

PP_343 LONG-TERM OUTCOME OF KIDNEY TRANSPLANT RECIPIENTS WITH END-STAGE KIDNEY DISEASES DUE TO TYPE II DIABETES MELLITUS

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Background: Compared with non-diabetic subjects, patients with type 2 diabetes and end-stage renal disease (ESRD) have seldom been selected for renal transplantation. This study aimed to compare the long-term prognoses of the two groups of patients after transplantation and to identify factors associated with allograft rejection.

Methods: We retrospectively studied 363 patients who underwent kidney transplantation between 1979 and 2014, including 84 with diabetic ESRD (DM group) and 270 with non-diabetic ESRD (NDM group) with no post-transplant diabetes mellitus. The mean follow-up in 338 out of 354 patients (93.1%) was 92±9 (0.1–386) months.

Results: Mean age was higher in the DM group (51.8 vs 44.6 years; P < .0001), and there was no significant difference in recipient gender, donor age, or donor source. There was no significant difference as regards pre-transplant hypertension or duration of dialysis. At the end of the follow-up also, there were no differences between the groups concerning blood pressure control and renal function (calculated creatinine clearance, 69±24 vs 68.4±24 ml/min/1.73 m2, respectively, P = 0.9). In total, 26 patients had acute transplant rejections [eight patients with diabetes (prevalence 16.3%) vs 18 patients without diabetes (prevalence 7.1%), P = 0.11]. There was no significant difference in post-transplant surgical complications such as wound dehiscence or infections. The incidence of rejection did not differ between the DM and NDM groups. There was a significantly high incidence of urinary tract infection rate in the DM group (17 vs 32 patients; P = .012). Four out of 22 patients died (18.2%) in the DM group and 10 out of 47 patients (21.3%) in the NDM group died from cardiovascular disease during the follow-up period (P = 0.17). The 1-, 5-, and 10-year patient survival rates in the DM and NDM groups were 97.5% vs 99% (ns), 74.4% vs 77.9% (ns), and 56.8% vs 58.8% (ns), respectively. The 1-, 5-, and 10-year graft survival rates were 97.5% vs 70.7% (ns), 77.2% vs 95.2% (P = 0.04), and 58.9% vs 66.1% (ns), respectively.

Conclusions: Renal transplantation in diabetic ESRD patients yields good results in terms of patient survival and complications, suggesting that renal transplantation can be performed in these patients and should become a more established treatment option.

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PP_344 GLYCEMIC VARIABILITY IN EARLY POST-TRANSPLANT PERIOD AND ITS IMPACT ON THE DEVELOPMENT OF LATER METABOLIC COMPLICATIONS

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Background: It is widely known that hyperglycaemia occurs frequently after kidney transplantation (KT), however prior data reveal that glycaemic variability (GV) may significantly effect later problems and patient outcome. The aim of our study was to use the continuous glycaemic monitoring (CGM) to determine how GV in the early post-transplant period affects metabolic problems.

Methods: This prospective study was conducted in University Hospital Martin, Slovakia, Transplant-nephrology department patients following primary KT. Adults without diabetes or prediabetes received a Dexcom G6 CGM before KT. This smartphone-connected gadget recorded blood glucose for 7 days after KT. We collected all patients' demographic and clinical information on day 0, 5, and the third and twelfth month, including protocol biopsy and donor-specific antibody results. Oral glucose tolerance was tested in months 3 and 12. All patients received the same immunosuppression for 12 months.

Results: The data analysis includes 20 patients (mean age 47,5 ± 14,6; 65% men) who have completed the follow-up period. The study included 10 patients with post-transplant diabetes mellitus (PTDM) (n = 7) and prediabetes (n = 3). We discovered no significant changes in baseline characteristics between the control and study groups. On the fifth day after KT, the study group had higher HbA1c (p = 0.0382) and lower insulin 2 hours post-load (p = 0.0417). We found substantially greater HbA1c (p = 0,0420), homeostatic model assessment index for insulin resistance, HOMA-IR, and fasting insulin (p = 0,0219) at month 3 and month 12 in the study group than in the control group. By analysing the 7-day CGM data, we found a significantly higher average glucose (p = 0,0208), standard deviation - SD (p = 0,0006), estimated A1c (p = 0,0169), time in hyperglycaemia (TIH) – high (p = 0,0423), TIH – very high (p = 0,0194), and lower time in normal range (p = 0,0365) in the CGM models based on ROC curve analysis with a sensitivity of 70 and specificity of 80 predicted PTDM/prediabetes with an SD criteria of > 2,1.

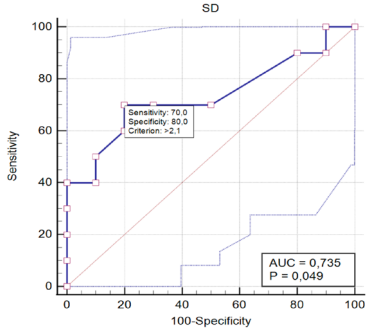
Conclusions: The first results of our study demonstrate the impact of GV in the early post-transplant period on the development of glucose metabolism disorders in the third and twelfth months after KT. CGM is an ideal tool for measuring GV in the early period after KT.

Table 1: The comparison of CGM parameters between study and control group

n = 20	control group (n = 10)	PTDM (n = 10)	P value
average glucose (mmol/l)	6,6 ± 1,2, median 6,5	8,4 ± 1,9, median 8,4	**0,0208**
standard deviation ± SD, median	1,2 ± 0,7, median 1,8	2,9 ± 1,1 median 2,8	**0,0006**
coefficient of variation ± SD, median	28,8 ± 6,8, median 27,3	33,6 ± 8,8, median 31,2	0,1819
coefficient of variation > 36 (%)	10 (n = 1)	40 (n = 4)	0,6124
estimated A1c (%)	6,1 ± 0,6, median 6	7 ± 0,9, median 6,9	**0,0169**
IGR 25/75 ± SD, median	2,4 ± 1, median 2,2	3,3 ± 1,7, median 2,7	0,1662
time in normal range – TIR (%) ± SD, median	88,4 ± 8,3, median 91,5	72,8 ± 20,2, median 74	**0,0365**
time in hyper – TIHyper high (%) ± SD, median	5,8 ± 5,8, median 4,5	19,2 ± 18,5, median 13,5	**0,0423**
time in hyper – TIHyper very high (%) ± SD, median	1,3 ± 2,1, median 0	8,8 ± 9, median 10,5	**0,0194**
time in hypo – TIHypo low (%) ± SD, median	4,3 ± 7,4, median 1	1,8 ± 1,8, median 1,3	0,3130
time in hypo – TIHypo very low (%) ± SD, median	0,5 ± 1, median 0	0,5 ± 0,7, median 0	1,0000

PTDM – post-transplant diabetes mellitus, IQR – interquartile range

Figure 1: ROC analysis for standard deviation as a predictor of PTDM / prediabetes occurrence using CGM



PP_346 A COHORT STUDY ASSESSED DESENSITIZATION THERAPY'S IMPACT ON BK VIRUS VIREMIA AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Desensitization has enabled immunologic incompatible living donor kidney transplantation across HLA/ABO barriers, providing survival benefits over long-term dialysis. However, desensitization therapy carries a heightened risk of infectious complications, particularly BK virus (BKV) infection, which can compromise graft outcomes.

Methods: This observational cohort study aimed to investigate the differential impact of desensitization therapy on the incidence of BKV viremia among 1356 living donor kidney transplant recipients. Among them, 454 patients (33.5%) received pre-transplant desensitization therapy. Patients were categorized by desensitization therapy: rituximab without intravenous immunoglobulin (IVIG), rituximab combined with low-dose IVIG (cumulative dose ≤ 1g/kg), rituximab combined with high-dose IVIG (cumulative dose > 1g/kg), and a control group with no desensitization.

Results: Over a median follow-up period, 129 patients (9.5%) developed BKV viremia. Multivariable analysis revealed that the rituximab without IVIG group had a 2.2-fold increased risk, and the rituximab plus low-dose IVIG group had a 1.9-fold increased risk of BKV viremia compared to the no desensitization group. Notably, the rituximab plus high-dose IVIG group exhibited a similar risk to the control group, suggesting that high-dose IVIG may mitigate the risk of BKV viremia associated with rituximab. BKV viremia was independently associated with an increased risk of death-censored graft loss (hazard ratio, 1.870; 95% confidence interval, 1.127–3.103).

Conclusions: In conclusion, use of rituximab as part of desensitization therapy appears to increase the risk of BKV viremia, whereas IVIG mitigates this risk. Our findings emphasize the importance of carefully considering potential infectious complications, especially BKV infection, associated with desensitization therapy in kidney transplant recipients.

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Infectious diseases, malignancies & long term challenges

PP_347 IGA DOMINANT POSTINFECTIOUS GLOMERULONEPHRITIS IN KIDNEY TRANSPLANT RECIPIENT

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Background: IgA Dominant Postinfectious Glomerulonephritis (IgA-DPG) is an acute glomerulonephritis form mainly linked to staphylococcal infections with very limited data on its occurrence in kidney transplant patients.

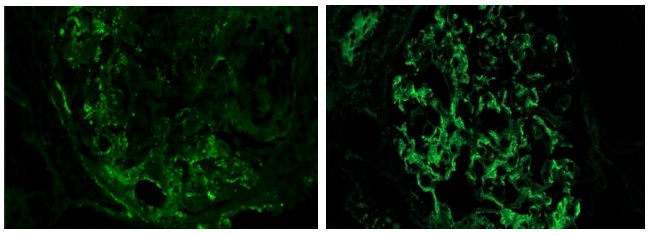
Methods: We describe a clinical case of a 50-year-old male kidney transplant recipient who presented with reduced urine output, lower extremity swelling, hypertension, joint pain and fatigue over two days. Two years after transplant, he had stable renal function, his medical history included Familial Mediterranean fever, psychosis and hepatitis B and C. Eight days prior, he had surgery for trunk phlegmon and was still on clindamycin after Staphylococcus aureus was identified. Physical examination showed hypertension , pretibial edema, and purpuric lesions suggesting vasculitis; treatment began with Methylprednisolone (MP) pulses. Despite rash improvement, renal function deteriorated, patient developed nephrotic syndrome, an active urinary sediment, Kidney biopsy revealed 3 ischemic glomeruli with bowmen capsule thickening/replication and GBM wrinkling. 6 glomeruli showed segmental fibrinoid necrosis with neutrophil infiltration, 5 of them with segmental cellular and fibrocellular crescent formation. 1 glomerulus showed circular fibrocellular crescent. One glomerular structure showed segmental GBM replication. IF revealed granular positivity for IgA (3+); C3c (2+/3+) Kappa and Lambda (3+) along the GBM. ANCA -negative. Diagnosis of IgA dominant postinfectious crescentic glomerulonephritis- was made. Treatment with Cyclophosphamide (CP) was started. 2 weeks later the patient developed fever, abdominal MRI revealed gluteal infiltrates, Clindamicin was switched to Vankomycine and CP was restarted in 3 days.

Results: Patient's kidney function recovered, proteinuria decreased (table1), nonetheless, patient didn't have full remission

Conclusion: (IgA-DPG) can mimic vasculitis and it should be distinguished from IgA nephropathy and IgA vasculitis.

	Admission	Day 5	2 weeks	1 month	3 months	1 year
Crea (mcmol/l)	145	270	180	145	110	130
Urine Protein/Crea ratio mg/mgCrea	0.3	2	8	7g	6.5	1.2
AlB g/l	35	33	27	29	29	38
ANCA	neg				neg	neg
Crioglobulins	neg					
Hep C PCR	neg					
Hep B PCR	44400 IU/ml					
C3/C4	WNL					

Table 1



C3C IgA

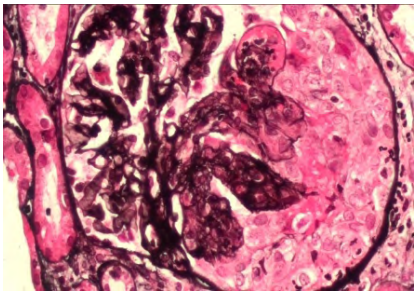


Figure 1

Transplant immunology & immunosuppression

PP_348 BIOPSY-BASED TRANSCRIPTOMICS AND DIAGNOSIS OF KIDNEY AMR IN CLINICAL PRACTICE

Jeanne Dandonneau[1], Arnaud François[2], *Dominique Bertrand*[3], Sophie Candon[4], Tristan De Nattes[5]

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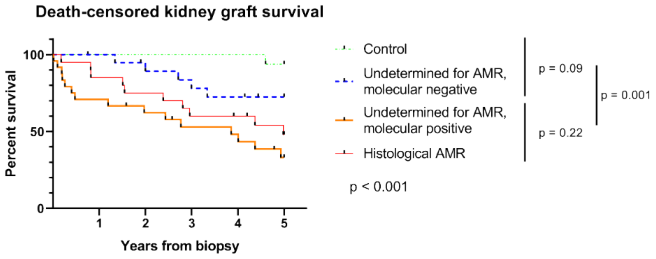
Background: To diagnose kidney transplant antibody-mediated rejection, biopsy-based transcriptomics can substitute for some histological criteria according to the Banff classification. However, clinical accessibility of these assays is still limited. Here, we aimed to evaluate the impact of integrating a routine-compatible molecular assay for the diagnosis of antibody-mediated rejection in clinical practice.

Methods: All biopsies performed in our center between 2013 and 2017 were retrospectively included. These biopsies were classified into three groups: "Antibody-mediated rejection biopsies" which displayed the full 2019 Banff criteria of antibody-mediated rejection independently of biopsy-based transcriptomics; "Undetermined for antibody-mediated rejection" biopsies which did not meet antibody-mediated rejection histological criteria, but would have been considered as antibody mediated rejection if biopsy-based transcriptomics had been positive; and control biopsies which showed no features of rejection.

Results: Within the inclusion period, 342 biopsies had a complete Banff scoring. Thirty-six of the biopsies already met antibody-mediated rejection criteria, and 43 out of 306 (14%) were considered as "undetermined for antibody-mediated rejection." Among these biopsies, 24 out of 43 (56%) had a molecular signature of antibody-mediated rejection, reclassifying them into the "antibody-mediated rejection" category. Five-year death-censored survival of these biopsies was unfavorable and statistically equivalent to that of the "antibody-mediated rejection" category (p = 0.22), with 15 out of 24 (63%) graft loss (figure 1).

Conclusion: A significant proportion of biopsies could benefit from a biopsy-based transcriptomics for antibody-mediated rejection diagnosis according to the Banff classification. Using a routine compatible molecular tool, more than the half of these biopsies were reclassified as antibody mediated rejection and associated with poor allograft survival.



Number at risk	0 year	1 year	2 years	3 years	4 years	5 years
Histological AMR	20	18	16	13	12	10
Undertermined for AMR, molecular positive	24	18	16	12	11	7
Undertermined for AMR, molecular negative	19	19	18	16	14	12
Control	17	17	17	17	17	16

Figure 1 : Death-censored kidney graft survival at five years according to histological and biopsy-based transcriptomics. AMR: antibody-mediated rejection.

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Transplant immunology & immunosuppression

PP_349 SIMPLE BIOPSY-BASED TRANSCRIPTOMICS FOR THE ASSESSMENT OF KIDNEY TRANSPLANT BIOPSIES

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Introduction: The Banff Classification for Allograft Pathology recommendations for the diagnosis of kidney transplant rejection includes molecular assessment of the transplant biopsy. However, implementation of molecular tools in clinical practice is still limited, partly due to the required expertise and financial investment. The reverse transcriptase multiplex ligation-dependent probe amplification (RT-MLPA) assay is a simple, rapid and inexpensive assay that permits simultaneous evaluation of a restricted gene panel using paraffin-embedded tissue blocks. The aim of this study was to develop and validate a RT-MLPA assay for diagnosis and classification of rejection.

Methods: A retrospective cohort of 220 kidney transplant biopsies from two centres, which included with 52 antibody-mediated rejection, 51 T cell-mediated rejection and 117 no-rejection controls was assessed. A 17-gene panel was identified, based on relevant pathophysiological pathways. A support vector machine classifier was developed. A subset of 109 biopsies was also assessed using the Nanostring B-HOT panel to compare the two assays.

Results: The support vector machine classifier train and test accuracy scores were 0.84 and 0.83, respectively. In the test cohort, the F1-score for antibody mediated rejection, T cell-mediated rejection and control were 0.88, 0.69 and 0.86, respectively. Using ROC curves, AUC for class predictions were 0.96, 0.89 and 0.91, respectively, with a weight-average at 0.94. Classifiers' performances were highest for antibody mediated rejection diagnosis with 94% correct predictions, compared to 88% correct predictions for control biopsies and 60% for T-cell mediated rejection biopsies. Gene expression levels assessed by RT-MLPA or Nanostring correlated: r = 0.68, p < 0.001, and gene expression profiles obtained with these assays were comparable in 81% of samples.

Conclusions: The 17-gene panel RT-MLPA assay, developed here for formalin-fixed paraffin-embedded kidney transplant biopsies, classifies kidney transplant rejection with an overall accurate prediction ratio of 0.83.

PP_350 DDCFDNA IS INDEPENDENTLY ASSOCIATED WITH HEART REJECTION AND IMPROVES INDIVIDUAL RISK STRATIFICATION

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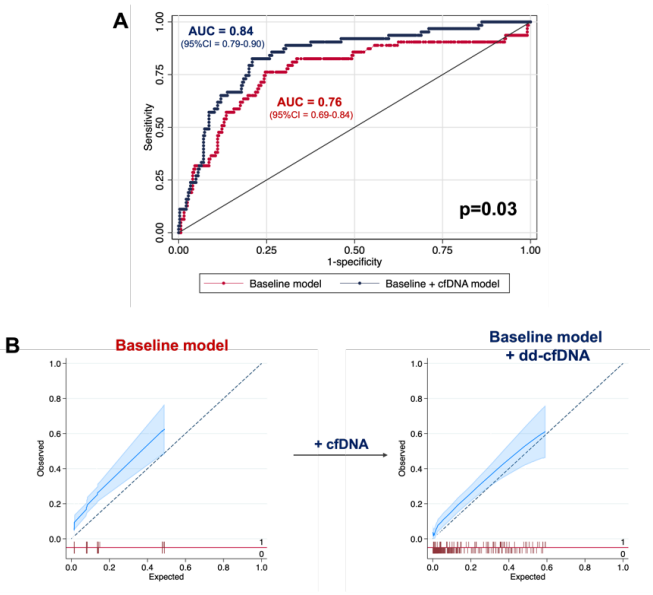
Background: Donor-derived cell-free DNA (dd-cfDNA) is a robust non-invasive biomarker for detecting allograft injury. However, its independent association with rejection and its ability to improve the individual risk stratification of allograft rejection have not yet been explored.

Methods: We designed a longitudinal prospective study involving 2 heart transplant centers. Patients were included from October 2022 to June 2024. Plasma samples were collected at the time of endomyocardial biopsies. Among 1542 samples representing 320 patients, 391 were selected to be representative of the landscape of rejection. dd-cfDNA was quantified using the AlloSeq cell-free DNA assay. Rejection was defined as cellular ≥ 2R, antibody-mediated ≥ pAMR 1 and/or acute allograft dysfunction. Mixed effect logistic regression was used to test the association between dd-cfDNA and rejection. The additional clinical value of dd-cfDNA was assessed using a previously validated robust clinico-biological model stratifying the risk of allograft rejection (including the following variables: time post-transplant, pre-transplant sensitizing event, prior history of rejection, circulating anti-HLA donor-specific antibodies [DSA], acute allograft dysfunction).

Results: Overall, 391 samples from 185 patients were analyzed. Patients were mostly males (n=135, 73%). Median time between transplant and visit was 201 days (IQR 74-1048). DSA were present in 74 cases (18.9%). Rejection was diagnosed in 63 cases (16.1%). Median dd-cfDNA was 0.20% (IQR 0.11-0.49). dd-cfDNA was independently associated with rejection after adjustment for circulating DSA, time post-transplant, graft function, pre-transplant sensitizing event and prior history of rejection (log dd-cfDNA: OR = 2.37, 95%CI = 1.49-3.76, p<0.001). Adding dd-cfDNA on top of the baseline model significantly improved discrimination (AUC 0.84, 95%CI = 0.79-0.90 compared to 0.76, 95%CI = 0.69-0.84, p = 0.03, Figure 1A), calibration (Figure 1B) and reclassification indices (NRI and IDI: p<0.001).

Conclusions: In this prospective longitudinal study, dd-cfDNA was independently associated with rejection and improved the individual risk stratification of rejection. These results support the routine use of dd-cfDNA for the monitoring of allograft rejection.



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PP_352 EARLY ULTRASTRUCTURAL FINDINGS IN RENAL TRANSPLANTS: LINKING MICROVASCULAR CHANGES AND IMMUNE MARKERS TO PREDICT THE TYPE OF REJECTION AND LONG-TERM GRAFT SURVIVAL

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Background: Early ultrastructural (US) alterations may provide valuable insights into unraveling the intricate mechanisms involved in the rejection process and may offer opportunities for intervention and therapeutic strategies. Thus, we aimed to evaluate the early US changes in renal allografts with different types of acute rejection (AR), and we compared these findings with capillary HLA-DR and VEGF expressions.

Methods: In 62 cases, T-cell-mediated rejection (TCMR), antibody-mediated rejection (ABMR), and mixed AR (MAR) were observed in 12, 32, and 18 patients, respectively, with biopsies taken within 3 months post-transplant. Early US changes included endothelial cell (EC) swelling, vacuolization, fenestration loss, and EC serration in glomeruli and peritubular capillaries (PTCs). Multilamellation of the microvascular capillary's basement membranes was evaluated. Microvascular HLA-DR and VEGF were analyzed, along with follow-up biopsies for transplant glomerulopathy (TG) and interstitial fibrosis (IF).

Results: Early US changes in glomeruli and PTCs were most pronounced in MAR and least in TCMR ($p<.001$). These changes correlated positively with PTC destruction, glomerulitis, macrophage infiltration, C4d grade, and neutrophil infiltration ($p<.001$), but negatively with VEGF and HLA-DR expression in PTCs and glomeruli. TG developed in 12.5%, 72.4%, and 82.4% of TCMR, ABMR, and MAR cases, respectively ($p<.001$), with shorter times to TG in MAR and ABMR. Early US changes strongly correlated with TG and IF development in follow-up biopsies ($p<.001$). VEGF and HLA-DR expression were negatively associated with TG and IF development ($p<.001$). Ten-year graft survival was significantly higher with higher VEGF grades in PTCs and glomeruli ($p<.001$).

Conclusions: Early US changes and VEGF expression in capillaries offer critical insights into the dynamics of AR, transcending their diagnostic value. These findings provide a deeper understanding of rejection mechanisms, enabling improved prediction, diagnosis, and intervention strategies to enhance graft survival and outcomes.

PP_353 MICRO RIBONUCLEIC ACID MAESTROS: PREDICTIVE BIOMARKERS OF ALLOGRAFT FATE IN KIDNEY TRANSPLANTS

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Background: In the intricate molecular symphony of the human body, microRNAs (miRNAs) serve as master regulators, orchestrating critical processes like immune modulation, inflammation, and tissue repair. Among these key players, miR-142-5p and miR-192-1 stand out, profoundly influencing renal transplant outcomes. Our study delves into their pivotal roles, unraveling how their interplay shapes the delicate balance of immune responses and tissue integrity, ultimately impacting the fate of renal transplants.

Methods: The study analyzed plasma levels of miRNAs using real-time PCR in 100 kidney transplant recipients. Groups included patients with long-term stable allograft function (n = 29), T-cell-mediated rejection (TCMR) (n = 16), antibody-mediated rejection (ABMR) (n = 28), and mixed rejection (n = 27). It also explored correlations between histological parameters and circulating miRNAs and evaluated the incidence of diffuse interstitial fibrosis (>50%) in follow-up biopsies.

Results: Significant upregulation of miR-142-5p ($p<.001$) and miR-192-1 ($p<.001$) was observed in recipients with acute rejection (AR) and interstitial fibrosis (IF) development. These miRNAs were strongly associated with key pathological features, including interstitial inflammation, eosinophil and plasma cell infiltration, peritubular capillary (PTC) C4d expression, PTC inflammation and destruction, glomerulitis, vascular rejection, thrombotic microangiopathy, tubular HLA-DR expression, AR episodes, and graft loss. The 5-year risk of IF development was 23% for patients with low miR-142-5p versus 52% for those with high levels ($p=0.002$), and 21% for low miR-192-1 versus 57% for high levels ($p<.001$). Similarly, 5-year graft survival rates were 94% (low miR-142-5p) versus 64% (high miR-142-5p, $p=0.001$) and 93% (low miR-192-1) versus 61% (high miR-192-1, $p<.001$).

Conclusions: Our study highlights the critical role of miR-142-5p and miR-192-1 in renal transplant pathology, particularly in AR and IF progression. These circulating microRNAs strongly correlate with AR type, inflammation, and microvascular injury, positioning them as promising, accessible biomarkers for monitoring AR, IF, and related vascular pathologies.

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Transplant immunology & immunosuppression

PP_354 TEN-YEAR OUTCOMES AFTER ALEMTUZUMAB VERSUS BASILIXIMAB INDUCTION IN RENAL TRANSPLANTATION

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Background: Our previous randomized controlled study compared Alemtuzumab with Basiliximab induction in renal transplantation (1) with long term follow up embedded. 10 year outcomes are reported.

Methods: Patients consented for long-term follow up at enrollment. Data collection was via regional network systems. Statistical analyses: t-tests for continuous variables; Chi Square/Fisher's tests for categorical data; log-rank test for survival curves.

Results: 116 adult patients were originally randomized to either the Basiliximab group (BAS) induction followed by Tacrolimus and Mycophenolate, or the Alemtuzumab group (ALEM) induction followed by Tacrolimus monotherapy (1). 96.6% of patients had 10year data. Median overall follow up was 10.0years (IQR 9.9-10.2years) and was not significantly different between the groups. Patient survival was 84.2% in the ALEM group and 73.2% in the BAS group (p=0.12). There was no significant difference in causes of death between the groups. Death censored graft survival was 94.5% in ALEM and 83.6% in BAS (Figure 1, p=0.21). Mean creatinine and eGFR at 10 years were comparable between the groups: Creatinine: ALEM 153.0±90.8µmol/L; BAS 157.8±67.6µmol/L, p=0.80. eGFR: ALEM 47.8±18.7ml/min; BAS 45.8±19.7ml/min, p=0.63). The number of rejection episodes was not significantly different between groups (p= 0.40). There was no evidence of a different viral disease rates. A numerically higher incidence of malignancy in BAS (n=24, 42.9%) compared to ALEM (n=17, 30.4%) did not reach statistical significance, p= 0.17. Five patients in BAS developed post-transplant lymphoproliferative disorder (PTLD) vs. two in ALEM (p=0.44).

Conclusions: Ten-year outcomes were similar between the two groups. The ALEM group benefitted from tacrolimus monotherapy, and some non-significant trends (patient/graft survival, malignancy rates) favored that group. Overall long-term outcomes were comparable.

References: Welberry Smith et al. Transplantation 96(12):1082-8(2013)

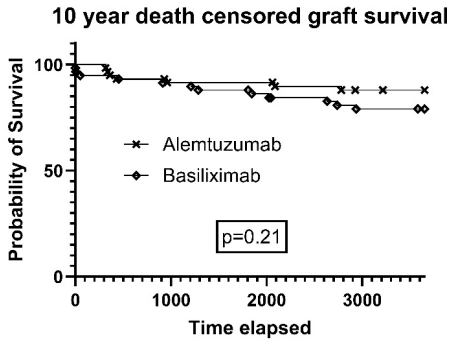

Figure 1: Death censored graft survival

PP_355 STREAMLINING IMMUNE SURVEILLANCE FOR SARS-COV-2 AND CMV IN TRANSPLANT PATIENTS: THE TOSCA PROJECT

Arianna Precisi o Procissi[1], Mauro Pistello[2], Roberto Lupi[3], Anna-Lisa Capria[2], Maria Sidoti[4], Chiara Lazzeri[5], Adriano Peris[6]

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Background: The TOSCA project aims to improve the monitoring of cell-mediated immune responses against SARS-CoV-2 and CMV. CMV reactivation can lead to severe multi-organ complications, while persistent SARS-CoV-2 infections in immunocompromised hosts lead to chronic disease and the emergence of immune-escapevariants. Since cell-mediated immunity plays a pivotal role in controlling both infections, enhanced methods for immune monitoring may lead to better therapeutic intervention in this high-risk population.

Methods: As part of the TOSCA initiative, we collaborated with clinicians to develop pre- and post-transplant protocols for monitoring CMV- and SARS-CoV-2-specific cell-mediated immune responses. Initial analyses relied on enzyme-linked immunospot (ELISPOT) assays, but to streamline and increase throughput, we are establishing protocols for gene expression profiling of T cells stimulated with CMV antigens. Viral persistence and genetic evolution in tissues were investigated using molecular assays to track viral adaptation and immune evasion.

Results: The protocols were initially set up and carried out in healthy individuals and oncology patients. In oncology patients, SARS-CoV-2 was found to persist in specific tissues, inducing chronic inflammatory damage. Genetic analysis of the virus revealed the accumulation of mutations enabling immune evasion. For CMV, initial comparisons between ELISPOT and gene expression analysis demonstrated comparable results, suggesting that gene expression profiling could soon offer a simpler and faster method for tracking CMV-specific immune responses.

Conclusions: Effective monitoring of cell-mediated immune responses is essential for managing CMV reactivation and persistent SARS-CoV-2 infections in transplant patients. Our findings suggest that the protocols established under TOSCA may support the development of individualized antiviral therapies and optimized immunosuppressive regimens.

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PP_357 IMPACT OF EARLY BELATACEPT CONVERSION ON RENAL TRANSPLANTS WITH DONOR-DERIVED VASCULAR DISEASE

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Background: Efforts to minimize organ nonuse have increased allografts with vascular disease. Calcineurin inhibitors (CNI) reduce rejection but cause nephrotoxicity, compromising such allografts. This study examined if early conversion to belatacept (Bela) based immunosuppression therapy (IST) improves glomerular filtration rate (GFR) in deceased donor renal transplants (DDRT) with vascular disease.

Methods: DDRT recipients at our center (2012-2024) were retrospectively screened for donor-derived vascular disease (arteriolar hyalinosis and alternative arteriolar hyalinosis ≥ 2 per Banff). Donor-matched pairs were included if 1 of 2 recipients transitioned from CNI to Bela IST within 1 year of transplant. Cohort was split according to Bela use, using the 1st Bela dose (or matched post-transplant time for non-Bela group) as baseline. Renal function data was collected over 2 years. Outcomes were GFR change from baseline to 6 months (primary) and from baseline to 1 and 2 years (secondary). Two-sample t tests or Wilcoxon Rank Sum tests were used to compare patient characteristics between groups. Linear mixed effect modeling, incorporating an interaction between time and Bela use, was used to assess outcomes over time. A random effect for donor ID was included to account for within-donor correlation.

Results: Ten donor-matched recipient pairs were analyzed, with no differences in age, sex, cause of kidney disease, immunologic risk and IST between groups (Table 1). Baseline renal function as well as GFR changes from baseline to 6 months and 1 year were comparable between groups. However, the Bela group had a significantly greater increase in GFR from baseline to 2 years with a 15.15 mL/min/1.73m^2 higher difference (p=0.03). This was despite cellular rejection grade 1A in two Bela patients after conversion.

Conclusions: Early conversion to Bela may improve GFR in DDRT recipients with donor-derived vascular disease. Larger studies are needed to validate these findings.

Figure 1

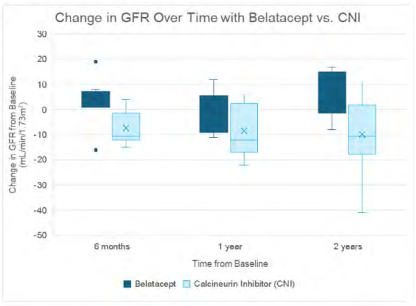

Table 1

Variable	Bela group (n=10)	Non-Bela group (n=10)	p value
Patient characteristics			
Age at the time of transplant, years	56 ± 14	58 ± 9	0.70
Sex, male	7 (70%)	6 (60%)	>0.99
Body mass index at the time of transplant, kg/m²	25.8 ± 5.2	25.1 ± 3.6	0.71
Cause of end stage kidney disease			>0.99
Diabetic nephropathy	0 (0%)	5 (50%)	
Hypertensive nephrosclerosis	1 (10%)	1 (10%)	
Focal segmental glomerulosclerosis	3 (30%)	0 (0%)	
Others	6 (60%)	4 (40%)	
Initial kidney transplant	9 (90%)	10 (100%)	>0.99
Duration on dialysis >5 years	4 (40%)	5 (50%)	>0.99
Panel reactive antigen at the time of transplant	15 ± 30	25 ± 34	0.48
Donor specific antibody present at the time of transplant	1 (10%)	1 (10%)	>0.99
Induction dose of Thymoglobulin, mg/kg	3.74 ± 1.71	5.26 ± 1.78	0.067
Maintenance immunosuppression at discharge			>0.99
Tacrolimus	10 (100%)	10 (100%)	
Mycophenolate	10 (100%)	10 (100%)	
Prednisone maintenance	4 (40%)	4 (40%)	
Prednisone withdrawal	6 (60%)	6 (60%)	
Graft function			>0.99
Immediate graft function	6 (60%)	5 (50%)	
Delayed graft function	4 (40%)	4 (40%)	
Primary non-function	0 (0%)	1 (10%)	
Index biopsy & belatacept conversion			
Number of days from transplant to index biopsy	91 ± 23	93 ± 19	0.86
Dialysis dependence at time of index biopsy	0 (0%)	1 (10%)	>0.99
Number of days from transplant to first dose of Belatacept	205 ± 75	n/a	n/a
Number of days from transplant to last dose of Tacrolimus	255 ± 78	n/a	n/a
Maintenance immunosuppression at baseline*			>0.99
Belatacept	10 (100%)	0 (0%)	
Mycophenolate	10 (100%)	8 (80%)	
Prednisone maintenance	4 (40%)	5 (50%)	
Prednisone withdrawal	6 (60%)	5 (50%)	
Tacrolimus	0 (0%)	9 (90%)	
Outcomes			
Creatinine, mg/dL			
Baseline*	1.97 ± 0.8	1.48 ± 0.4	0.12
Baseline* + 6 months	1.77 ± 0.6	1.65 ± 0.3	0.60
Baseline* + 1 year	1.94 ± 0.6	1.76 ± 0.4	0.49
Baseline* + 2 years	1.73 ± 0.7	1.58 ± 0.3	0.75
GFR*, mL/min/1.73m²			
Baseline*	42.1 ± 15.7	46.9 ± 21.2	0.57
Baseline* + 6 months	46.5 ± 18.1	39.6 ± 18.6	0.41
Baseline* + 1 year	41.2 ± 16.0	38.5 ± 21.2	0.75
Baseline* + 2 years	47.8 ± 19.5	37.0 ± 21.4	0.27
Change in GFR from baseline*, mL/min/1.73m²			
6 months	4.4 ± 4.8	-7.3 ± 4.8	0.09
1 year	-0.9 ± 4.8	-8.4 ± 4.8	0.27
2 years	5.2 ± 5.0	-9.9 ± 4.8	0.03

*Baseline is defined as time of first dose of belatacept in the recipient in the Bela group and the matched time post-transplant in the recipient in the non-Bela group
*Calculated using CKD-EPI 2021 creatinine equation

PP_358 RANDOMIZED CONTROLLED TRIAL COMPARING IMMEDIATE VERSUS EXTENDED RELEASE TACROLIMUS

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Background: Tacrolimus is the cornerstone of immunosuppressive treatment post lung transplantation (LTx). Extended release (LCP) tacrolimus has a higher bioavailability resulting in lower peak and more stable trough levels than immediate release (IR) tacrolimus. Previous studies have shown similar efficacy profiles for both forms of tacrolimus. Because of high immunogenicity of transplanted lungs, target tacrolimus trough levels in LTx are high, with the potential drawback of increased tacrolimus related adverse effects; renal toxicity, post transplantation diabetes mellitus (PTDM), hypertension and infections. The aim of the REVOLUTION study is to compare LCP to IR tacrolimus in LTx recipients, with the hypothesis that LCP tacrolimus has less adverse effects compared to IR tacrolimus (ClinicalTrials.gov:NCT05001074).

Methods: From October 2020 to October 2021, 75 adult LTx recipients were randomized to LCP or IR tacrolimus in an open label trial. Follow up lasted 2 years with study visits and laboratory analyses every 6 months. The CKD-EPI creatinine-cystatin C equation was used to estimate renal function. Absolute change in estimated glomerular filtration (eGFR) slope was used to assess the potential difference in renal toxicity. The final patient visit will take place in May 2025. Data-analyses will start thereafter. The primary endpoint is renal toxicity. Secondary outcomes include incidence of infection, acute cellular rejection, PTDM and new onset hypertension. Analyses will be performed by an intention to treat approach in the primary analysis population, defined as all enrolled patients who had measurements at both baseline and 2 years. The primary hypothesis will be tested depending on the distribution (t-test/Mann-Whitney U-test). Furthermore an eGFR difference of ≥ 1.51 ml/min/1.73m^2 in favor of the intervention group is considered clinically relevant surrogate endpoint for kidney failure.

Results: The final patient will visit in May 2025. There are no results to share at the moment of abstract submission deadline.

Conclusions: After the last patient visit data will be analyzed and from these results we might conclude that in this randomized open label trial in LTx patients LCP tacrolimus has less severe adverse effects when compared to IR tacrolimus.

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Transplant immunology & immunosuppression

PP_359 EXTRACORPOREAL PHOTOPHERESIS AS A TREATMENT FOR CLAD: THE BELGIAN EXPERIENCE

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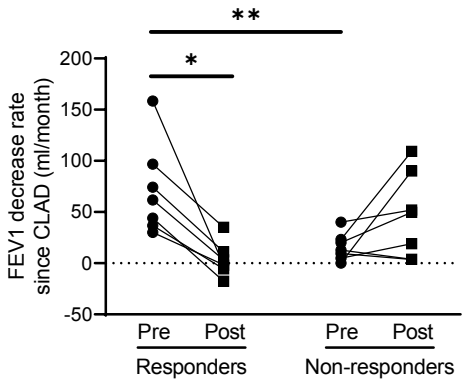
Background: Chronic lung allograft dysfunction (CLAD) remains a significant challenge after lung transplantation (LTx), representing the leading cause of mortality beyond the first post-transplant year and thus limiting long-term survival. Extracorporeal photopheresis (ECP), an immunomodulatory therapy involving the reinfusion of photosensitized, UV-A-irradiated leukocytes, is now recognized as a therapeutic option for CLAD. However, as ECP is not reimbursed in Belgium, no national data have been reported to date.

Methods: We retrospectively analyzed clinical and pulmonary function test data from 14 LTx recipients who underwent ECP between 2011 and 2024 at the two largest Belgian LTx centers: UZ Leuven (n=3) and CHU UCL Namur (n=11), where institutional funding enabled the implementation of ECP. The rates of decline in forced expiratory volume in one second (FEV_1) prior to ECP (since CLAD diagnosis) and in the 6 months following ECP were measured. Responders were defined as patients experiencing a reduction of ≥30 mL/month in the rate of FEV_1 decline after 6 months of ECP.

Results: The median time since LTx was 65.9 [IQR: 43.1–83.6] months, and the median time since CLAD diagnosis was 422 [249–662] days. Seven patients (50%) were classified as responders, while the remaining seven were non-responders. Responders exhibited a significantly higher pre-ECP rate of FEV_1-decline compared to non-responders (61.8 vs. 12.8 mL/month, p=0.0023, Figure 1). Additionally, responders had a shorter median duration since CLAD diagnosis (283 vs. 628 days, p=0.026). No differences were observed between the two groups regarding the initial respiratory disease, immunosuppressive regimens, or other CLAD treatments. A trend toward a higher response rate in male patients was observed but did not reach statistical significance.

Conclusions: ECP reduced the rate of FEV_1-decline in half of the patients. Faster pre-ECP FEV_1- decline, more recent CLAD diagnosis, and male sex were associated with better response to ECP, consistent with previous findings. These results, in addition to demonstrating the feasibility of ECP in Belgium, may help inform the selection of candidates for ECP therapy.



PP_360 USING TTV AS A SERIAL MONITORING TOOL FOR PREDICTING REJECTION AND INFECTION IN KIDNEY RECIPIENTS

Akhil Singla[1], Kenny Chen[2], Connor Lantz[2], John Friedewald[3], Lihui Zhao[2], Rohita Sinha[4], Sanjay Mehrotra[2], Sook Park[5], Steve Kleiboeker[6], Zixuan Zhu[6]

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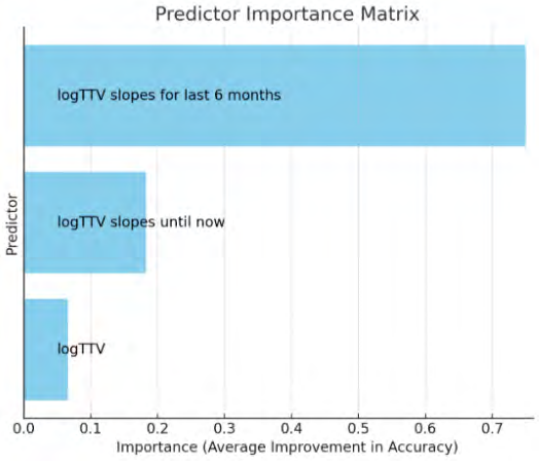
Background: Torque Teno Virus (TTV), an anellovirus ubiquitous in the human virome, has emerged as a potential biomarker reflecting the net state of immunosuppression (IS). However, instantaneous TTV viral load (VL) alone does not provide a complete picture of IS, and patient-specific factors affect the TTV range, necessitating patient-specific trajectory analysis for assessing rejection and infection risks and enabling personalized IS adjustments.

Methods: We analyzed longitudinal data from the CTOT-08 trial, which included blood and urine samples from 307 kidney transplant recipients, collected across an average of 7.7 visits per subject over two years, with over 600 biopsy samples and reported infection events. Patient-specific IS trajectory predictors—such as historical TTV averages, instantaneous VL, and longitudinal slopes of logTTV—were incorporated into a decision tree (DT) model to predict subAR (131 events) versus TX (365 events) versus infection (107 events). A logistic regression model using a TTV-based longitudinal slope variable was used to identify its impact on the chances of rejection and infection.

Results: Average logTTV VL was significantly lower during subAR compared to TX (p-value: 0.0001) and TX compared to infection events (p-value: 0.1). Our DT model, incorporating patient-specific trajectories, achieved an AUC of 0.7 for predicting subAR and 0.6 for predicting infection. We also showed that a 1.2-fold change in TTV VL over the past 3 months significantly increases the odds of infection compared to TX by 73.8% (95% CI: 6.7% to 329%). Similarly, a 0.95-fold change in TTV VL over a period exceeding one year significantly increases the odds of subAR compared to TX by 70% (95% CI: 32% to 127%).

Conclusions: TTV-based trajectories show promise as a serial monitoring tool for personalized risk predictions and IS adjustment, capturing a complete picture of immune response changes.

Event Type	Average logTTV Viral Load
subAR	4.64 (95% CI: 4.4 to 4.9)
TX	5.28 (95% CI: 5.1 to 5.4)
Infection	5.80 (95% CI: 5.2 to 6.4)



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Transplant immunology & immunosuppression

PP_361 INNATE-LIKE CD8T CELL RESPONSE TO KIDNEY GRAFT: A MULTIMODAL PROFILING STUDY OF TRANSPLANT REJECTION

Kevin Louis[1], Jiefei Wang[2], Nicole Nourié[3], Alexis Piedrafita[4], Camila Macedo[5], Uma Chandran[6], Parmjeet Randhawa[7], Alexandre Loupy[8], Diana Metes[9], Carmen Lefaucheur[10]

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Background: Uncontrolled CD8 T cell responses can lead to cell-dependent cytotoxicity and graft rejection. However, only few studies have delineated the immune phenotype, clonal repertoire and transcriptional profiles of CD8 T cells involved in graft rejection.

Methods: We performed single-cell RNA/T-cell repertoire sequencing to investigate blood CD8 T cells from kidney recipients with antibody-mediated rejection (AMR) n=6, T-cell mediated rejection (TCMR) n=6 or without rejection (stable) n=6 at time of graft biopsy. We established a single-cell transcriptional signature of 12 unique CD8 T cell subsets and applied this blood signature to profile CD8 T cells in 438 graft biopsies.

Results: Single-cell CD8 T cell profiles could distinguish stable patients from those with graft rejection. Compared to TCMR, AMR patients displayed accumulation of effector memory cells re-expressing CD45RA (TEMRA) characterized by unique expression of FCGRIIIA/CD16a, interferon-gamma and CD160 with expanded T cell clonotypes. In contrast, TCMR was characterized by increased number and clonally expanded mucosal-associated invariant T (MAIT) and natural killer T (NKT)-like cells with high expression of Eomesodermin, granulysin and perforin, supporting potent cytotoxic functions. Stable patients did not show blood accumulation of the rejection-specific TEMRA, MAIT nor NKT-like subsets. Cell deconvolution and gene-set enrichment analysis identified evidence for CD8 graft infiltration of TEMRA in AMR, and both MAIT and NKT-like cells in TCMR with only few transcripts overlap, and significant correlation with AMR and TCMR-specific Banff lesions respectively.

Conclusions: We identified previously unrecognized CD8 subsets with innate-like features involved in TCMR and the unexpected importance of a $CD16a^{+}$-CD8 T cell component in AMR. Thus, this study uncovers uncontrolled CD8 T cell responses in patients undergoing rejection and supports specific CD8 T cell targeting for treatment of graft rejection.

PP_362 INTESTINAL MICROBIOME AND ACUTE REJECTION OF TRANSPLANTED KIDNEY - RESULTS OF CASE-CONTROL STUDY

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Background: Kidney transplantation (KTx) is the preferred form of renal replacement therapy. However, acute rejection of transplanted kidney (AR) shortly after KTx may impair long-term survival of the kidney graft and the recipients. Although previous studies suggest the gut microbiota influences immune system activity, the relationship between gut microbiota and kidney rejection remains underexplored. This study aimed to investigate the relationship between gut microbiome and the risk of AR shortly after KTx.

Methods: In this single-center, retrospective case-control study, ten patients with biopsy proved AR shortly after KTx (mean age 44.7±12.3 years; 8M/2F) were matched by sex and age with 20 patients without AR during one year follow up after KTx (mean age 43.7±10.7 years; 16M/4F). Stool samples were collected 2-3 days after KTx for microbiome analysis using Illumina shallow shotgun sequencing. Bioinformatic analysis included taxonomic and functional profiling, with predictive modeling performed using a random forest model. Model performance was evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC).

Results: No significant differences in clinical characteristics or microbiota diversity were observed between two groups. Differential abundance analysis identified Bacteroides dorei/vulgatus and Clostridium as differentially abundant in AR patients, but no consistent taxonomic markers were found. Predictive models varied in performance, with functional KEGG pathway profiles showing the highest predictive value (AUC = 0.740). Key metabolic pathways implicated included lipid metabolism (e.g., sphingolipid metabolism, glycerophospholipid metabolism, and secondary bile acid biosynthesis), glycan biosynthesis, and terpenoid and polyketide metabolism.

Conclusions: 1. No universal taxonomic gut microbiota marker of AR was identified. 2. Functional profile of the gut microbiome may be related with AR, with specific metabolic pathways potentially involved in the underlying mechanisms. 3. These findings suggest a role for immunomodulation, inflammation, and metabolic regulation in AR, highlighting the need for further research to understand these associations and their impact on kidney transplant outcomes.

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PP_363 PLASMA AND WHOLE BLOOD TACROLIMUS CONCENTRATIONS DURING PREGNANCY IN KIDNEY AND LIVER TRANSPLANT RECIPIENTS

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Background: Pregnancy-related physiological changes influence tacrolimus disposition, yet data on pharmacokinetics remain scarce. Conventional whole blood (WB) tacrolimus concentration monitoring may be suboptimal during pregnancy, due to changes such as the relative increase of plasma volume. Plasma tacrolimus concentration might better reflect dosage needs. This study aimed to assess plasma and WB tacrolimus concentrations before, during, and after pregnancy in transplant recipients.

Methods: This prospective single-center cohort study included kidney and liver transplant recipients using tacrolimus during pregnancy. WB and plasma tacrolimus concentrations were measured via liquid chromatography-tandem mass spectrometry before, during, and up to one year postpartum. Concentrations (µg/L) were divided by dose (mg) to calculate concentration-to-dose (C/D) ratios. Changes in C/D ratios were analyzed using linear mixed model analysis.

Results: Nine women (10 pregnancies) were included, of which six had a kidney, two a liver and one a combined kidney-liver transplant. In six pregnancies extended-release tacrolimus (Advagraf®) and in four an immediate-release tacrolimus (Prograft®) was used. Based on WB tacrolimus concentration, the prescribed dosage increased from 3 to 7.5 mg/day (+150%) in the third trimester. Median WB tacrolimus C/D ratios decreased from 1.48 pre-pregnancy to 1.00 in the first trimester (-32%) and to 0.58 in the second and third trimester (-61%) (Figure 1). Median plasma tacrolimus C/D ratios decreased from 0.028 pre-pregnancy to 0.017 in the first trimester (-39%) and remained stable afterward. WB tacrolimus C/D ratios significantly changed over time (overall effect p<0.001) (Table 1). The effect of time became non-significant after adjusting for hematocrit (p=0.40). In contrast, the C/D ratio of plasma tacrolimus remained stable across time periods (p=0.33).

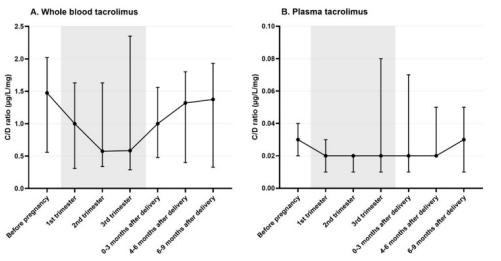
Conclusions: This study demonstrates that plasma tacrolimus C/D ratios remained stable during pregnancy, while WB C/D ratios decrease by up to 61% in the third trimester, which is largely explained by changes in hematocrit during pregnancy. These findings suggest that the increased dosages typically prescribed during pregnancy, based on WB concentrations, may not be necessary.

Table 1. Estimated Marginal Means of tacrolimus concentration-to-dose ratios derived from linear mixed model analysis

Time period	Estimated Marginal Means	95% Confidence Interval	P values*
Whole blood tacrolimus			
Before pregnancy	1.45	1.11-1.78	Reference
1st trimester	1.06	0.74-1.38	0.16
2nd trimester	0.70	0.38-1.02	**<0.001**
3rd trimester	0.80	0.48-1.11	**0.01**
0-3 months after delivery	1.04	0.72-1.36	0.43
3-6 months after delivery	1.22	0.88-1.56	1.00
6-9 months after delivery	1.30	0.96-1.63	1.00
Plasma tacrolimus			
Before pregnancy	0.03	0.02-0.05	Reference
1st trimester	0.03	0.01-0.04	1.00
2nd trimester	0.02	0.01-0.04	0.78
3rd trimester	0.03	0.01-0.04	1.00
0-3 months after delivery	0.03	0.01-0.04	1.00
3-6 months after delivery	0.03	0.01-0.04	1.00
6-9 months after delivery	0.03	0.02-0.05	1.00

* P value comparison with prepregnancy value (=baseline). Crude model, including time period as the sole predictor.

Figure 1. Concentration-to-dose ratio of whole blood and plasma tacrolimus



Median concentration-to-dose values with range within the given time-period before, during and after pregnancy. *Abbreviation: C/D: concentration-to-dose*

PP_364 USING TTV AS A MARKER OF IMMUNE RESPONSE STATUS AND ITS TRAJECTORY IN KIDNEY TRANSPLANT RECIPIENTS

***Akhil Singla*[1], Kenny Chen[2], Connor Lantz[2], John Friedewald[3], Lihui Zhao[2], Rohita Sinha[4], Sanjay Mehrotra[2], Sook Park[5], Steve Kleiboeker[6], Zixuan Zhu[6]**

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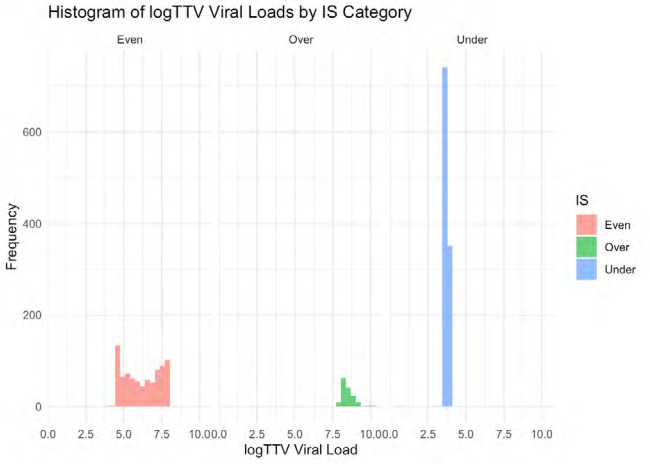
Background: Torque Teno Virus (TTV), an anellovirus ubiquitous in the human virome, has emerged as a potential biomarker reflecting the net state of immunosuppression (IS). Unlike other biomarkers, TTV can capture both the status of immune response (IR) and its trajectory, enabling more informed adjustments to IS therapy.

Methods: We analyzed longitudinal data from the CTOT-08 trial, which included blood and urine samples from 307 kidney transplant recipients, collected across an average of 7.7 visits per subject over two years, with over 600 biopsy samples and reported infection events. We used a multi-criteria decision approach to establish optimal two-sided thresholds for TTV viral load, leveraging data from biopsy phenotypes, clinical infections, and longitudinal viral loads. We developed a decision tree (DT) model to predict infection (107 events) versus subAR (131 events) using patient-specific, logTTV-derived predictors.

Results: We classified immune response (IR) status into under-IS (logTTV < 4), even-IS (logTTV between 4 and 8), and over-IS (logTTV > 8) categories. The average logTTV values were 3.8, 6.2, and 8.5, while the average historical logTTV slopes were negative, nearly zero, and positive in the under-, even-, and over-IS categories, respectively. Subjects in the under-IS category had 1.6 times the risk of subAR compared to those in the over-IS category. Conversely, subjects in the over-IS category had triple the risk of infection compared to those in the under-IS category. Our decision tree (DT) model, incorporating patient-specific TTV predictors, achieved an AUC of 0.71, with a sensitivity of 47%, specificity of 91%, PPV of 82%, and NPV of 66% for predicting infection versus subAR.

Conclusions: TTV enables the classification of IR into under-, even-, or over-IS categories and tracks personalized IR trajectories. These findings provide insights for preemptive IS adjustments by assessing both the current IS state and the direction of IR changes.



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Transplant immunology & immunosuppression

PP_365 REFERENCE INDICATORS FOR ANTI-THYMOGLOBULIN DOSING IN KIDNEY TRANSPLANT

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Background: Anti-thymoglobulin (ATG) is widely used for induction therapy in kidney transplantation, but a standardized dosing regimen remains undefined. The common protocol involves 1.5–2 mg/kg intraoperatively, followed by 1.5–2 mg/kg daily for 2 to 4 days. Excessive T cell suppression increases infection risk, while insufficient suppression may jeopardize graft function. A reliable biomarker to optimize ATG dosing is crucial for enhancing its clinical efficacy.

Methods: From August 2018 to December 2023, all kidney transplants at our hospital were included, excluding cases with ABO incompatibility, atypical hemolytic uremic syndrome, thrombotic microangiopathy, donor-specific antibody positivity, or donation after circulatory death. ATG was given intraoperatively at 1–1.5 mg/kg, with subsequent doses of 0.5 mg/kg daily guided by peripheral CD4/total lymphocyte count (TLC) and CD8/TLC ratios until both fell below 10%. Graft function, rejection episodes, and infection rates were monitored to assess the efficacy and safety of this approach.

Results: This study included 81 patients, with 40 receiving living-related and 41 deceased donor kidney transplants. The median ATG dosage was 1.5 mg/kg. Notably, 39 patients achieved CD4/TLC and CD8/TLC ratios <10% with a single intraoperative dose. Acute T cell-mediated rejection occurred in one case due to poor medication adherence. BK viruria and *Escherichia coli* were the most common infections, with no significant difference in ATG dosage between patients with and without infections.

Conclusions: Guiding anti-thymoglobulin (ATG) dosing in kidney transplantation using CD4/TLC and CD8/TLC ratios <10% is effective and safe. This approach maintained graft function with minimal rejection, including one acute T cell-mediated rejection due to poor adherence. The median ATG dose of 1.5 mg/kg, lower than traditional regimens, was linked to infections, suggesting higher doses may further increase infection risk.

PP_366 EVEROLIMUS-BASED IMMUNOSUPPRESSION EXPANDS REGULATORY T-CELLS AND PRESERVES EFFECTOR MEMORY T-CELLS

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Background: Everolimus (EVR) is known for limited nephrotoxicity and tolerance-inducing properties compared to mycophenolate mofetil (MMF) following kidney transplantation. EVR may be beneficial for elderly patients with increased frailty and comorbidities, presenting with a different risk profile for kidney transplantation. This study aimed to evaluate T-cell differentiation and exhaustion marker profiles in patients on everolimus-tacrolimus-prednisolone (EVR-IS) versus MMF-tacrolimus-prednisolone (MMF-IS) post-transplant.

Methods: In the multicenter OPTIMIZE study (EudraCT number: 2018-003194-10), blood samples were collected from kidney transplant recipients aged ≥65 years before transplantation and at 12 and 24 months after transplantation. Participants were randomized to either MMF-IS or EVR-IS. Circulating T-cells (N=86 EVR-IS, N=83 MMF-IS) were analyzed for differentiation status, transcription factor and exhaustion marker expression using multiparameter flow cytometry. Data were analyzed through assessing predefined T-cell subsets and marker expression and by unsupervised analysis (FlowSOM).

Results: MMF-IS resulted in a significant decrease in percentages of central (CD45RA-CCR7+, Tcm) and effector (CD45RA-CCR7-, Tem) memory CD4+ and CD8+ T-cells, as well as regulatory CD4+ T-cells (Tregs) at 12 months, with stabilization by 24 months. In contrast, EVR-IS led to an increase in Tregs at 12 months ($P<0.05$), while CD4+ and CD8+ Tem percentages remained stable. Unsupervised analysis identified three significantly different clusters of cells at 12 months, largely confirming the traditional analysis. One cluster represented Tregs (2.4-fold higher in EVR-IS), one less differentiated CD4+ Tem co-expressing Ki-67 (1.9-fold higher in EVR-IS), and one cluster contained terminally differentiated CD8+ Tem expressing Tbet (2-fold lower in EVR-IS). The expression of exhaustion markers did not differ between the two arms with no significant changes in time after transplantation.

Conclusions: EVR-IS promotes Treg expansion while maintaining stable CD4+ and CD8+ Tem percentages, unlike MMF-IS. These findings suggest that tolerance induction by EVR could be an important mechanism which allows for lower levels of tacrolimus in elderly transplant recipients

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Transplant immunology & immunosuppression

PP_367 PATHOLOGICAL FACTORS AND SURVIVAL OUTCOMES IN ABO-INCOMPATIBLE LIVING-DONOR KIDNEY TRANSPLANTATION

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Background: Advancements in desensitization therapy have significantly improved the graft survival rate of ABO-incompatible (ABO-I) living-donor kidney transplantation, making it comparable to that of ABO-compatible (ABO-C) transplants. However, challenges remain, including higher incidences of antibody-mediated rejection and infections. In this study, we investigated the pathological factors affecting graft survival in ABO-I transplantation.

Methods: Among 718 living-donor kidney transplantations performed by the Osaka University Kidney Transplant Group since 2010, 523 ABO-C cases and 195 ABO-I cases were retrospectively analyzed and compared. Propensity score matching (PSM) was also conducted based on factors showing significant differences between the two groups. Desensitization therapy included splenectomy and plasma exchange until 2013, and rituximab and plasma exchange from 2014 onward.

Results: The 10-year graft survival rates were 93.6% for ABO-C and 91.5% for ABO-I, with no significant difference. However, the 10-year patient survival rates were significantly lower for ABO-I (95.5% for ABO-C vs. 89.4% for ABO-I, p = 0.008). After PSM, the 10-year patient survival rates were 93.0% for ABO-C and 88.9% for ABO-I, with no significant difference observed (p = 0.055). However, there was a trend toward lower survival rates in ABO-I, mainly due to a higher incidence of infections. No significant differences were observed between the two groups regarding the incidence of hypertension, diabetes, cardiovascular disease, or malignancies. Pathological findings revealed that C4d deposition was significantly more common in ABO-I (81.3%) than in ABO-C (13.4%). While microvascular inflammation (MVI) did not occur more frequently in ABO-I, its presence was associated with significantly lower graft survival compared to cases without MVI (p = 0.0018, 94.4% for ABO-C vs. 88.6% for ABO-I).

Conclusions: While graft survival in ABO-I kidney transplantation has become comparable to ABO-C transplantation, patient survival remains lower due to higher infection rates. Although MVI is not more frequent in ABO-I, its presence significantly impacts graft survival. Addressing infection risks and the consequences of MVI is crucial for improving ABO-I outcomes.

PP_368 T-CELL EPITOPE MISMATCHES PREDICT REJECTION IN KIDNEY TRANSPLANTS UNDERGOING BASILIXIMAB INDUCTION

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Background: T-cell mediated rejection is the commonest type of rejection in the first 12 months post kidney transplantation. We previously showed that the level of sensitisation at the time of transplant is a poor predictor of rejection in patients undergoing induction with non-depleting antibodies. Hence, we analysed the association of T-cell epitope mismatches and rejection in a multi-ethnic population undergoing kidney transplantation with basiliximab induction.

Methods: Adult patients who underwent kidney alone transplantation with basiliximab induction at a single centre between 2012-2023 were included. T-cell epitope mismatches were quantified using Predicted Indirectly ReCognizable HLA Epitope (PIRCHE-II) scores (https://www.pirche.com). Scores were transformed as ln(PIRCHE + 1) for analysis. We determined the impact of epitope mismatches on rejection rates, and death-censored allograft survival (DCGS) over a follow-up of 5-years post-transplant.

Results: 825 kidney transplant recipients (KTRs) were included, mean age 50 ± 13.5 years, 296 (35.9%) female, and 466 (56.5%) from black and minority ethnic groups. 211 (25.6%) patients were sensitised (cRF 1-84%), and 92 (11.2%) were highly sensitised (crf 85-100%) at the time of transplant. Mean ln(PIRCHE+1) scores were 4.249 ± 0.583 and 3.973 ± 1.005 in patients with and without rejection at 12-months (p=0.022), and 4.102 ± 0.669 and 3.909 ± 0.987 in patients with and without rejection at 60-months (p=0.27) (**Figure 1a**). Rejection of any type at 12 months occurred in 9 (5.63%) patients with PIRCHE scores in the lowest quartile (Q1 PIRCHE) and 16 (10.74%) patients with scores in the highest quartile (Q4 PIRCHE) (p=0.29). There was a stepwise increase in rejection with each increase in PIRCHE quartile, but this did not reach statistical significance (**Figure 1b**). There were no differences in DCGS or rejection free allograft survival when patients were stratified by PIRCHE scores (**Figure 1c**). Ln(PIRCHE+1) was associated with rejection at 12-months in multivariable analyses (Odds Ratio 1.57, 95% CI 1.01-2.61), whereas levels of sensitisation were not (**Table 1**).

Conclusions: T-cell epitope mismatches inform rejection risk in the first-year post kidney transplant in patients undergoing non-depleting induction, but no impact on graft survival was seen.

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Figure 1: Association between PIRCHE scores and rejection
a. ln(PIRCHE+1) scores in patients with no rejection, any rejection, TCMR / mixed rejection and ABMR at 12 months. Mean and SD values plotted.
b. ln(PIRCHE+1) scores in patients with no rejection, any rejection, TCMR / mixed rejection and ABMR at 60 months. Mean and SD values plotted.
c.12-month rejection rates in patients divided into PIRCHE score quartiles. Rates of any rejection and TCMR / mixed rejection plotted.
d. DCGS and rejection free allograft survival in patients stratified by PIRCHE quartile.

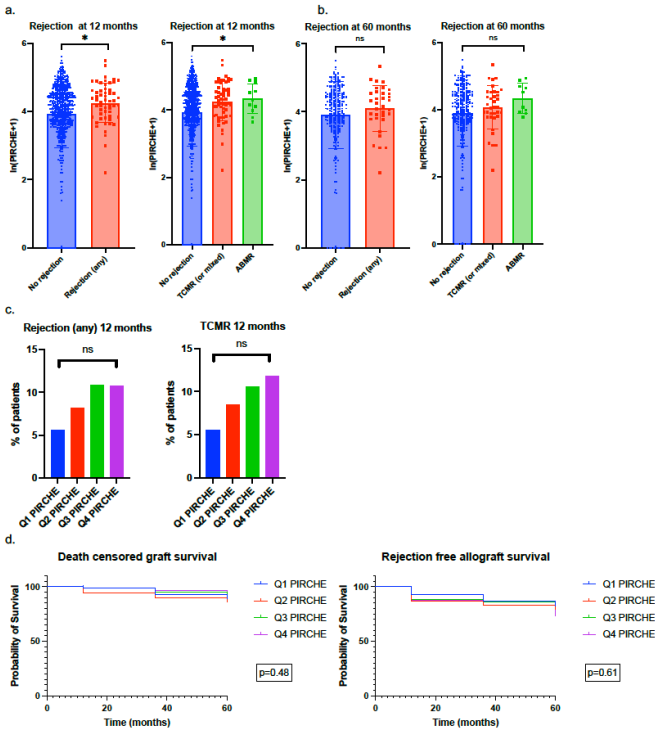

Table 1: Multivariable logistic regression analysis of clinical variables associated with rejection (any type) at 12-months.

Clinical Variable	*Odds Ratio for Rejection at 12-months*	*95% confidence interval*
Age at Transplant	0.9842	0.9627 to 1.006
Male Sex [reference = female]	0.8231	0.4594 to 1.499
Ethnicity [black; reference = white]	0.9235	0.4522 to 1.846
Ethnicity [Asian; reference = white]	0.7687	0.3639 to 1.560
DBD transplant [reference = live transplant]	0.5734	0.2686 to 1.234
DCD transplant [reference = live transplant]	0.9267	0.4242 to 2.041
Total HLA Mismatch	1.058	0.8143 to 1.374
cRF as continuous variable	1.005	0.9958 to 1.013
Pre-emptive transplant [reference = not pre-emptive]	1.290	0.6404 to 2.489
Multiple grafts [reference = first graft]	1.268	0.5695 to 2.667
ln(PIRCHE+1) as continuous variable	**1.574**	**1.009 to 2.610**

PP_369 EXPANSION OF DONOR-SPECIFIC REGULATORY T-CELLS AND INCREASED TREG/TEFFECTOR RATIO UNDER EVEROLIMUS

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Background: Everolimus-tacrolimus-prednisolone (EVR-IS) immunosuppression allows for lower tacrolimus trough levels than mycophenolate mofetil-tacrolimus-prednisolone (MMF-IS) in kidney transplant recipients. EVR-IS leads to the expansion of regulatory CD4+ T cells (Tregs), while the effector memory T cell population remains mostly unaffected. MMF-IS, however, causes a progressive loss of donor-specific effector memory T cells, especially in CD4+ T cells. Whether EVR-IS induced changes in T cell subpopulations are reflected in frequencies of donor-specific T cells is not known but important to interpret the clinical significance of Treg expansion.

Methods: PBMCs from 20 kidney transplant recipients (10 EVR-IS and 10 MMF-IS) prior to, and at 12 and 24 months after transplantation were short-term stimulated with CD3-depleted donor cells. The activation-induced marker CD137 was used to identify donor-reactive regulatory (Treg) and effector (Teff) T cells by multiparameter flowcytometry. Tregs were identified as CD4+CD25++CD127- T cells.

Results: The proportion of donor-specific Tregs increased in the EVR-IS group, while it decreased in the MMF-IS group. At 12 months, the average percentage of CD137+ Tregs was 0.19% for EVR-IS versus 0.05% for MMF-IS (P<0.05). Donor-specific CD4+ Teff declined in both arms, but more sharply in the MMF-IS group, with 0.14% and 0.06% CD137+ CD4+ Teff at 12 months, respectively. The decline in donor-specific CD8+ Teff occurred earlier in EVR-IS (60% reduction from 0.91% to 0.31%) compared to MMF-IS, where it was delayed until 24 months. The Treg/Teff ratios for both CD4+ and CD8+ Teff significantly increased in EVR-IS (P=0.01), from 1.2 to 1.9 and 0.3 to 0.9, respectively, at 24 months. In contrast, these ratios decreased in the MMF-IS arm.

Conclusions: EVR-IS leads to a significant expansion of donor-specific Tregs and a reduction in donor-specific CD8+ and CD4+ Teff over time. The resulting increase in the Treg/Teff ratio may explain the observation that an EVL-IS regimen allows for lower tacrolimus trough levels.

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PP_370 LYMPHOCYTE DEPLETION POST ALEMTUZUMAB IN IMLIFIDASE ENABLED KIDNEY TRANSPLANTS; A UK CASE SERIES

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Background: Imlifidase temporarily cleaves IgG, providing a short window for kidney transplantation in highly sensitised patients.High-quality, large-scale trials are lacking, leaving uncertainty around optimal induction immunosuppression, particularly around timing of induction agents which are also inactivated by imlifidase.

Methods: In 2024, pharmacists from three UK centres reviewed treatment of 4 imlifidase-enabled kidney transplant patients, and collaboratively shared insights and reflections to inform future practice. **Patient 1 (Trust A):** A 56-year-old male, second transplant (February), end of chain altruistic offer via deceased donor list. **Patient 2 (Trust B):** A 47 year old male, third transplant (June), end of chain altruistic offer via deceased donor list. **Patient 3 (Trust A):** A 34-year-old female, third transplant (July), deceased donor transplant (DBD). **Patient 4 (Trust C):** A 52-year-old female, first transplant (October), deceased donor transplant (DBD). All four patients received induction with alemtuzumab (timing attenuated by experience) and centre specific intensified triple therapy (IV/PO corticosteroids, mycophenolate mofetil and tacrolimus (target trough 8 -14ug/L)).

Results: At day 28, 3 of 4 patients remained in-patients, see figure 1.

Conclusions: This series highlights the evolution of imlifidase-enabled kidney transplants. Timing and choice of induction remains unclear due to variability in imlifidase's half-life and its effect on them. Imlifidase has a half-life of 60-238 hours (mean 89). The need for intense clinical scrutiny and prompt immunosuppression adjustments according to clinical circumstance are essential. Early TCMR was seen in 3 of 4 cases so future strategies, including alemtuzumab pre-imlifidase, repeat dosing of alemtuzumab and alternative agents like eATG, will need to address this. Protocolised biopsies could inform earlier decision making. All must balance the risks of ischaemic time, immunosuppressive burden, and long-term outcomes.

Figure 1: Lymphocyte depletion timeline

Day	0	1	4	5	7	8	10	12	13	17	28
Patient 1 (Trust A)	Imlifidase		Alemtuzumab						Alemtuzumab		
Lymphocytes (x10⁹/L)	0.64	2.53	1.05	0.55	1.61	0.76	1.53	0.93	1.35	0.00	0.01
Creatinine (umol/L)	448	171	121	133	131	134	119	109	133	120	89
Methylprednisolone (MP)		MP (4 days) then prednisolone from D5							MP (D13-15)		
	Cumulative DSA MFI pre-imlifidase, Class I: 1900, Class II: 8000. MM 1-2-1. Dialysis independent at day 28										
DSA post imlifidase	Negative	Negative					DSA Positive				Positive
Patient 2 (Trust B)	Imlifidase				Alemtuzumab						
Lymphocytes (x10⁹/L)	0.3	0.4	0.6	0.4	0.3	0.4	0.02	0.09	0.09	0.08	0.2
Creatinine (umol/L)	757	702	708	521	338	504	541	569	617	704	545
Methylprednisolone (MP)		MP (4 days) then prednisolone from D5					MP (D9-10)* (patient unable to tolerate)				
							rATG (D10-25; 4 doses in total)				
										PEx (D17-32; 10 cycles in total)	
	Cumulative DSA MFI pre-imlifidase, Class I: 5804, Class II: 2862. MM 0-2-1. Remained dialysis dependent at day 28										
DSA post imlifidase	Negative	Negative								DSA Positive (D15)	DSA's rising (D21)
Patient 3 (Trust A)	Imlifidase							Alemtuzumab			
Lymphocytes (x10⁹/L)	1.28	0.35	0.42	0.41	0.57	0.69	0.38	0.46	0.00	0.00	0.00
Creatinine (umol/L)	661	480	647	581	717	572	623	642	655	609	454
Methylprednisolone (MP)		MP (4 days) then prednisolone from D5				MP (D8-11)					
	Cumulative DSA MFI pre-imlifidase, Class I: 10,050, Class II: DSA Negative. MM 0-1-0. Dialysis independent at day 28										
DSA post imlifidase	Negative	Negative					Weak DSA Positive			DSA Positive (D18)	Positive
Patient 4 (Trust C)	Imlifidase		Alemtuzumab		Alemtuzumab						
Lymphocytes (x10⁹/L)	1.36	0.55	0.17 (post alemtuz)	0.06	0.1	0.04	0.03	0.03	0.03	0.06	0.14
Creatinine (umol/L)	602	781	815	817	531	646	650	562	604	575	346
Methylprednisolone (MP)		MP (D1-15) then prednisolone from D16									
	Cumulative DSA MFI pre-imlifidase, Class I: 15000, Class II: DSA negative. MM 2-2-0. Remained dialysis dependent at day 28										
DSA post imlifidase	Negative	Negative									Negative

PP_371 SYSTEMATIC TRANSPLANTECTOMY VERSUS CONVENTIONAL CARE AFTER KIDNEY GRAFT FAILURE (DESYRE)

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Background: The optimal approach to managing kidney transplant patients returning to dialysis, particularly regarding immunosuppression (IS) and transplantectomy, needs to be better defined. The practice of performing a systematic transplantectomy upon return to dialysis under immunosuppressive cover to prevent sensitization related to graft retention after IS discontinuation has never been prospectively evaluated.

Methods: The DESYRE prospective randomized study compared systematic transplantectomy followed by rapid IS withdrawal over two months versus slow IS tapering over nine months with the graft in place, assessing the risk of anti-HLA sensitization (measured by Luminex) one year after return to dialysis (primary endpoint). Secondary endpoints included the kinetics of anti-HLA antibody (Ab) development, inflammatory syndrome, nutritional status, anemia, and IS-related complications in both arms.

Results: Fifty-six patients (28 in each arm), instead of the 118 initially planned, were included due to recruitment challenges related to randomizing a surgical procedure. The immunization rate was similar between the groups, with 77% developing at least one new anti-HLA Ab in class I or II within one year. Patients in both groups developed Abs against 20% of the available eplet antigen repertoire for Ab formation. The onset and peak of anti-HLA Abs were correlated with the duration of IS tapering, with no direct link to transplantectomy. The study's secondary endpoints will be reported during the congress presentation.

Conclusions: The DESYRE study's results have significant implications for the management of kidney transplant patients. The study demonstrates no benefit in anti-HLA sensitization from a strategy combining systematic transplantectomy after return to dialysis with subsequent rapid IS withdrawal. This suggests that maintaining immunosuppression is the best strategy to avoid sensitization in patients awaiting re-transplantation.

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PP_372 EXPLORING A NEW URINE-DERIVED RENAL EPITHELIAL AND WHARTON'S JELLY MESENCHYMAL CELLS 3D MODEL

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Background: The set-up of more in vivo-like conditions is a main goal of the newest culture techniques. Different cell types can be combined into hybrid and multicellular 3D structures, to study how they interact and distribute. Urine Renal Epithelial Cells (URECs) are a heterogeneous cells population voided in urine from the upper urinary tract; these cells are rarely detected in healthy subjects, while their number increases in presence of acute kidney damage and after kidney transplant. Here, we aimed to establish a 3D model combining URECs with Wharton's Jelly Mesenchymal Stromal Cells (WJ-MSCs), to evaluate structure, cell distribution and viability of the newly generated spheroids. Immunomodulatory properties were analysed by coculturing spheroids with Peripheral Blood Mononuclear Cells (PBMCs); the proliferation of CD4 and CD8 T cells, as well as the percentage of Treg cells and Granzyme B positive cells were evaluated after coculture.

Methods: URECs and WJ-MSCs were combined to obtain spheroids by testing different condition and ratio: URECs or WJ-MSCs only, URECs:WJ-MSCs 1:1 and 2:1 ratio. Spheroids formation and cell distribution were analysed using Incucyte, and by staining URECs and WJ-MSCs with different fluorochromes. The viability was assessed by Live/Dead assay at different time point. Spheroids were then cultured with PBMCs, and after 72h immune cells were analysed by flow cytometry, comparing the results with activated PBMCs set as control.

Results: Stable spheroids were obtained combining URECs and WJ-MSCs, with a higher viability compared to WJ-MSCs spheres, while URECs alone could not self-aggregate (Fig.1a-b-d). URECs were mostly located in the core of the 3D model, while WJ-MSCs were in the outer layer (Fig. 1c). In coculture with PBMCs, hybrid spheroids reduced CD4 and CD8 T cell proliferation, and the percentage of Granzyme B producing cells, while increasing the regulatory T cell subset (Fig. 1 e-f-g).

Conclusions: Our data showed long term stability and promising immunomodulatory effects for UREC:WJ-MSCs spheroids. These findings may provide the background for studies testing previously unknown effects of this new hybrid 3D cell model.

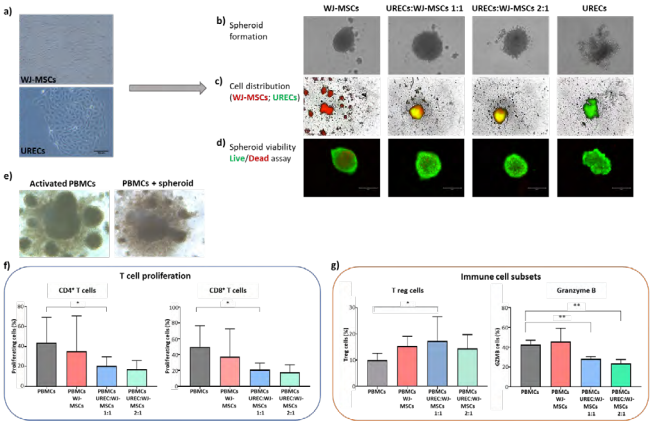

Fig.1: **a)** WJ-MSCs and UREC representative pictures. **b)** Morphology of WJ-MSCs, UREC:WJ-MSCs (1:1; 2:1 ratio) and UREC spheroids. **c)** WJ (red) and UREC (green) distribution in spheroids cultured for 72h. **d)** Live and Dead assay on spheroids cultured for 72h. **e)** Representative pictures of Activated PBMCs (control) and PBMCs-spheroids coculture. **f)** Evaluation of CD4 and CD8 T cell proliferation after PBMCs-spheroids coculture. **g)** Analysis of CD4+CD25+Foxp3+ Treg and Granzyme B percentage after PBMCs-spheroids coculture. * p<0.05; ** p<0.01

PP_373 EARLY HLA ANTIBODY SCREENING IN THE FIRST MONTH POSTTRANSPLANT AND KIDNEY GRAFT OUTCOMES

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Background: Donor-specific HLA antibodies (DSA) are related to antibody-mediated rejection (ABMR) and graft failure. The indication and frequency of screening for anti-HLA antibodies in stable patients are not established. The aim of our study is to evaluate the impact of early DSA appearance in the first month post-transplant on graft outcomes.

Methods: All kidney transplant recipients between 01/01/2012-12/31/2022 with anti-HLA antibody screening by Luminex during the first month post-transplant were included. Patients with preformed or historical DSA and those with DSA detection after graft loss were excluded. The mean fluorescence intensity cut-off was 1,500.

Results: Three hundred fifty-three patients were included and the median time from transplant to first antibody test was 30.0 days. During 3.8 years of follow-up, graft loss occurred in 9.1% and 19.5% had ABMR. A total of 8.5% developed early-DSA in the first month. Patients with early-DSA detection had more HLA sensitization at the time of transplant (p<0.001) and were associated with lower ABMR-free survival (**Figure 1**). Multivariable analysis showed that the presence of early-DSA was an independent risk factor for ABMR.

Conclusions: In conclusion, patients with HLA sensitization at the time of transplant have a higher risk of DSA formation in the first month, probably reflecting alloimmune memory, therefore early HLA antibody screening should be performed in this high-risk population.

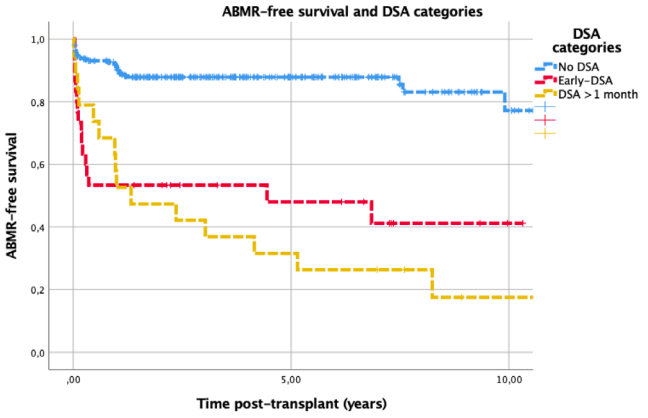

Figure 1. Kaplan–Meier survival analysis of antibody-mediated rejection (ABMR) for DSA categories.

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PP_374 VORTEX-ACTUATED CELL SORTING BOOSTS HUMAN REGULATORY T CELL THROUGHPUT AND GROWTH

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Background: Cell sorting is crucial to produce cells of interest at high purity for the manufacturing of cell therapies. Magnetic-activated cell sorting (MACS) can be used to enrich for cells of interest before fluorescence-activated cell sorting to reduce sorting time. Cell sorting using different techniques can be cumbersome and data comparing different enrichment methods is scarce. Highway1, a Good Manufacturing Practice-compliant cell sorter, sorts cells using transient vortices (i.e. vortex-actuated cell sorting, VACS) which may be gentler and improve cell viability. We compared VACS enrichment with CD25 MACS enrichment before purifying human regulatory T cells (Tregs) with VACS.

Methods: Peripheral blood mononuclear cells were isolated from blood cones from blood donors. Tregs were sorted using the Highway1 after CD25 MACS enrichment (MP), CD4CD25 VACS enrichment (VP) or directly without enrichment (DP), then expanded with CD3/CD28 stimulation beads, IL-2 and rapamycin (Figure 1a).

Results: Sorting using MP, VP and DP produced Tregs of high and comparable purity (95.3±3.8%, 96.5±2.6 vs 94.5±3.1%, mean±SD, p=0.45, Figure 1b). Both MP and VP reduced sorting time compared to DP (2.1±1.3, 6.1±1.5 vs 19.8±0.8 minutes per 10 million cells, Figure 1c). Treg yield (Figure 1d) from VP (13.6±4.0%) was lower than DP (27.3±11.0%) but higher than MP (8.6±3.3%). Tregs from VP and DP expanded more than MP after 6 (3.6±2.0, 5.1±2.7 vs 1.2±1.0 fold expansion, Figure 1e) and 14 days (60.2±54.0, 69.0±52.1 vs 3.3±2.8 fold expansion, Figure 1f). CD25 expression was lower in Tregs produced by MP at day 6 compared to VP and DP, though Foxp3, Helios, TIGIT, CTLA-4 CD62L expression did not differ (Figure 1g).

Conclusions: CD4CD25 VACS enrichment reduced time needed for Treg sorting, had greater yield and produced Tregs that expanded better than CD25 MACS enrichment.

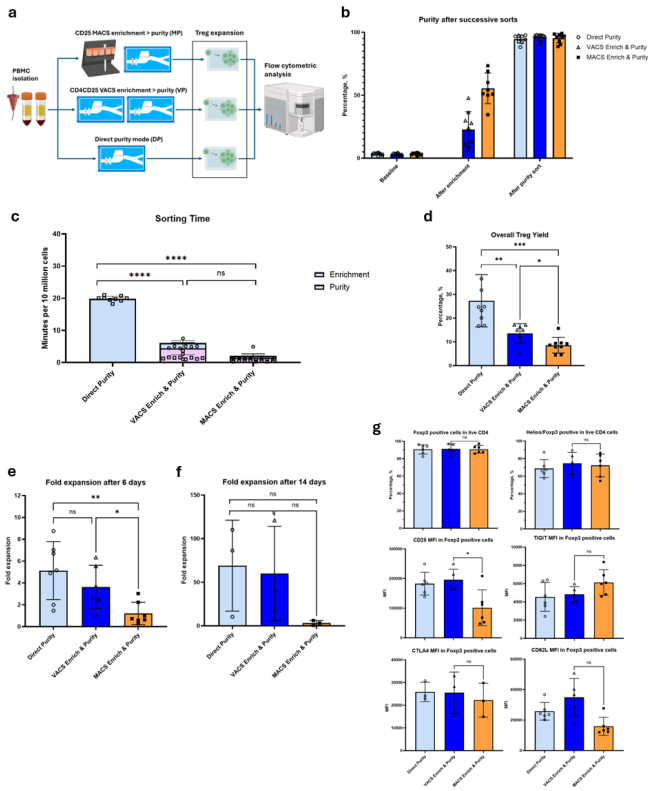

Figure 1a. Overall study design **b.** Purity for regulatory T cell (Tregs) after successive sorts after CD25 MACS enrichment (MP), CD4CD25 VACS enrichment (VP) or directly without enrichment (DP) **c.** Sorting time **d.** Treg yield **e.** Fold expansion at day 6 and **f.** at day 14 **g.** Treg functional and phenotypic markers at day 6 comparing MP, VP and DP. PBMC, Peripheral blood mononuclear cells; MACS, magnetic-activated cell sorting; VACS, vortex-actuated cell sorting. *p<0.05, **p<0.01, ***p<0.001****, p<0.0001, ns, not significant

PP_375 THE ROLE OF ENDOTHELIAL DYSFUNCTION AND MICROVASCULAR THROMBOSIS IN RENAL ALLOGRAFT SURVIVAL

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Background: Antibody-mediated rejection (ABMR) involves complex immunological mechanisms. Key factors include TNF-α, driving inflammation, and VEGF, a regulator of vascular remodeling, contributing to endothelial dysfunction marked by reduced nitric oxide (NO) and altered von Willebrand factor (vWF). This study aims to unravel the dynamic interplay of these factors, shedding light on their roles in the ABMR.

Methods: ABMR cases (n:128) were analyzed for renal expression of TNF-α alongside interstitial infiltration by macrophages and lymphocytes. VEGF, NO, vWF, and CD61 expression were graded in glomeruli and peritubular capillaries (PTCs). Follow-up biopsies were assessed for the progression of interstitial fibrosis (IF), transplant glomerulopathy (TG), and glomerulosclerosis (GS) exceeding 15%.

Results: The intensity of inflammatory cells in glomeruli, PTCs, and interstitium, combined with interstitial and tubular TNF-α expression, demonstrated a strong positive correlation with increased vWF and CD61 in glomeruli and PTCs (p<.001). In contrast, these parameters were inversely correlated with VEGF and NO expression in the same regions (p<.001). CD61(+) thrombosis increased in glomeruli and PTCs in parallel with elevated microvascular vWF, while VEGF and NO expression decreased in microvasculature. Patients with increased glomerular and PTC vWF and CD61 expression, coupled with reduced VEGF and NO levels, exhibit in follow-up biopsies a higher prevalence of proteinuria, PTC destruction, IF, TG, GS, and graft loss as evidenced by follow-up biopsies (p<.01).

Conclusions: Elevated vWF and CD61(+) thrombosis in glomeruli and PTCs, alongside diminished VEGF and NO levels, significantly exacerbate microvascular injury, leading to accelerated IF, TG, and GS. These are strongly associated with poorer graft prognosis, including heightened proteinuria and irreversible graft loss. The findings underscore the detrimental impact of endothelial dysfunction and microvascular thrombosis on renal allograft survival, highlighting their importance as therapeutic targets to mitigate graft failure.

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PP_376 KIDNEY TRANSPLANT IN SENSITIZED PATIENTS WITH DONOR SPECIFIC ANTIBODIES USING A DELISTING STRATEGY

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Background: Highly sensitized patients face challenges in kidney transplantation (KT) due to limited donor compatibility and high rejection risks. Delisting forbidden HLA antigens is a strategy to expand transplantation opportunities.

Methods: This retrospective, multicenter study included highly sensitized patients (cPRA≥98%) undergoing delisting strategies before KT from December 2018 to June 2024. Initially, KT was allowed with low-intensity anti-HLA antibodies (MFI <4000). If cPRA remained high, a more aggressive approach permitted antibodies with MFI up to 10,000. Complement-binding antibodies and those targeting previous transplant antigens were excluded. The primary objetive was to analyze the outcomes of KT following the delisting of forbidden HLA antigens, aiming to reduce cPRA to <98%.

Results: Seventeen patients from three Andalusian hospitals were included, all with preformed donor-specific antibodies (DSA) after applying delisting strategies. All patients had a negative complement-dependent cytotoxicity crossmatch, average age 50±10 years, 65% female, and median dialysis duration of 59 months. Time from delisting to KT was 16 [4–23] months. Sixty-five percent had a prior transplant. Mean cPRA decreased from 99.5±0.6 to 88±14 after delisting. The mean number of mismatches was 5.2±1.3, with 2 [1.5–3] DSAs at KT. Post-transplant desensitization was performed in 82%, with all receiving Thymoglobulin induction. Six patients experienced acute rejection (five humoral, one mixed) within 12 [9–35] days post-transplant. Infections occurred in 47%, including CMV in 23%. Graft functionality at 7 [4–50] months was 93%, with renal function at 6 and 12 months at 48 and 54 ml/min, respectively. Patient survival was 100%.

Conclusions: The implementation of delisting strategies optimizes the chances of KT in highly sensitized patients with preformed donor-specific antibodies. Despite a high incidence of acute rejection and infections, the majority of grafts remain functional with acceptable renal function. These findings highlight the effectiveness of delisting in improving access to transplantation in this complex population.

PP_377 CLINICAL CHARACTERISTICS AND OUTCOMES IN RECURRENT AND NATIVE IMMUNOGLOBULIN A NEPHROPATHY

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Background: Immunoglobulin A nephropathy (IgAN) is the most prevalent primary glomerular disease and a major cause of end-stage kidney disease (ESKD). IgAN can recur post-transplant (rIgAN) in 9–53% of cases, and graft survival after recurrence is poor. Newer targeted treatments are being investigated in IgAN but are currently limited to native IgAN (nIgAN). Understanding the similarities and differences between rIgAN and nIgAN could help in translating these treatments and potentially improve outcomes in rIgAN.

Methods: This single-centre retrospective study at Manchester University Hospitals, UK, analysed data from 63 patients with nIgAN and 21 with rIgAN. Demographics, clinical features, histology and outcomes including ESKD during follow up were assessed. Findings were supplemented with Kaplan-Meier analysis of time to ESKD.

Results: Median age at diagnosis was higher in the rIgAN group (47 vs. 37 years). Male predominance was seen in both cohorts (90.5% vs. 73.0%). Median time from transplant to IgAN diagnosis was 44 months. Serum creatinine at presentation was significantly elevated in rIgAN (227 µmol/L vs. 128 µmol/L, p < 0.001). All the MEST scores were higher in rIgAN group. Serum creatinine in the rIgAN group showed consistent deterioration over time. rIgAN was associated with higher graft failure rates (52.4% vs. 22.2% in nIgAN, p = 0.019) and earlier onset (17 vs 50 months). Kaplan-Meier analysis showed significant acceleration to kidney failure in rIgAN compared to nIgAN (Fig. 1, p = 0.0002).

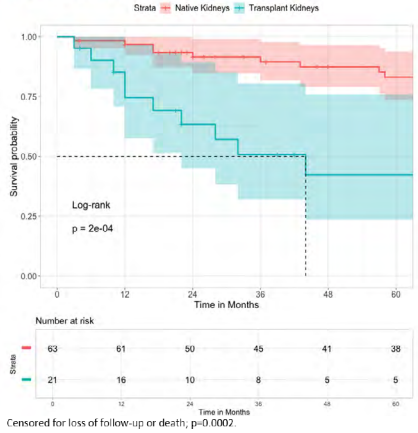
Conclusions: Recurrent IgAN is diagnosed in later stages of CKD, exhibits higher adverse histological features and has a more aggressive course. The significantly shorter time to ESKD underscores the need for earlier diagnosis and investigation of predictive markers. There is an urgent need for application of newer therapies and translating the use of agents in native IgAN seems the next logical approach to improve outcomes in rIgAN.

Table:

Variable	Overall	nIgAN	rIgAN	p
Number	84	63	21	
Age at time of Biopsy	41.50 [30.50, 51.25]	37.00 [28.00, 50.50]	47.00 [41.00, 55.00]	0.07
Males, n (%)	65 (77.4)	46 (73.0)	19 (90.5)	0.175
Transplant to Diagnosis, months	NA	NA	44.00 [33.50, 62.50]	
Systolic BP, mm Hg	146.79 (23.38)	145.51 (23.25)	151.05 (23.94)	0.368
Diastolic BP, mm Hg	86.68 (13.61)	86.78 (13.71)	86.37 (13.65)	0.909
MAP, mm Hg	106.74 (15.23)	106.41 (15.40)	107.84 (15.00)	0.722
RASI, n (%)	62 (73.8%)	55* (87.3)	7 (33.3)	<0.001
MEST Score				
M1	51 (60.7)	34 (54.0)	17 (81.0)	0.053
E1	26 (31.0)	13 (20.6)	13 (61.9)	0.001
S1	39 (46.4)	20 (31.7)	19 (90.5)	<0.001
T1 -2	26 (30.9)	13 (20.6)	13 (61.9)	0.001
Creatinine at presentation, (µmol/L)	147.00 [103.75, 211.75]	128.00 [94.00, 188.50]	227.00 [162.00, 288.00]	<0.001
uPCR at presentation (mg/mmol)	188 [101.25, 343.5]	164 [100, 339]	211 [105, 345]	0.902
Follow up, months	66 [22, 104]	87 [27, 108.5]	22 [12 ,44]	0.003
Kidney Failure, n (%)	25 (29.8)	14 (22.2)	11 (52.4)	0.019
Time to kidney failure, months	28.00 [12.00, 58.00]	50.00 [18.75, 77.50]	17.00 [11.00, 30.00]	
Death, n (%)	7 (8.3)	5 (7.9)	2 (9.5)	1

Data represented as number (proportion) or median [inter-quartile range] or mean (standard deviation).
*Data was not available for 3 patients.

Fig 1: Time to ESKD in native and transplant kidneys



Censored for loss of follow-up or death; p=0.0002.

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Transplant immunology & immunosuppression

PP_380 URINARY EXOSOMAL MIRNA BIOMARKERS FOR ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: This study aimed to identify urine-derived exosomal miRNAs as diagnosis biomarkers associated with antibody-mediated rejection (ABMR) after kidney transplantation.

Methods: Exosomal miRNAs using differential ultracentrifugation were isolated in urine from 24 donors and kidney transplant recipients with 12 ABMR, 8 T cell-mediated rejection (TCMR), 5 BK virus nephropathy (BKVN), and 11 no major abnormality (NOMOA). We characterized exosomes using transmission electron microscopy, nanoparticle tracking analysis, Western blotting and analyzed miRNAs using RNA sequencing to identify exosomal miRNA candidates in the discovery cohort.

Results: Up-regulated miRNAs in the ABMR group were miR-8485, miR-221-3p, miR-192-5p, miR-126-5p, miR-328-5p, miR-103a-3p, miR-455-3p, and miR-126-3p whereas down-regulated miRNAs in the ABMR group were miR-let-7d-3p, miR-10a-5p, and miR-10b-5p. Up-regulated miRNAs in the TCMR group were miR-8485, miR-221-3p, miR-192-5p, miR-345-5p, miR-215-5p, miR-1273g-3p, miR-19a-3p, and miR-223-3p. Thereafter, we quantified the expression of miRNA candidates using RT-qPCR in a validation cohort consisted of 20 ABMR, 5 TCMR, 8 NOMOA, and 8 donors. The diagnostic potential of the exosomal miRNAs was evaluated by receiver operating characteristic (ROC) curves. Four miRNAs consisting of miR-221-3p, miR-455-3p, miR-126-3p, and miR-215-5p were significantly higher in the ABMR group than in NOMOA group. Additionally, miR-221-3p and miR-215-5p were highly expressed in the tissue of patients with ABMR.

Conclusions: In this study, we found that the four combined exosomal miRNAs consisting of miR-221-3p, miR-455-3p, miR-126-3p, miR-215-5p can improve the prediction performance from ROC value in the validation set. Thus, the combined exosomal miRNAs show potential in monitoring and early detection of ABMR.

PP_381 CLAZAKIZUMAB TREATMENT EFFECTS ON PERIPHERAL BLOOD AND KIDNEY TRANSCRIPTOMES IN LATE AMR

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Background: Antibody-mediated rejection (AMR) is a major cause of late kidney allograft loss, with no licensed treatments. Clazakizumab (CLZ), an IL6-neutralizing antibody, showed potential efficacy in a phase 2 randomized trial in patients with late AMR (Doberer *et al.*, 2021), where prolonged treatment reduced donor-specific antibodies (DSA) and renal function decline.

Methods: We studied the transcriptional changes in blood and kidney samples taken at baseline, 11-weeks and 51-weeks in 20 patients recruited to this CLZ in AMR trial. Patients were given 12 weeks of CLZ or placebo (Phase A), followed by 40 weeks of CLZ in both groups (Phase B).

Results: In peripheral blood, short-term CLZ treatment in Phase A reduced major antibody effector pathways, with variable individual responses and some patients showing a rebound in these pathways in phase B despite ongoing CLZ treatment. Weighted gene co-expression network analysis (WGCNA) identified a gene module in blood that significantly correlated with an AMR molecular score in the kidney and was downregulated by CLZ treatment, suggesting that peripheral blood could be used to non-invasively assess treatment efficacy. In the kidney, WGCNA showed that long-term CLZ treatment was associated with a reduction in degenerative tubular signatures (*cyan*) and preservation of podocyte signatures (*darkred*; Fig. 1). Furthermore, a module containing several humoral immunity-associated hub genes (*saddlebrown*), including *PRDM1* (a plasma cell-defining transcription factor (TF)) and *POU2AF1* (a TF that supports germinal centre development), was positively correlated with circulating antibody titres, suggesting that kidney-resident plasma/B cells contribute to DSA production, though this module was not downregulated by long-term CLZ treatment.

Conclusions: Our data indicate that CLZ-treatment prevents the tubular damage and podocyte loss associated with late AMR, providing further evidence of its therapeutic potential.

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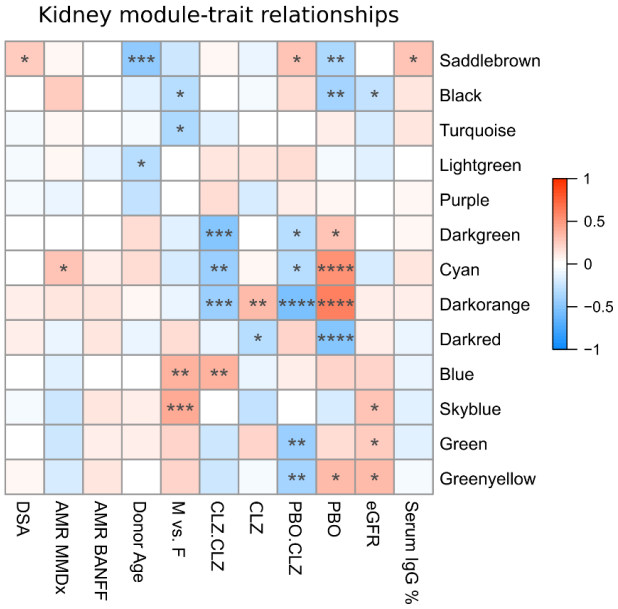

Module-trait relationships for kidney samples between identified modules (rows) and clinical parameters of interest (columns). Heatmap colours indicate correlation between module eigengene and clinical parameter. Asterisks indicate nominally-significant P-values of correlations (*, ≤ 0.05; **, ≤0.01; ***, ≤0.001; ****, ≤0.0001).

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Transplant immunology & immunosuppression

PP_382 THE IMPACT OF AGE ON INFECTION-RELATED MORTALITY AND GRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Older kidney transplant (KT) recipients have a lower risk of graft loss due to rejection, but a higher risk of infections. Less intensive immunosuppressive regimens (IS) may reduce infection risk without increasing rejection risk. We investigated whether an age threshold could be determined to identify recipients who might benefit from less intensive IS.

Methods: Data on KTs performed since 2000 in a single center were obtained from the Dutch national database. Age-related differences in mortality and graft loss were analyzed using Cox regression with adjustment for confounders (e.g. donor age, year of KT). To investigate whether hazards reached a plateau at a certain age, analyses were repeated with recipient age dichotomized at various cut-off points.

Results: 2,671 KTs were included (mean age 51 years, 55% living donor). With increasing age at time of KT, the hazard of mortality post-KT increased (all-cause: hazard ratio [HR] 1.07 per year of increasing age [95% CI 1.06;1.08]; infection-related: HR 1.03 [1.01;1.06]; malignancy-related: HR 1.02 [1.00;1.05]). All-cause and infection-related death hazards increased continuously with advancing age, while malignancy-related death hazard plateaued at age 60. The hazard of all-cause graft loss also increased with advancing age (HR 1.03 [1.02;1.04]), but the hazard of death-censored (DC) graft loss (mainly due to rejection) decreased (HR 0.98 [0.97;0.99]), indicating that with increasing age, a larger proportion of the patients died with a functioning graft. DC graft loss plateaued between ages 55 and 60.

Conclusions: While the risk of infection-related death continues to increase with advancing age, the age-related decrease in the risk of DC graft loss already plateaued between the ages of 55 and 60 years at time of KT. Since 44% of KT recipients are currently aged 55 or older, these data do not allow to identify a specific subset of KT recipients who might benefit from less intensive IS.

PP_383 THE PRO-INFLAMMATORY ROLE OF EVS IN CHRONIC LUNG REJECTION: NFKB SIGNALLING AS A POSSIBLE TARGET

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Background: Chronic lung allograft rejection (CLAD) is the leading cause of morbidity and mortality following lung transplantation (LT). Although much progress has been made, little is known about the pathogenic mechanisms underlying chronic rejection. We explored CLAD in the lung microenvironment by characterising and profiling LT patients' extracellular vesicles (EVs) from bronchoalveolar lavage (BAL).

Methods: We extracted EVs from the BALs of CLAD (n=10) and non-rejecting (CTR, n=10) patients. We characterised EVs for specific markers (CD63, TSG101) and phenotyped them using Nanoparticle Tracking Analyses (NTA) and the Leprechaun platform. By co-culturing the EVs with a human bronchial epithelium cell line (HBEpC) for 48/72h, we profiled them for transcriptome by nCounter Nanostring and protein expression.

Results: The LT patients were stratified into stable and severe based on lung function after CLAD. The immunophenotypic characterisation confirmed the leucocytic origin of EVs, given the positivity for the CD45 marker. The HBEpC co-cultured with CLAD-EVs showed transcriptional up-regulation of REL and CHUCK (both involved in the NF-kB signalling) and the downregulation of CXCL8, a neutrophil-attracting chemokine. Proteomic analysis showed the up-regulation of CCL25, chemotactic for macrophages and dendritic cells, and DNER. The pathways analysis revealed the up-regulation of TRAF6-mediated transcription factor NF-kB pathway and the MAPK mediated by MAP3K8.

Conclusions: Our results suggest the involvement of the NF-kB pathway as a possible immunological scenario associated with severe CLAD, with the activation of chemotaxis and the recruitment of macrophages and dendritic cells. The mediator TRAF6 also indicates a possible canonical pathway of NF-kB signalling and the involvement of Toll-like receptors that are even expressed by macrophages. CCL25 and NF-kB might be therapeutic targets to limit chronic graft rejection.

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PP_384 THE ROLE OF HLA-DQ ANTIBODY ON THE DEVELOPMENT OF ADVERSE EVENTS IN HEART TRANSPLANT RECIPIENTS

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Background: Assessment of the recipient's immunological status allows for early diagnosis and treatment of acute heart transplant rejection, as well as the correct selection of supportive immunosuppressive therapy. The problem of heart transplant dysfunction and persistent high immunological load remains, in particular, the problem of complex elimination of anti-HLA-DQ, which carry with them severe heart transplant dysfunction.

Methods: In the period from January 2018 to November 2024, blood samples were evaluated from 373 heart recipients who underwent heart transplantation at the Shumakov National Research Medical Center. All heart transplant recipients underwent endomyocardial biopsy, coronary angiography and examination of anti-HLA IgG levels in blood serum.

Results: Among 373 heart recipients who underwent cardiac graft function assessment and de novo donor-specific antibody screening, 96 patients had laboratory evidence of anti-HLA circulation in their blood serum. Only 9 patients had anti-HLA-DQ circulation. Taking into account the development of heart transplant dysfunction, 88.9% of heart recipients underwent pulse hormone therapy with methylprednisolone for three days, also four patients (44.4%) received immunomodulatory therapy with human immunoglobulin and plasmapheresis sessions. Clinical remission of heart transplant dysfunction was achieved in 88.9% of cases. However, only 11.1% managed to achieve complete elimination of anti-HLA-DQ. 44.4% of patients developed repeated heart transplant dysfunction within 1-3 months, which in one case resulted in death.

Conclusions: Thus, based on the data obtained, it is possible to note a persistent dependence of the presence of anti-HLA-DQ in the blood serum and the development of severe heart transplant dysfunction, occurring with frequent relapses, despite the specific therapy. Due to the morphological specificity of anti-HLA-DQ molecules, its identification in blood serum is difficult and may lead to the unplanned development of rapid heart transplant dysfunction with the development of undesirable events.

PP_385 DISEASE-SPECIFIC IMMUNOSUPPRESION WITH ANTI-THYMOCYTE GLOBULIN: REJECTION AND SURVIVAL OUTCOMES

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Background: Acute rejection (AR) affects up to 25% of liver transplant (LT) recipients and can lead to graft loss. Anti-thymocyte globulin (ATG) has been used as induction immunosuppression (IS). However, no studies have addressed selective use of ATG in disease-specific populations. Our study reports on a selective IS strategy limiting ATG use to patients with autoimmune liver diseases: autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), or primary sclerosing cholangitis (PSC).

Methods: This was a retrospective study comparing two eras based on changes in IS protocol in response to the COVID19 pandemic at a single large-volume LT center in the U.S. (Era 1: 1/2016-3/2020, Era 2: 4/2020-12/2023). Patients in Era 1 received ATG regardless of primary disease; in Era 2, only those with AIH/PBC/PSC received ATG. For the entire duration, patients with age >65, extreme frailty, or recent active infection did not receive ATG. Pediatric recipients, simultaneous multiorgan transplants, and retransplants were excluded. AR was diagnosed based clinical suspicion and histologic confirmation.

Results: Of a total of 1017 patients, 515 were in Era 1 and 502 in Era 2. Baseline characteristics and differences between cohorts are reported in Table 1. ATG was given to 87% of patients in Era 1 and 13% in Era 2 (p<0.001). The proportion of AIH/PBC/PSC patients receiving ATG during Era 1 and Era 2 were 87% vs 61% (p<0.001). Overall, 156 patients (15.3%) experienced AR. AR was more common in Era 2 (19% vs. 12% in Era 1, p=0.001) and in patients with AIH/PBC/PSC (21% vs. 14% other etiologies, p = 0.037). The frequency of AR in patients with non-autoimmune etiologies was significantly higher in Era 2 (19% vs. 10% in Era 1, p<0.001); it was not different between the two eras for AIH/PBC/PSC (19.5% vs 23.5%, p=0.69). In multivariable analysis, the predictors of AR were younger age (p=0.001), non-ATG IS (p=0.041), and AIH/PBC/PSC (p=0.043). Death after transplant or graft loss were not statistically different between the two eras (p>0.05 for both, Figure 1).

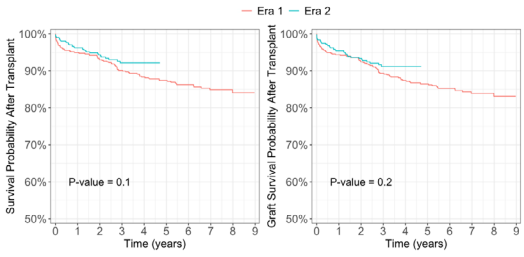
Conclusions: A shift in IS strategy to ATG induction for only AIH/PBC/PSC etiologies led to a dramatic reduction in ATG use from 87% to 14%, but a modest but statistically significant increase in the risk of AR without affecting graft loss.

Table 1: Baseline characteristics and outcomes for two eras of induction IS with ATG for LT (Era 1 not disease-specific, Era 2 disease-specific)

	Overall N=1017	Era 1 N=515	Era 2 N=502	p-value Era 1 vs. Era 2
Age at transplant, mean (S.D.)	55.53 (11.39)	56.23 (10.75)	54.82 (11.97)	0.049
Male gender, N (%)	624 (61.36%)	332 (64.47%)	292 (58.17%)	0.046
Indication for transplant				
Alcohol, N (%)	402 (39.53%)	196 (38.06%)	206 (41.04%)	0.364
Viral (Hep B + Hep C), N (%)	180 (17.70%)	111 (21.55%)	69 (13.75%)	0.001
MASH, N (%)	312 (30.68%)	174 (33.79%)	138 (27.49%)	0.035
HCC, N (%)	226 (22.22%)	123 (23.88%)	103 (20.52%)	0.224
Autoimmune hepatitis, N (%)	54 (5.31%)	25 (4.85%)	29 (5.78%)	0.606
PSC/PBC, N (%)	104 (10.23%)	46 (8.93%)	58 (11.55%)	0.202
All others, N (%)	138 (13.57%)	74 (14.37%)	64 (12.75%)	0.508
BMI at transplant, mean (S.D.)	29.79 (5.65)	29.78 (5.87)	29.81 (5.38)	0.944
Carlson comorbidity index at transplant, mean (S.D.)	7.49 (3.97)	7.56 (3.95)	7.41 (3.99)	0.572
MELD at Transplant, mean (S.D.)	22.73 (7.63)	22.25 (6.82)	23.23 (8.38)	0.045
Donor Gender Male, N (%)	641 (63.03%)	315 (61.17%)	326 (64.94%)	0.237
Donor Type, N (%)				
CAD	815 (80.14%)	422 (81.94%)	393 (78.29%)	<0.001
DCD	172 (16.91%)	93 (18.06%)	79 (15.74%)	
LRT	9 (0.88%)	0 (0.00%)	9 (1.79%)	
LUT	21 (2.06%)	0 (0.00%)	21 (4.18%)	
ATG given for induction, N (%)	510 (50.15%)	446 (86.60%)	64 (12.75%)	<0.001
Acute rejection, N (%)	156 (15.34%)	60 (11.65%)	96 (19.12%)	0.001
Time to rejection, days (median, IQR)	130 [30.0, 263.5]	139.5 [26.5, 402.3]	124 [37.8, 212.8]	0.372
Time to rejection, days, N (%)				0.485
7-30 days	40 (3.93%)	17 (3.30%)	23 (4.58%)	
31-90 days	23 (2.26%)	8 (1.55%)	15 (2.99%)	
91-365 days	59 (5.80%)	19 (3.69%)	40 (7.97%)	
365 days over	34 (3.34%)	16 (3.11%)	18 (3.59%)	
Death after transplant, N (%)	108 (10.62%)	75 (14.56%)	33 (6.57%)	0.100
Graft loss after transplant, N (%)	118 (11.60%)	80 (15.53%)	38 (7.57%)	0.200

*P-value: Chi-square test was used for categorical variables. T-test and Mann-Whitney U test was used for continuous variables. Survival and graft loss differences were analyzed using log-rank test.

Figure 1: Patient survival and graft survival for two eras of induction IS with ATG for LT (Era 1 not disease-specific, Era 2 disease-specific)



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PP_386 OUTCOMES IN SENSITISED KIDNEY TRANSPLANT RECIPIENTS AFTER NON-DEPLETING ANTIBODY INDUCTION THERAPY

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Background: Lymphocyte depleting antibody induction therapy is recommended for kidney transplant recipients (KTRs) at high immunological risk, which includes sensitised patients with detectable anti-HLA antibodies prior to transplantation. Data to support improved long-term outcomes with this approach are sparse. We investigated outcomes in sensitised KTRs undergoing transplantation with non-depleting induction.

Methods: Adult patients who underwent kidney alone transplantation with basiliximab induction at a single centre between 2012-2023 were included. We determined rejection rates, patient, and allograft survival at 1-, 3- and 5-years post-transplant. We compared patients who were unsensitised (cRF 0%), sensitised (cRF 1-84%), and highly sensitised (cRF 85-100%) at the time of transplantation.

Results: 1348 KTRs underwent induction with basiliximab and were included. Of these, 859 (63.7%) patients were unsensitised, 344 (25.5%) were sensitised, and 145 (10.8%) were highly sensitised. Highly sensitised patients were younger, more commonly female, less commonly white, less frequently underwent living or pre-emptive kidney transplantation, and had a better total match at HLA-A, -B, and -DR loci. Patient and allograft survival were not different according to cRF categories, whereas death censored graft survival (DCGS) was lower in highly sensitised patients compared to other cRF groups (**Figure 1**). Rejection in the first year occurred in 20 (16.3%) highly sensitised patients, 23 (8.0%) sensitised patients, and 58 (8.7%) unsensitised patients (p=0.029). BK and CMV viremia were not different between groups. Cox regression analyses were undertaken to determine clinical variables associated with patient and allograft survival over 5 years follow-up (**Table 1**); cRF was not associated with any outcomes.

Conclusion: Sensitisation at the time of transplant did not impact patient or allograft survival in KTRs undergoing induction with basiliximab. This supports the use of non-depleting antibody induction in sensitised KTRs.

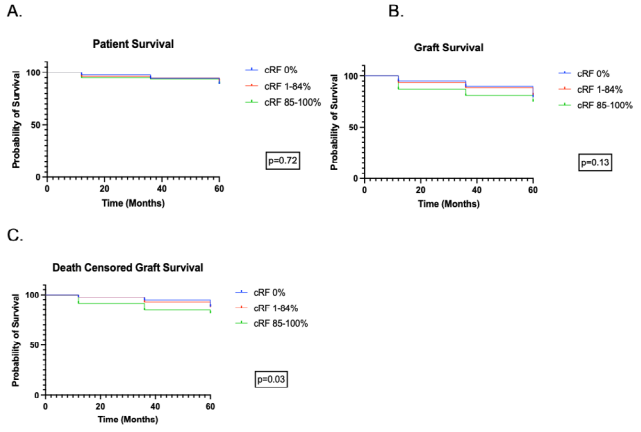

Figure 1: Transplant Outcomes in patients undergoing induction with basiliximab stratified by cRF.

	PATIENT SURVIVAL		GRAFT SURVIVAL		DEATH-CENSORED GRAFT SURVIVAL		REJECTION-FREE ALLOGRAFT SURVIVAL	
Clinical Variable	*Hazard ratio*	*95% confidence interval*	*Hazard ratio*	*95% confidence interval*	*Hazard ratio*	*95% confidence interval*	*Hazard ratio*	*95% confidence interval*
Age at Transplant	**1.070**	**1.040 to 1.103**	**1.026**	**1.009 to 1.043**	1.004	0.9821 to 1.026	0.9883	0.9733 to 1.003
Male Sex [reference = female]	1.153	0.6029 to 2.328	0.8195	0.5319 to 1.276	0.5823	0.3262 to 1.038	**0.6413**	**0.4315 to 0.9560**
Ethnicity [black; reference = white]	**0.3862**	**0.09489 to 0.7009**	0.8007	0.4733 to 1.330	1.366	0.7078 to 2.613	1.046	0.6684 to 1.651
Ethnicity [Asian; reference = white]	0.8563	0.4248 to 1.667	0.7744	0.4617 to 1.274	0.7504	0.3500 to 1.548	0.7081	0.4214 to 1.161
DBD transplant [reference = live transplant]	1.483	0.5791 to 4.587	1.574	0.8189 to 3.290	1.668	0.6955 to 4.670	0.8640	0.5091 to 1.497
DCD transplant [reference = live transplant]	0.9685	0.3546 to 3.102	1.724	0.8673 to 3.698	2.699	1.099 to 7.687	1.309	0.7603 to 2.298
Total HLA Mismatch	0.9655	0.7356 to 1.264	0.8370	0.6917 to 1.011	0.7808	0.6029 to 1.009	0.9258	0.7715 to 1.109
cRF 1-84% [reference = cRF 0%)	0.9498	0.4438 to 1.908	1.129	0.6834 to 1.825	1.305	0.6714 to 2.482	0.9891	0.6169 to 1.555
cRF 85-100% [reference = cRF 0%)	0.6393	0.1678 to 1.911	1.404	0.6857 to 2.707	2.183	0.9356 to 4.784	1.548	0.8328 to 2.748
Pre-emptive transplant [reference = not pre-emptive]	**0.07169**	**0.004021 to 0.3355**	**0.3421**	**0.1499 to 0.6790**	0.5648	0.2241 to 1.225	1.074	0.6594 to 1.697
Multiple grafts [reference = first graft]	1.735	0.5861 to 4.499	0.9775	0.4847 to 1.845	0.7565	0.2908 to 1.724	1.244	0.7057 to 2.104
ln(PIRCHE+1) as continuous variable	1.184	0.7618 to 1.925	1.146	0.8633 to 1.554	1.145	0.8014 to 1.693	**1.341**	**1.026 to 1.796**

Table 1: Cox regression analyses of clinical variables associated with patient and transplant outcomes.

PP_387 A MULTIPLEX DIGITAL DROPLET PCR ASSAY FOR DETECTION OF KIDNEY-SPECIFIC CELL-FREE DNA

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Background: Kidney transplantation is the optimal treatment for end-stage kidney disease, but graft survival is limited by rejection and alloimmunity. Biomarkers for monitoring graft health could improve outcomes. Organ injury releases cell-free DNA (cfDNA) into circulation, which can be quantified and used as a biomarker. CfDNA derived from allografts is an emerging and promising marker of injury. We aimed to develop a multiplex digital droplet PCR assay to measure kidney-specific cfDNA using differentially methylated regions (DMRs) and to explore the dynamics of the biomarkers during the first year post-transplant in 20 kidney transplant recipients, as well as their association with baseline characteristics.

Methods: Five kidney-specific DMRs were selected as biomarkers from The Cancer Genome Atlas and Gene Expression Omnibus and combined into a multiplex digital droplet PCR assay. The presence of the biomarkers was tested in kidney implantation biopsies and plasma from 20 kidney transplant recipients without rejection, with samples collected pre-transplant and on days 5, 30, 90, 180, and 360 post-transplant.

Results: All five biomarkers were detected in kidney tissue. In plasma, kidney-specific cfDNA levels peaked on day 5 post-transplant. Four biomarkers returned to levels similar to pre-transplant, while one had a higher level post-transplant than pre-transplant. No significant associations were observed between the kidney-specific cfDNA levels and pre-transplant dialysis status, immunosuppressive regimen, age, or gender.

Conclusions: We successfully developed and tested a multiplex digital droplet assay to detect kidney-specific cfDNA based on DMRs. The post-transplant kidney-specific cfDNA peak supports its potential as a biomarker for kidney injury. Stable kidney-specific cfDNA levels resembling baseline throughout the first year in four of five markers suggest minimal allograft contribution in the absence of kidney injury, providing a reference for future studies.

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Transplant immunology & immunosuppression

PP_388 ESTIMATION OF THE EFFICACY OF FELZARTAMAB TO TREAT ANTIBODY-MEDIATED REJECTION USING THE IBOX

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Background: Felzartamab, a fully human monoclonal CD38 antibody, has been recently investigated for the treatment of antibody-mediated rejection (AMR) in kidney transplant recipients (KTRs), in a phase 2 randomized, double-blind, placebo-controlled trial (EDURACT: 2021-000545-40). Despite promising results, the trial's small sample size and short duration precluded the assessment of long-term clinical endpoints. The present study aimed to use the iBox, an EMA- and FDA-qualified surrogate endpoint, to predict the long-term allograft survival in this trial.

Methods: We performed a prespecified post-hoc analysis using data from the Felzartamab trial (n=22; 11 felzartamab, 11 placebo). Patients were followed for one year and underwent transplant biopsies at baseline, 24 weeks (end of the exposure period), and 52 weeks (end of the observation period). The iBox was used to estimate 5-year graft survival probabilities at each biopsy. Linear mixed-effects modeling was used to estimate the treatment effect, accounting for baseline differences between groups.

Results: At baseline, the iBox-estimated 5-year graft survival was 50.0% in the felzartamab group and 29.8% in the placebo group (difference: 20.2%, 95% CI: -11.4% to 51.8%). During the study period, graft survival probabilities increased in the felzartamab group (+6.4% per year, 95% CI: -0.4% to 13.1%), and decreased in the placebo group (-7.6% per year, 95% CI: -14.5% to -0.6%). Treatment effect was observed solely during the exposure period (0-24 weeks). During the observation period (24-52 weeks), both groups showed a similar decline in survival probabilities, suggesting that treatment effect achieved during the exposure period was maintained over time. Results were consistent in several sensitivity analyses using alternative strategies to handle missing data or to account for treatment effect.

Conclusions: Our study suggests that felzartamab improves graft survival in KTRs with AMR. A phase 3 trial with a larger cohort and longer follow-up is essential to confirm felzartamab's efficacy in preventing graft failure.

PP_389 OPTIMIZING AN ORGANOID MOUSE MODEL TO STUDY T-CELL SUBSETS IN FIBROSIS IN KIDNEY TRANSPLANTATION

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Background: Long-term kidney allograft function is often compromised by the development of fibrosis, arising from both immune-related (antigen-dependent) and non-immune-related events. Immune-related events are driven by mismatched HLA and non-HLA antigens. Previous studies indicate that circulating non-HLA antigen-reactive CD4+ T cells correlate with the degree of fibrosis in kidney transplant recipients, yet their specific role remains unclear. A vascularized human kidney organoid immune-deficient mouse model allows for studying human immune responses in transplantation by injection of immune cells. Understanding whether isolated T cell populations can successfully graft in this model is essential for studying the role of these T cell subsets.

Methods: To assess the role of CD4+ T cell subsets, sorted CD4+ T cells were expanded for two weeks using anti-CD3/anti-CD28-coated beads and exogenous IL-2 and IL-15. The expanded cells were either frozen for later use or tested immediately. Two weeks after implantation of kidney organoids into immune-deficient mice, different doses (2 and 5 million) of autologous CD4+ T cells were injected intraperitoneally to facilitate engraftment. After four weeks, blood samples were collected, and spleen and organoids were harvested for analysis. T cell populations in the blood and spleen were quantified using flow cytometry.

Results: After injecting 2 or 5 million fresh CD4+ T cells, median levels of human CD45+ lymphocytes in the spleens of four mice per group were 35% and 87%, respectively, indicating better engraftment with the higher dose. By comparison, after injecting 2 or 5 million frozen CD4+ T cells, median levels of human CD45+ lymphocytes in the spleens of two mice per group were 71% and 88%, respectively, suggesting that frozen CD4+ T cells perform comparable to fresh cells in this model. Mice injected with 5 million CD4+ T cells exhibited substantial CD3e gene expression in implanted kidney organoids, confirming successful T cell infiltration in autologous kidney organoids.

Conclusions: Five million CD4+ T cells, either fresh or frozen, successfully engraft in a vascularized kidney organoid mouse model, enabling detailed studies on the role of non-HLA antigen-reactive CD4+ T cells in induction of fibrosis in kidney transplantation.

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Transplant immunology & immunosuppression

PP_390 DARATUMUMAB AND BELATACEPT DUAL TARGETING IMPACTS ON B-CELL IMMUNITY IN HIGHLY SENSITIZED PATIENTS

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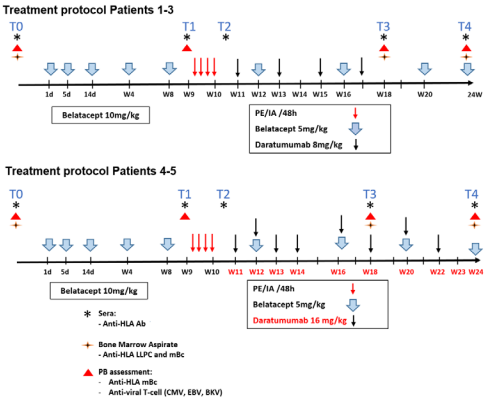
Background: Current desensitization therapies show limited success in reducing anti-HLA antibodies (Ab) in highly sensitized (HS) Kidney transplant (KT) candidates. Both central Bone Marrow (BM)-residing long-lived plasma cells (LLPCs) and peripheral memory B cells (mBC) in collaboration with T Follicular Helper Cell (TFH) contribute to Ab formation. We designed a prospective, phase-I/II, exploratory trial (COMBAT; NCT05145296) using a dual-target approach with co-stimulation blockade (belatacept) and an anti-CD38 mAb (daratumumab).

Methods: 5 HS patients (cPRA≥99.9%) on the deceased donor KT waiting list without a compatible donor for >3 years were included. The protocol involved 5 doses of Belatacept 10mg/kg (T0-T1), followed by 4 sessions of apheresis (T1-T2), and then daratumumab (4 doses (8mg/kg) biweekly for patients 1-2 or 4 doses (16mg/kg) weekly and 4 biweekly for patients 3-4), combined with 4 additional monthly belatacept doses (5mg/kg) (T2-T4) (Figure). Changes in serum anti-HLA Ab, cPRA and different peripheral and bone-marrow B-cell subsets with spectral flow cytometry prior, during and after therapy were assessed.

Results: Four patients completed the study; one patient was withdrawn due to infectious colitis. No other severe adverse events occurred. 3/4 patients displayed significant reduction of class I and II anti-HLA Ab MFI values, already after 5 initial belatacept doses (T0-T1), which increased after daratumumab, achieving complete negativization in >20% class I Ab (Table). However, the impact on cPRA was minimal. Multidimensional spectral cytometry revealed profound depletion of CD38-expressing cells, including plasma cells, plasmablasts, and CD38+ switched(sw)-mBCs (p<0.005), while no changes were observed in total sw-mBC or CD4+CXCR5+PD1+ TFH. A reduction in circulating plasma cells and plasmablasts already occurred prior to daratumumab. Similar effects were observed within BM immune cells. Notably, the lowest daratumumab dose similarly impacted on peripheral and BM cell subsets.

Conclusions: Dual targeting of central and peripheral B cell alloimmune compartments with daratumumab and belatacept seems to be a safe strategy to reduce the main cellular subsets contributing to sensitization burden of HS patients, eventually facilitating access to HLA compatible KT.



Patient	MFI (median (IQR))	T0	T1	T2	T3	T4	P value (T4 vs T0)	T0-T4 MFI negativization (<500 MFI)
002	HLA Class I (n=80)	6845.5 (742 – 18761.75)	4936.5 (529 – 16737.75)	3686.5 (389 – 14942.75)	2933 (370.25 – 14101.25)	2719 (282.75 – 14695.25)	<0.0001	33/80 (41.25%)
	HLA Class II (n=64)	20327 (10192.75 – 20966.25)	20150.5 (8898.5 – 21176.75)	18465 (5006 – 21791)	17897.5 (6911 – 20479.5)	19415.5 (9227 – 20005.75)	<0.0001	0/64 (0%)
003	HLA Class I (n=33)	14596 (6764.5 – 20481.5)	17371 (7723 – 20414)	17638 (11748.5 – 20746.5)	14445 (9018.5 – 19723.5)	15646 (9620 – 20152.5)	0.406	0/33 (0%)
	HLA Class II (n=48)	17425.5 (1002 – 20482)	18399 (1326.75 – 19805.25)	18891.5 (4075.25 – 20980.5)	19085.5 (1890.25 – 19927.5)	19204.5 (1219 – 19957)	0.088	0/48 (0%)
004	HLA Class I (n=36)	2232 (1195.25 – 4014.25)	1522 (942.5 – 4040.5)	422 (284 – 1518.75)	1095 (640.5 – 4607.5)	948 (506 – 4281)	0.009	8/36 (22.22%)
	HLA Class II (n=60)	18200.5 (13528 – 19744.25)	16220.5 (10043 – 18639.5)	6873.5 (3968.25 – 11987.5)	16403 (10968.5 – 18465.25)	16718 (10721.75 – 18402.25)	<0.0001	0/60 (0%)
005	HLA Class I (n=91)	805 (628 – 4971)	760 (557 – 4776.5)		675 (505.5 – 3910)	692 (497.5 – 3790.5)	<0.0001	19/81 (23.45%)
	HLA Class II (n=59)	6933 (4439 – 16049)	6262 (3039 – 12868)		5565 (2444 – 13613)	6937 (3473 – 15279)	0.014	3/59 (5.08%)

PP_391 RAPID LIQUID BIOPSY ASSESSMENT THROUGH GENE PROFILING FROM THE KIDNEY BIOPSY TRANSPORT MEDIUM

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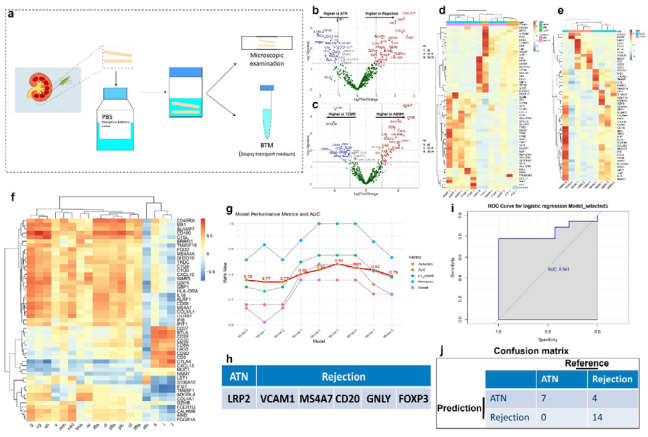
Background: Rapid diagnosis is pivotal in renal transplantation for timely and precision therapy. Conventional microscopic assessment relies on extra sample processing, making same-day diagnosis impractical. Therefore, we introduce the biopsy transport medium (BTM) (Figure 1-a), a byproduct of the biopsy tissue storage process that could serve as a source of biomarkers, accelerating the assessment workflow through pre-classification.

Methods: We created BTM mimics for homogenization, allowing optimization of RNA extraction procedure. We analyzed RNA quantity, integrity, and biomarkers through qPCR and conducted gene signature profiling using the Banff Human Organ Transplant (B-HOT) panel on the NanoString nCounter platform. Following that, select a small gene panel based on the previous results. We measured the expression of the panel in BTM derived from renal allograft biopsy tissues of an individual cohort. We investigated the importance of the genes in distinguishing between rejection and non-rejection, and the most relevant genes were selected to build a prediction model.

Results: The results showed that storage time (the duration a biopsy is floating in BTM), ranging from 0.5 to 24 hours did not significantly affect RNA quality and yield. Differential gene expression (DGE) analysis of allograft rejection BTM identified specific rejection profiles (Figure 1-b,c,d,e), correlating with Banff lesion scores (Figure 1-f). The small gene panel including 19 genes and a cohort involving 85 patients was established. The dataset was divided into training (70%) and testing (30%) subsets to train and evaluate the prediction model. Finally, 6 genes were selected as the most relevant genes: *LRP2, VCAM1, MS4A7, CD20, GNLY,* and *FOXP3*. The performance on the independent test set achieved an F1-Score of 0.88, and the area under the receiver operating characteristic curve (AUC-ROC) for the test set was 0.84 (Figure 1-g,h,i,j).

Conclusions: This study confirmed the capability of BTM to provide transcriptomic information relevant to the renal allograft. In addition, we developed a complementary tool to facilitate rapidly assessing renal allograft rejection. When integrated with qPCR, the gene panel we built showed promise for same-day molecular diagnosis, particularly in cases with narrow diagnostic windows.

Figure 1. (a) The procedure for routine kidney biopsy: Two biopsy slides are floated in BTM (PBS) for transport. Pathologists remove the biopsies for microscopic examination, while the BTM is left behind. (b-e) Differentially expressed genes (DEGs) on 12 real BTM: b, The red dots represent statistically significant genes that are higher in rejection compared to ATN, and the blue dots represent the genes higher in ATN; c. The red dots represent statistically significant genes that are higher in ABMR compared to TCMR, and the blue dots represent the genes higher in TCMR; d. Hierarchical clustering suggests significant heterogeneity between rejection and ATN. Of the 770 genes, 31 were higher and 23 were lower in rejection; e. Hierarchical clustering suggests significant heterogeneity between ABMR and TCMR. Of the 770 genes, 37 were higher and 12 were lower in ABMR. (f) A Spearman's rank correlation heat map comparing the DEGs with Banff lesion scores in real BTM in the setting of delayed graft function (DGF). (g) Model performance metrics and the receiver operating characteristic (ROC) curve for testing across nine rounds. (h) The genes included in the highest-performing model (model 5). (i) The area under the curve (AUC) value of model 5. (j) The confusion matrix of the model 5, based on the test set.



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PP_392 A FOUR-METABOLITE MODEL BEATS CLINICAL MODELS IN PREDICTING ANTIBODY-MEDIATED REJECTION

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Background: Antibody-mediated rejection and microvascular inflammation (AMR/MVI) contribute to graft loss after kidney transplantation. Its presentation is often subclinical and diagnosis is delayed. On-time immunosuppression tunings or novel treatments may modify its prognosis. Early identification of risk may improve outcomes.

Methods: We selected 57 recipients with a normal biopsy (Bx) and divided them according to a 2nd Bx 2 years later into 28 cases with AMR/MVI and 29 matched controls with no damage. Serum samples at 1st Bx were analyzed using targeted metabolomic methods including 124 metabolic markers belonging to several critical pathways in inflammation, renal function and immune system. We applied out-of-bag recursive feature elimination to clinical and metabolomic variables, identifying 5 key features after 100 iterations. We evaluated these features using a random forest model and then used to construct a decision tree, with hyperparameters optimized via leave-one-out cross-validation based on AUC. Further external validation is ongoing.

Results: The 1st Bx in the AMR/MVI group was more frequent per indication (37.9 vs. 4.4%), they had lower GFR (49,5 vs 60,4 ml/min) with similar creatinine (1.59 vs 1.34 mg/dl) compared to controls; histology was alike, except that 5 cases had glomerulitis score=1. The metabolomics analysis showed 12 metabolites significantly altered in the later AMR/MVI group 2 years before diagnosis, 6 showed p< 0.1 even after false discovery correction. A model using clinical variables alone achieved a moderate separation between groups with a ROC AUC of 0.615 (95% CI [0.5948, 0.6414]). Adding metabolomic markers to the model improved this separation, a model containing a clinical variable and 4 metabolites reached a ROC AUC of 0.819 (95% CI [0.8054, 0.8326]). We also explored the potential of a decision tree based on 3 metabolites that achieved a separation of the cohorts with a sensitivity of 0.82 (95% CI: 0.68-0.96) and a specificity of 0.90 (95% CI: 0.79-1.00) **[Figure 1].**

Conclusions: Metabolic alterations may complement clinical variables in the early identification of AMR/MVI risk. If confirmed in ongoing independent cohorts, the use of metabolomics may become a powerful predictive biomarker of AMR/MVI

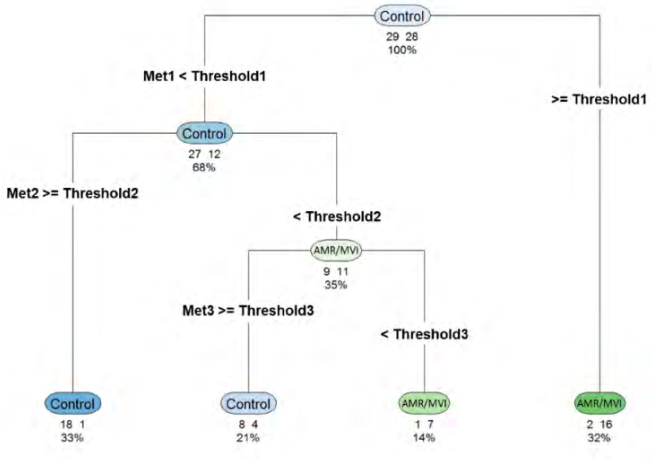

Figure 1. Decision tree based on the concentration of 3 metabolites

PP_393 OPAL MULTIPLEX IMMUNOFLUORESCENCE FOR IDENTIFYING MONONUCLEAR CELLS IN KIDNEY ALLOGRAFT REJECTION

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Background: Graft rejection remains a challenge in kidney transplantation, with the roles of intragraft monocytes and natural killer (NK) cells in antibody-mediated rejection (ABMR) and T-cell-mediated rejection (TCMR) not yet fully understood. Multiplex immunofluorescence (mIF) assays, using Opal reagents, offer enhanced diagnostic precision by enabling the simultaneous detection of multiple immune cell markers within a single tissue section. The objective of this study was to quantify and compare the densities of various immune cell subsets, in kidney allograft biopsies from patients with ABMR, TCMR, and no rejection (NR) via Opal mIF.

Methods: In this retrospective cohort study of 38 kidney transplant recipients undergoing for-cause allograft biopsies, mIF via Opal was used to stain and quantify mononuclear cell subsets. CD14+CD11c+ and CD3-PAX8-CD16+CD57+ cells were identified as key subsets for analysis. Quantitative differences in cell densities were statistically analyzed, and Cox proportional hazards regression assessed their predictive value for graft survival.

Results: In the kidney allograft biopsies, the density of CD14+CD11c+ monocyte-derived dendritic cells was significantly higher in ABMR compared to TCMR (P = 0.011, Bonferroni-corrected threshold for significance: P < 0.0167), implicating their involvement in ABMR. CD3-PAX8-CD16+CD57+ mature NK cells also showed significantly higher densities in ABMR than TCMR (P = 0.008) indicating a potential role in cytotoxicity-mediated graft damage. A receiver operating characteristic (ROC) curve analysis for these two subsets combined demonstrated an AUC of 0.79 (95% CI: 0.65–0.93), suggesting good discriminatory power for distinguishing ABMR from other rejection types. Cox regression showed CD14+CD11c+ cells were not significantly associated with survival (HR = 0.62, p = 0.40), while CD3-PAX8-CD16+CD57+ cells showed a trend toward increased risk (HR = 2.73, p = 0.09).

Conclusions: These findings highlight the potential involvement of CD14+CD11c+ and CD3-PAX8-CD16+CD57+ cells in ABMR, suggesting the potential for improving the diagnosis and management of kidney allograft rejection.

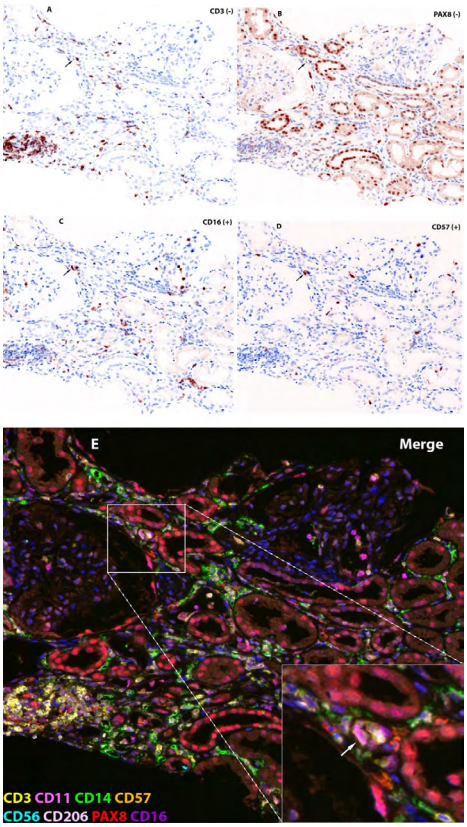

Figure 1. Opal mIF of ABMR kidney. Arrows: CD3- (A), PAX8- (B), CD16+ (C), CD57+ NK cells. Inset: CD16+CD57+ NK cells, X200

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Transplant immunology & immunosuppression

PP_394 GUT MICROBIOME DYNAMICS IN ORGAN TRANSPLANT PATIENTS: INSIGHTS FROM A MULTIORGAN COHORT STUDY

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Background: The gut-organ axis is increasingly recognized as critical in transplantation outcomes. This study analyzed fecal microbiome profiles in 65 transplant recipients (37 liver, 14 kidney, 6 heart, 1 pancreas, 2 lung) to characterize microbiome alterations before and after organ transplantation across different transplanted organs.

Methods: Fecal samples were collected from 65 transplant recipients: 37 liver, 14 kidney, 6 heart, 1 pancreas, and 2 lung transplant patients. Microbiome profiling was performed using full-length 16S rRNA sequencing on the PacBio Revio platform. Processed data were analyzed with QIIME2 (v2024.10), using DADA2 for amplicon sequence variant (ASV) generation and Greengenes2 for taxonomic assignment. Diversity analyses included alpha (Kruskal-Wallis) and beta (ANOSIM) metrics, with rarefaction at 24,100 reads.

Results: The gut microbiome exhibited organ-specific changes post-transplant. Liver recipients showed decreased *Bacteroidota* and increased *Pseudomonadota*, while kidney recipients showed no significant pre- or post-transplant changes. Individual variability in microbiome composition was evident. Alpha diversity was higher in kidney versus liver recipients ($p < 0.05$). Post-transplant, liver recipients showed a significant diversity decline ($p < 0.05$), with no changes in kidney recipients. Beta diversity (Unweighted UniFrac) revealed significant differences in microbiome composition among organ groups, including heart-kidney, kidney-liver, kidney-lung, and liver-lung ($p < 0.05$). Weighted UniFrac confirmed differences between heart-kidney, kidney-liver, and kidney-lung groups. Liver recipients also exhibited significant microbiome shifts post-transplantation ($p < 0.05$). Additionally, liver transplant recipients exhibited significant microbiome shifts post-transplantation ($p < 0.05$).

Conclusions: The gut microbiome undergoes organ-specific changes post-transplantation, with notable shifts in liver recipients. This study underscores the potential of microbiome profiling to advance our understanding of the gut-organ axis and highlights the need for larger studies.

This study was supported by the National Institute of Health research project (2024ER080600).

PP_395 DELAYED GRAFT FUNCTION: ENDOTHELIAL TO MESENCHYMAL TRANSITION INCLUDES HLA II EXPRESSION

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Background: There are several stages in kidney transplantation during which epithelial injury and endothelial activation in the graft can occur. When acute tubular necrosis delays recovery of renal graft function (DGF) immediately after the surgery, a biopsy is occasionally taken to estimate the risk of primary non-function, adapt immunosuppression, and eliminate acute rejection.

Methods: We investigated the phenotype of endothelial cells in peritubular capillaries in biopsy samples from recipients experiencing DGF, paying special attention to markers of partial endothelial-to-mesenchymal transition (pEndMT) and induction of expression of HLA II antigens. We also focused on the further development of de novo, donor specific, anti-HLA antibodies (dnDSA).

Results: The majority of patients with DGF (62%) had pEndMT, which was associated with the endothelial expression of HLA II antigens in peritubular capillaries (detectable in 55% of samples, and significantly correlated with pEndMT semi-quantitative score). Importantly, early pEndMT was significantly associated with later development of dnDSA (51.6% vs 8%, p=0.001), and with more antibody mediated rejection (ABMR) during follow-up (31.4% vs 7.14%, p=0.021), more graft dysfunction (estimated GFR 23.34±22.9 vs 40.2±22.5, p=0.0064) and loss (51.2% vs 14.8%, p=0.002). Microvascular inflammation score in early biopsies could not predict these events.

Conclusions: In the context of kidney transplantation, pEndMT markers are frequently observed in graft biopsies taken from recipients experiencing DGF. Here, pEndMT includes HLA II expression every other time, is a strong risk factor for the development of dnDSA, and associates with a high incidence of ABMR. This reasonably contributes to explain why DGF is a risk factor of ABMR, and the negative impact of DGF in the long run.

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Transplant immunology & immunosuppression

PP_396 EPO MODULATES REDOX HOMEOSTASIS AND IMMUNMODULATORY FUNCTIONS OF MONOCYTES IN KIDNEY TRANSPLANTATION

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Background: Erythropoietin (EPO) has been shown to exert immunomodulatory effects beyond its role in erythropoiesis. Immune cells, particularly monocytes, undergo metabolic reprogramming during activation, which affects their function. This study aims to investigate the immunomodulatory effects of EPO in human kidney transplantation, with a focus on elucidating the effects of EPO on the metabolic state of immune cell subsets using redox homeostasis as a proxy.

Methods: Healthy donor (HD) peripheral blood mononuclear cells (PBMC) and kidney transplant recipients (KTR) PBMC (without EPO treatment *in vivo*) were treated with EPO *in vitro* to assess direct EPO effects. Additionally, a cohort of stable KTR (n=34) with anemia (Hb <10.0 g/dL) was enrolled and studied before and after 4 weeks of EPO therapy. As a proxy for redox set point, glutathione (GSH) levels were monitored with FJF375, a novel small molecule selective GSH fluorescent sensor developed in the group. Immune phenotyping, cytokine quantification, and bulk RNA sequencing were performed to explore molecular mechanisms of EPO's effects.

Results: EPO treatment *in vitro* induced metabolic alterations in monocytes, as detected by our GSH sensor. While no significant changes were observed in T cells or B cells, monocytes significantly decreased GSH baseline levels after EPO treatment *in vitro* (p=0.005). KTR treated with EPO *in vivo* exhibited immune modulation associated with monocyte phenotypes. A significant decrease in GSH levels in monocytes (p = 0.017) was observed, correlating with a marked reduction of TNF-α release (p = 0.0037). RNA sequencing deconvolution analysis further revealed a tendency toward increased IL-4 levels, an anti-inflammatory cytokine associated with M2 macrophages.

Conclusions: EPO treatment induces cell-specific changes in GSH levels in monocytes, but not in T cells or B cells. EPO may influence immune cell function in KTR by promoting a shift in monocyte phenotyping from a pro-inflammatory M1 profile to an immunomodulatory M2 profile through alterations in redox homeostasis. Future studies are planned to investigate the functional consequences of these metabolic alterations in immune cells and their potential implications for transplantation outcomes.

PP_397 URINARY CHEMOKINES FOR THE NON-INVASIVE DETECTION OF KIDNEY ALLOGRAFT REJECTION

Valentin Goutaudier[1], Olivier Aubert[2], Maud Racape[3], Agathe Truchot[4], Marta Sablik[5], Éric Vicaut[6], Michelle Elias[7], Gillian Divard[8], Richard Danger[9], Beatrice Charreau[10], Didier Bouton[11], Christine Randoux-Lebrun[12], Jean-Luc Taupin[13], Pierre-Antoine Gourraud[14], Magali Giral[15], Moglie Le Quintrec[16], Emmanuel Morelon[17], Lionel Couzi[18], Christophe Legendre[19], Carmen Lefaucheur[20], Nassim Kamar[21], Sophie Brouard[22], Dany Anglicheau[23], Alexandre Loupy[24]

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Background: Urinary chemokines CXCL9 and CXCL10 have shown promise for detecting kidney allograft rejection, but the demonstration of their added value beyond standard of care patient monitoring requires further study.

Methods: We prospectively enrolled adult patients who underwent kidney transplantation in 7 transplant referral centers between July 2018 and December 2019 (ClinicalTrials.gov, NCT03582436). We quantified urinary CXCL9 and CXCL10 protein levels at the time of kidney allograft biopsies in the first year post-transplantation using an automated immunoassay platform. The primary outcome was allograft rejection defined according to the international Banff 2019 classification.

Results: Overall, 733 kidney transplant patients (64.1% male, 35.9% female) were included in the main analysis, with 1,549 biopsies paired with a urine sample. The cumulative incidence of rejection was 9.7%. Urinary CXCL9 and CXCL10 levels were significantly associated with overall allograft rejection (p < 0.001 for both), without discrimination between AMR and TCMR. For detecting allograft rejection, urinary CXCL9 and CXCL10 showed areas under the receiver operating curve (AUROC) of 0.70 (95% confidence interval [CI], 0.64-0.75) and 0.64 (95% CI, 0.58-0.71), respectively. Adding urinary CXCL9 to a standard of care model improved discrimination for allograft rejection (AUROC 0.75 [percentile bootstrap CI 0.70-0.79] to 0.78 [percentile bootstrap CI 0.73-0.83], p = 0.008, **Figure**), while urinary CXCL10 did not. There was a trend for an improvement of overall fit with the addition of urinary CXCL9 (Brier score changed from 0.056 [95% CI, 0.046-0.067] to 0.054 [95% CI, 0.045-0.064], p = 0.12), though this tended to overestimate the risk for allograft rejection for patients at high risk for rejection.

Conclusions: In this large, prospective, and unselected multicenter cohort study, urinary chemokine levels showed moderate clinical benefit in detecting kidney allograft rejection within the first year after transplantation.

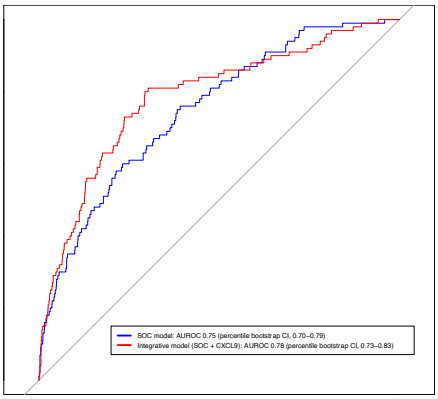

Figure. Added value of urinary chemokine levels beyond standard of care parameters for predicting allograft rejection in the KTD-Innov cohort.

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Transplant immunology & immunosuppression

PP_398 EFFECT OF EXTRACORPOREAL PHOTOPHERESIS ON GRAFT INTIMAL HYPERPLASIA IN THE FIRST YEAR AFTER HEART TRANSPLANTATION

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Background: Cardiac allograft vasculopathy (CAV) is a major cause of long-term mortality after heart transplantation (HTx) but prevention measures are still limited. Coronary intimal thickening that occurs during the first post-HTx year is an early sign of CAV. To our knowledge, only one study has reported of decreased intimal thickening in HTx recipients who received prophylactic extracorporeal photopheresis (ECP) in addition to maintenance immunosuppressive therapy (IST) consisting of cyclosporine, azathioprine, and steroid. The aim of this study was to evaluate the effect of prophylactic ECP on intimal thickening during the first post-HTx year as assessed by optical coherence tomography (OCT) in light of modern IST which includes mycophenolate mofetil, proven to have advantages over azathioprine in CAV prevention.

Methods: This is a pilot, prospective, randomized, open-label study. A total of 38 consecutive patients were randomized into two arms to receive either 10 cycles of ECP treatment in addition to standard IST or standard IST alone. OCT images from baseline and one year were recorded for the matched coronary segments and compared to assess intimal thickening. The primary endpoint was defined as the change in normalized total intimal volume, i.e. volume index (intimal volume/length).

Results: Follow-up was completed in 27 patients (13 in control and 14 in ECP group). The mean increase in volume index at 1-yr follow-up was significantly lower in the ECP group compared with the control group (1.054±1.756 mm^3/mm vs. 0.040±0.753 mm^3/mm, p=0.013).

Conclusions: This is the first prospective study that evaluated the effect of prophylactic ECP on intimal thickening in HTx recipients in the context of modern IST. Our study demonstrated significantly decreased intimal thickening in the first post-HTx year in patients receiving prophylactic ECP. The study is limited by a relatively small population size. The larger-scaled study is warranted to confirm our observation.

PP_399 EFFICACY OF INTRAVENOUS IMMUNOGLOBULIN FOR DONOR-SPECIFIC ANTIBODIES AFTER LUNG TRANSPLANTATION

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Background: De novo donor-specific antibodies (dnDSA) are associated with poor outcomes and reduced survival following lung transplantation. Despite their clinical significance, treatment protocols remain variable and lack consensus. This study aimed to evaluate the efficacy of intravenous immunoglobulin (IVIG) in eliminating dnDSA and to identify prognostic factors influencing treatment outcomes.

Methods: Between 2015 and 2019, 47 lung transplant recipients with dnDSA were treated with IVIG (1 g/kg initially, followed by 0.5 g/kg at four-week intervals, up to three doses). Patients were classified as responders (elimination of dnDSA, n=23) or non-responders (persistent dnDSA, n=24). HLA antibodies were assessed via Luminex Single Antigen Bead assays before, during, and after treatment.

Results: IVIG therapy resulted in dnDSA elimination in 49% of patients. Age and gender did not differ significantly between responders and non-responders (p=0.28 and p=1.0, respectively). However, non-responders were significantly more likely to have HLA Class II dnDSA (92% vs. 48%, p=0.003) and exhibited higher mean maximum MFI values (11,683 vs. 7,152, p=0.002). Time to dnDSA onset was significantly shorter in responders (61 days vs. 258 days, p=0.005). Multivariable logistic regression revealed that treatment initiated during subclinical antibody-mediated rejection (AMR) significantly improved dnDSA elimination (OR = 28.33, 95% CI 2.25–357.27, p < 0.005). This underscores the importance of early intervention, even in the absence of clinical symptoms or lung function decline.

Conclusions: The therapeutic approach for managing dnDSA following lung transplantation remains a topic of ongoing debate. Our findings suggest that early intervention targeting dnDSA may significantly enhance the likelihood of successful antibody elimination, potentially improving patient outcomes.

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PP_400 INTERIM ANALYSIS OF THE PROTECT RENVARSUS STUDY

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Background: As previously reported, fast tacrolimus (Tac) metabolizers can show an improvement in renal function after conversion from immediate-release (IR)-Tac to LCP-Tac whereas no recovery of kidney function was found in slow metabolizers [1]. In this study we intended to confirm these results in a multicentre trial.

Methods: In this retrospective European study, we aimed to include 300 renal transplant (RTx) patients who were converted from IR-Tac to LCP-Tac one month or later after RTx. The Tac concentration-to-dose ratio (C/D ratio) was calculated to define the metabolism groups (fast metabolizers: <1 ng/mL*1/mg and slow: ≥1) [2]. Kidney allograft function, acute rejections, infection rates, and the development of arterial hypertension were observed over a 5-year follow-up.

Results: A total of 305 patients have been included in this study to date. Initial results showed that fast metabolizers were of younger age and received considerable higher Tac doses at all time points. As early as 10 days after switching to LCP-Tac, the entire cohort showed an improvement in renal function. In particular, fast metabolizers who were switched to LCP-Tac 8.3 months (range: 1.0-253.1) after RTx showed a considerable increase in eGFR. Interestingly, kidney function in slow metabolizers only recovered until month 9 after conversion. Notably, slow metabolizers were switched to LCP-Tac at a noticeably longer time of 12.4 months (range: 1.0-203.6; p=0.010) after RTx. Adverse events were rare and comparable between the two groups.

Conclusions: Especially fast IR-Tac metabolizers may benefit from the C/D ratio calculation and switch to LCP-Tac early after RTx. Renal function in these patients can recover considerably and low rates of adverse events have been observed during 5-years of follow-up.

PP_403 MEDICATION ADHERENCE AMONG LIVER, HEART, LUNG AND KIDNEY TRANSPLANT RECIPIENTS

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Background: Non-adherence to immunosuppressive medication (IS) in solid organ transplantation (SOT) is associated with an increased risk of transplant rejection and graft loss. A joint initiative was taken to gain insight into medication adherence between recipients of different organs with the ultimate aim of promoting adherence in clinic.

Methods: The Basel Assessment of adherence to immunosuppressive Medication Scale (BAASIS) questionnaire was implemented as a post-transplant patient-reported outcome measure (PROM) from July 2023, starting with kidney, followed by heart, lung and liver transplant recipients. The BAASIS measures both taking (1 or more missed dosages of IS in the last 4 weeks) and timing (>2 hours before or after agreed time) of medication, persistence (stopped medication without consultation with the healthcare provider (HCP)) and adjustment (changing dosage without consultation with HCP). Recipients received questionnaires 3, 6, 9 and 12 months and yearly after SOT.

Results: 1577 BAASIS questionnaires were completed (response 77%, 60% Male), 202 heart, 193 lung, 371 liver and 816 kidney transplant recipients. Overall, 11% of SOT recipients were non-adherent on the taking scale (10% heart, 10% lung, 12% liver and 11% kidney transplant recipients). 25% SOT patients were non-adherent on the timing scale (24% heart, 18% lung, 34% liver and 22% kidney recipients). Liver recipients had a higher incidence of non-adherence in the timing scale, 0-6 months up to 45% and > 10 months up to 35%, whilst other SOT recipients showed an increase up to 27% >12 months. 3 kidney recipients completely stopped their medication without consent from the physician. 15 recipients changed the dosage of IS without consent from or informing their physician (3 heart, 2 liver, 2 lung and 8 kidney recipients).

Conclusions: Most recipients after SOT take their IS at the correct time, in the correct dosage and do not alter their medication use on their own initiative. More than 10% admitted being non-adherent. However, the adherence of recipients who did not (yet) complete the questionnaire, remains unknown. BAASIS is a useful tool to stimulate discussion about medication adherence with transplant recipients during their outpatient visits. Future research should focus on efficacy of interventions to promote adherence.

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PP_404 IS RITUXIMAB USEFUL OR HARMFUL IN BLOOD GROUP INCOMPATIBLE (ABOI) RENAL TRANSPLANTATION?

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Background: Rituximab has been proven to suppress anti-ABO titer rebound in ABOi renal transplantation. However, an increased risk of severe infectious disease and of acute antibody-mediated rejection (AMR) has been described after ABOi renal transplantation. We performed a prospective renal transplant study up to 5 years posttransplant to detect long-term immunological effects of rituximab administration.

Methods: Mononuclear cell subsets in peripheral blood, regional lymph nodes and protocol biopsies, and in-vitro T and B cell responses were assessed in 85 renal transplant recipients (living donation: n=25 ABOi, n=30 ABO compatible (ABOc); deceased donation (DD): n=30, all ABO compatible). IgG anti-HLA antibodies were assessed by single antigen assay.

Results: The frequency of severe infectious diseases was doubled in ABOi versus ABOc recipients (P=0.042 within 2 years). In ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years, together with impaired in-vitro B cell responses for 2 years (P=0.010, T-dependent; P=0.053, T-independent). CD4+ T cell counts were significantly lower up to 6 months (P=0.046). In regional lymph nodes of ABOi patients, we found a significant downregulation of naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation. ABOi patients showed an increased frequency of biopsy-proven acute rejection (3-12 months posttransplant, P=0.003) and of AMR (P=0.008 within 5 years). In protocol graft biopsies, we found rituximab-induced B cell depletion at 3 months (P<0.001), but even enhanced counts of T cells (P=0.041), macrophages (P=0.021) and plasma cells (P=0.033) at 1 year. IgG anti-HLA antibody formation was not significantly different between ABOi and ABOc patients.

Conclusions: An increased frequency of severe infectious diseases in rituximab treated ABOi renal transplant recipients may be explained by the rituximab-induced long-term immunological effects on CD4+ T cell counts and the prolonged depletion of B cell subsets together with compromised B cell responses. In protocol graft biopsies, rituximab induced early B cell depletion but counter-regulatory proinflammatory effects, coinciding with an increased acute rejection frequency. IgG anti-HLA antibody formation was not suppressed.

PP_405 INFLAMMATORY STATES AFFECT COMPOSITION OF PRETRANSPLANT PERIPHERAL BLOOD IMMUNE CELL COMPARTMENT

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Background: Stage 5 CKD patients have been at higher risk of various infections and malignancies due to uremia-associated alterations of the immune system. Little is known about other factors affecting peripheral blood immune cell compartment (PBICC) composition in this patient population.

Methods: This cross-sectional study included 107 kidney transplantation candidates (CKD5 patients) and 29 healthy controls. B cell, T cell, and dendritic cell populations were measured using a standardized and validated flow cytometry panel of The ONE study.

Results: CKD patients exhibited B and T cell lymphopenia with an immunosenescent phenotype predominantly in the CD4+ compartment and significantly higher counts of APCs. Multivariable PERMANOVAs identified smoking (R2 = 0.041, p < 0.001), CMV seropositivity (R2 = 0.05, p < 0001), age (R2 = 0.02, p = 0.03), past dialysis treatment (R = 0.035, p = 0.019), and presence of atherosclerotic cardiovascular disease (R2 = 0.02, p = 0.03) as factors associated with the changes in PBICC composition. Poisson regression models revealed that smoking was associated mainly with increase in switched memory B cells (RR = 2,4, adj.p = 0.18), CMV seropositivity with increase in CD4+ (RR = 5.8, adj.p < 0.001) and CD8+ (RR = 3, adj.p < 0.001) TEMRA cells, age with decrease in naive CD8+ T-cells (RR = 0.34, adj.p < 0.001), and dialysis with increase in marginal-zone B cells (RR = 2.3, adj.p = 0.007).

Conclusions: Factors associated with systemic inflammatory response significantly modify the composition of PBICC in patients prior to kidney transplantation. Whether such alterations of immune compartments represent a risk for adverse transplant outcomes needs to be explored further.

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PP_406 INTERNATIONAL PERSPECTIVE OF PHARMACISTS ROLE IN TRANSPLANT

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Background: Pharmacotherapy for solid organ transplant (SOT) recipients is complex. Pharmacists are recognized as part of the transplant team in the United States, but in other countries the role is less defined. Our objectives were to identify which countries have transplant pharmacists and to describe their role in SOT care.

Methods: An internet search identified contact information for SOT centers in countries other than the USA. (Search=*country name* + *transplant* + *center* OR *institution* OR *program*). Institutions were emailed a survey in one of their official languages (39 translations) to determine if they had a transplant pharmacist (Survey 1). Snowball distribution was undertaken via SOT networks. If 'yes', institutions were asked to share another electronic survey with pharmacists (Survey 2). If 'no', they were asked why. Survey 2 for pharmacists had 4 sections: demographics; assessment of roles; barriers to providing care; interest in joining a transplant network. Descriptive statistics were used for analysis.

Results: Of 193 countries, 127(65.8%) performed SOT. Survey 1 (sent to 1726 institutions) received responses from 130 institutions/40 countries. Survey 2 received responses from 128 pharmacists/17 countries. Of 42 countries responding in total, 43% had transplant pharmacists, 19% supplied mixed responses, and 38% did not; the most common reason was that pharmacists did not routinely provide clinical care. Most pharmacist respondents (n=128) were licensed for >5 years (81%), didn't have specialized transplant training (83%) and provided inpatient care (82%). Nearly all were confident in their ability to provide SOT care (94%) and perceived a demand for SOT pharmacists (99%). Having a variety of duties leaving insufficient time was the most common barrier (57%) Most (86%) perceived value in joining a network.

Conclusions: Transplant pharmacists are present in many countries and successes and barriers are identified. A professional network may facilitate international collaborations.

PP_407 IMPACT OF PERSISTENT AND RESOLVED DE NOVO DONOR-SPECIFIC ANTIBODIES ON KIDNEY TRANSPLANT OUTCOMES

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Background: *De novo* donor-specific antibodies (*dn*DSA) are recognized as a significant risk factor for graft failure in kidney transplantation. However, the prognostic significance of whether *dn*DSA persists or resolves after its initial detection remains unclear. This study aimed to evaluate the impact of persistent versus resolved *dn*DSA on graft survival in kidney transplant recipients.

Methods: We conducted a retrospective analysis on adult patients who underwent kidney transplantation at Severance Hospital between 2006 and 2022. Patients were divided into three groups: no dnDSA, resolved dnDSA, and persistent dnDSA. Among 1,395 patients, 390 (28.0%) developed dnDSA during follow-up. Graft survival rates were also analyzed and compared across the three groups.

Results: Death-censored graft survival was significantly lower in patients with *dn*DSA compared to those without *dn*DSA (P < 0.001). Among the 390 patients with *dn*DSA, 201 (51.5%) experienced resolution, while 189 (48.5%) had persistent *dn*DSA. The resolved dnDSA group developed dnDSA at a median of 20 months (IQR 5–70) after translantation, while the persistent dnDSA group developed dnDSA at a median of 44 months (IQR 12–83.5) post-transplant. Persistent *dn*DSA was associated with the presence of multiple *dn*DSA (30.7% vs. 15.4%, P < 0.001) and a higher median mean fluorescence intensity (4120 [IQR 1160-11750.5] vs. 1348 [IQR 814-2961], P < 0.001). Death-censored graft survival rates were 91.6% in the no *dn*DSA group, 87.2% in the resolved *dn*DSA group, and 72.7% in the persistent *dn*DSA group (P < 0.001).

Conclusions: Persistent *dn*DSA is strongly associated with poorer graft survival, whereas resolved *dn*DSA results in outcomes comparable to those without *dn*DSA. These findings highlight the importance of proactive management strategies to promote *dn*DSA resolution and improve long-term graft outcomes.

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PP_408 MHC-I DEFICIENT ISLET GRAFTS DO NOT TRIGGER MISSING SELF-INDUCED NK CELL REJECTION

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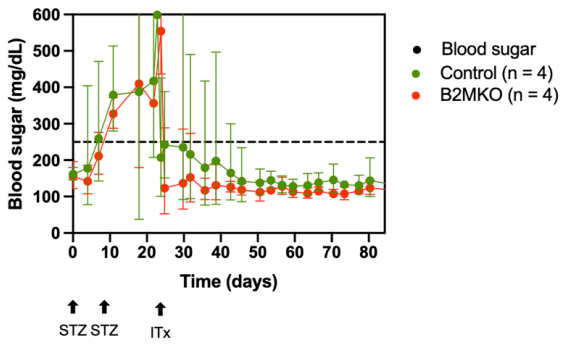
Background: Type 1 diabetes mellitus (T1DM) is an autoimmune disease caused by the destruction of insulin-producing pancreatic β cells by autoreactive CD8+ T cells. Islet transplantation is a promising treatment for T1DM, but long-term success is hindered by graft destruction from both autoreactive (T1DM recurrence) and alloreactive (rejection) recipient CD8+ T cells, which both target major histocompatibility complex class I (MHC-I) molecules on graft cells. While suppressing MHC-I expression in islets through genetic engineering is a logical strategy, our group has previously shown that MHC-I-deficient graft endothelial cells fail to provide inhibitory HLA-I signals to recipient NK cells, leading to microvascular inflammation and graft failure. However, since we also demonstrated that islet grafts are vascularized by recipient-derived vessels, it remains unclear whether MHC-I-deficient islet grafts are equally susceptible to missing self-induced NK cell rejection.

Methods: To investigate this, we developed a model in which MHC-I-deficient (B2M knockout) and wild-type WT C57BL/6 islets were transplanted under the kidney capsule of WT C57BL/6 recipients rendered diabetic by streptozotocin injection. This model excluded both autoreactive and alloreactive CD8+ T cells, focusing specifically on NK cell-mediated rejection. Grafts (350 islet equivalents per recipient) were monitored for function via blood glucose levels and histological analysis over 80 days.

Results: All recipients in both groups achieved normoglycemia (fasting blood glucose <250 mg/dL) within two weeks post-transplantation. Normoglycemia was sustained for eight weeks, with no significant differences in blood glucose levels between groups.

Conclusion: MHC-I-deficient islet grafts did not elicit missing self-induced NK cell rejection. Ongoing experiments aim to elucidate the mechanisms underlying this observation, providing valuable insights for improving islet transplantation outcomes.



PP_409 EARLY IMMUNE PROFILING AFTER KTX IDENTIFIES SCF AS A POTENTIAL BIOMARKER OF LONG-TERM GRAFT OUTCOME

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Background: Long-term graft survival remains disappointing following kidney transplantation (KTx), with around 30% loss rate after 10 years. Organ allocation is primarily based on donor and recipient's clinical and immunogenetic characteristics with poor prognostic accuracy. As current research often neglects the influence of early post-operative events, our study aimed to explore whether pre- and early post-operative biomarkers could predict long-term graft function and outcome.

Methods: We enrolled all consecutive adult patients, who received a KTx from living donation (LD), donation after brain death (DBD) or after cardiocirculatory death (DCD) at our hospital, from March 2022 to March 2023. We conducted a 12-month follow-up with detailed clinical and biological assessment of each patient. Pre- and early post-KTx (day 0 and day 2) peripheral blood cytokines levels and immune cell-subsets counts were respectively analyzed by multiplex and mass cytometry (CyTOF).

Results: 39 KTx recipients (female, 25.6%; median age, 60 years old) received a kidney from 14 LD, 10 DBD, and 15 DCD. Specific pro-inflammatory and hematopoietic signatures were observed before and after KTx. Women had lower IL-6 (p = 0.017) and higher GM-CSF (p = 0.047) pre-KTx levels than men. CXCL13 was the only factor to differ between donation types. Precisely, post-KTx CXCL13 levels were higher in DBD recipients, and were correlated with donor-specific anti-HLA antibody formation. More strikingly, higher pre- and post-KTx stem cell factor (SCF) levels were moderately to strongly associated with poorer 1-year allograft function. Finally, patients with higher post-KTx regulatory T cells counts displayed a better kidney function during follow-up.

Conclusions: Our comprehensive analysis of the immune landscape bridges a major gap in the knowledge of early immune responses in KTx recipients. These findings, pending further validation, could improve kidney allocation, and guide new diagnostic and therapeutic strategies.

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PP_410 GRAPH NEURAL NETWORKS IN THE NEPHROPATHOLOGICAL DIAGNOSIS OF ANTIBODY-MEDIATED REJECTION (AMR)

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Background: Antibody-mediated rejection (AMR) remains a significant cause of late allograft failure. However, considerable variability exists in its diagnosis, even among experts. Weakly supervised machine learning applied to renal biopsy whole slide images (WSIs) could offer cost-efficient and accurate diagnostics with perfect reproducibility. In this study, we build on our previous work developing diagnostic models for AMR using a multi-institutional dataset including adversarial samples such as accommodation, transmitted, recurrent, and de novo diseases.

Methods: A dataset of 1,183 periodic acid-Schiff WSIs from 348 patients from four different institutions was automatically segmented into tissue compartment crops. Graph neural networks (GNNs) were employed to classify AMR and non-AMR (including adversarial samples like accommodation, transmitted and de novo glomerulopathy). The WSIs were represented as fully connected graphs, with glomerular crops as nodes, capturing global spatial relationships. Feature vectors for individual glomerular crops were computed using both supervised (Swin Transformer) and self-supervised (MAE and SimCLR) architectures. Classification was performed using Graph-Transformer and three novel models: SimpleGCN, DenseGCN, and SimpleGAT. These WSI-level classifiers were compared to state-of-the-art patch-level classification methods (Swin and ConvNeXt). Performance was determined in 5-fold internal cross-validation experiments.

Results: The GNN-based methods outperformed baseline patch-level classification models. The best-performing model, SimpleGCN with Swin-extracted features, achieved an accuracy of 71.00% and an AUC of 0.7858, significantly better than the Swin model (accuracy of 65.66% and an AUC of 0.7265).

Conclusions: This study shows the potential of graph-based representations to model contextual information in nephropathology images. Our approach permits easy upscaling of training cohorts for cost-efficient and even more accurate diagnostic support systems. To this end and for further validation we are actively seeking collaborators. GB and JUB contributed equally.

PP_411 OPTIMIZING MTOR INHIBITOR USE IN HYPERSENSITIZED KIDNEY TRANSPLANT RECIPIENTS: INSIGHTS FROM A PROPENSITY SCORE ANALYSIS

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Background: mTOR inhibitors (mTORi) are not usually considered in high immunological risk kidney transplant recipients (KTR) for a perceived increased risk of rejection. However, in most of the studies that examined the combination of mTORi with calcineurin inhibitors (CNI), hypersensitized patients have been excluded from enrollment. The aim is to analyze our clinical experience with the use of mTORi in association with CNI in this subset of patients.

Methods: Analysis of 202 consecutive KTR with a baseline calculated panel reactive antibody (cPRA)≥50% who received a graft from June 2013 to December 2019 at our Institution. Immunosuppression was based on CNI, steroids and, alternatively, mycophenolic acid (MPA; n = 92) or mTORi (n=116) depending on the active Institution's protocol at the time of transplantation. A propensity score to receive mTORi was calculated based on the inverse probability of treatment weighting (IPTW) from the following parameters: age and sex of donor and recipient, BMI, previous transplants, diabetes, cPRA, dialysis before transplantation, dialysis vintage, type of donor, HLA-mismatches, induction and ischemia time. Median follow-up was 2.7[1.45-4.24]years.

Results: Baseline characteristics showed significant imbalances favoring mTORi in age, BMI, and diabetes, while donor type and cold ischemia time favored MPA. IPTW corrected these imbalances (STD ≤ 0.10). Immunological profiles, including DSA presence, type, and intensity, were similar between groups. Clinical outcomes, such as rejection rates, graft failure, and survival, showed no significant differences overall. In HLA-incompatible patients, mTORi had lower acute rejection and ABMR rates but similar graft loss and mortality. CNI trough levels were slightly lower in the mTORi group early post-transplant. Immunosuppressive therapy changes were more frequent in the mTORi group, often due to complications. Surgical outcomes favored mTORi with fewer infections and leaks but more hematomas. Post-transplant complications, including infections and delayed graft function, were similar between groups.

Conclusions: mTORi are a viable alternative to MPA in high immunological risk KTR, with comparable outcomes in terms of rejection rates, graft survival, patient survival, and the development of de novo DSA.

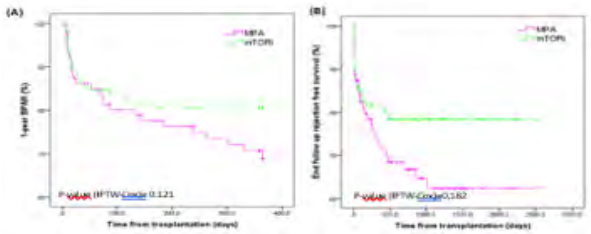

Figure 1. Kaplan-Meier estimates of survival for 1-year acute rejection (A), end follow up rejection (B)

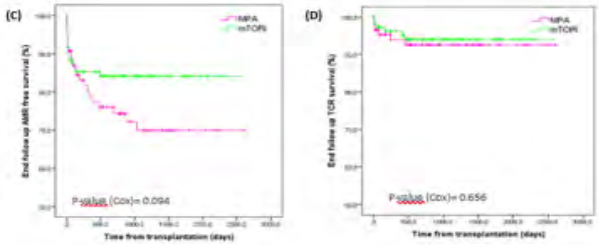

Figure 1. Kaplan-Meier estimates end follow up AMR free survival (C) and end follow up TCR survival (D).

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PP_412 INVESTIGATION OF BLOOD MYCOPHENOLIC ACID CONCENTRATIONS AND INFLUENCING FACTORS IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background: Immunosuppressants for kidney transplantation (KTx) mainly consist of tacrolimus and mycophenolate mofetil (MMF); however, there is a lack of consensus on the optimal concentration of mycophenolic acid (MPA). We thus measured and evaluated the factors that affect MPA concentration.

Methods: In total, 375 kidney transplant recipients were enrolled in this study. MPA concentrations were measured before the morning dose (12-hour trough) and divided into three groups (Group A: <2 μg/mL, Group B: 2–3.5 μg/mL, and Group C: ≥3.5 μg/mL) to analyze differences (Table).

Results: Correlation analysis indicated significant negative correlations between blood MPA concentration, and both estimated glomerular filtration rate (eGFR; p<0.0001) and body mass index (BMI; p<0.0001) (Figure1). The Kruskal–Wallis and Steel–Dwass tests revealed that higher MPA blood levels were associated with significantly lower eGFRs (47.9 ± 16 in Group A, 42.7 ± 11.2 in Group B, and 38.7 ± 12.1 in Group C; p<0.0001) and BMIs (23.1 ± 4.0 in Group A and 21.0 ± 2.8 in Group C; p<0.0001) than those in patients with low MPA levels. Multiple regression analysis revealed that eGFR, BMI, and total MMF dose significantly influenced blood MPA concentration (Figure2. p<0.0001, p<0.0001, and p=0.0002, respectively). It was assumed that a 1 unit increase in eGFR would lead to a 0.03 unit decrease in MPA blood level, while a 1 unit increase in BMI would result in a 0.11 unit decrease in MPA blood level, as a predictive model.

Conclusions: eGFR and BMI are considered reasonable indices for adjusting MPA concentration.

	group A (<2.0)	group B (2.0—3.5)	group C (3.5≥)	p	A/C	B/C	A/B
n	130	128	117				
age (years)	56.0 ± 12	51.9 ± 12.3	52.6 ± 11.9	0.0287	0.0913	0.9995	0.0762
MPA trough (μg/dL)	1.3 ± 0.4	2.2 ± 0.13	4.9 ± 1.4	<.0001	<.0001	<.0001	<.0001
MMF total (mg)	835 ± 237	851 ± 212	880 ± 190	0.1047	0.2598	0.9929	0.2267
MMF morning (mg)	458 ± 124	462 ± 103	477 ± 90	0.2257	0.2361	0.9668	0.4112
MMF evening (mg)	377 ± 143	388 ± 136	402 ± 130	0.1445	0.1887	0.9936	0.2327
duration from KTx (days)	3059 ± 2004	2701 ± 2182	3366 ± 2231	0.4408	0.6519	0.9862	0.5517
BMI (kg/m^2)	23.1 ± 4.0	22.1 ± 3.6	21.0 ± 2.8	<.0001	<.0001	0.0250	0.1917
eGFR	47.9 ± 16	42.7 ± 11.2	38.7 ± 12.1	<.0001	<.0001	0.0253	0.0223
serum creatinine (mg/dL)	1.3 ± 0.6	1.3 ± 0.3	1.5 ± 0.6	<.0001	0.0103	0.0557	0.8114
TAC trough (ng/mL)	4.7 ± 1.1	4.6 ± 1.4	4.5 ± 1.4	0.5219	0.5816	0.7267	0.9701
WBC (/μL)	6559 ± 2127	5993 ± 1963	5903 ± 2179	0.0130	0.0332	0.2261	0.6559
Hemoglobin (g/dL)	13.6 ± 1.5	13.5 ± 1.8	12.8 ± 1.7	0.0009	0.002	0.0219	0.7275
AST (IU/L)	21 ± 9	21.2 ± 8.0	19.7 ± 5.1	0.1025	0.0534	0.2145	0.7733
ALT (IU/L)	19 ± 14	19 ± 17	15.1 ± 7.2	0.0032	0.0108	0.2943	0.322
T-Bil (mg/dL)	0.8 ± 0.3	0.8 ± 0.2	0.8 ± 0.2	0.2839	0.3547	0.59	0.9088

Table. Baseline characteristics according to the concentration of mycophenolic acid grade

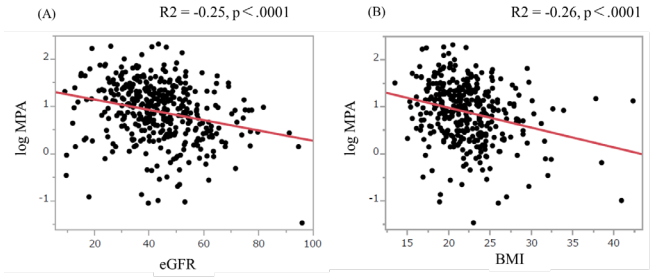

Figure 1.Univariate analysis of the correlation between mycophenolic acid and expected influencing factors

Correlation between blood MPA concentration and (A) eGFR, or (B) BMI

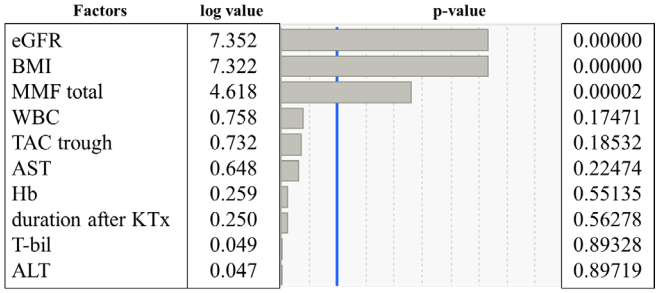

Figure 2. Logistic regression analysis of the relationship between expected influencing factors and the concentration of mycophenolic acid

PP_416 MMP9 EXPRESSION AS A POTENTIAL PREDICTIVE AND DIAGNOSTIC BIOMARKER OF CHRONIC ABMR IN RENAL TRANSPLANTATION

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Background: Chronic antibody-mediated rejection (cABMR) is the main cause of late kidney graft failure today, but the molecular triggers of cABMR beyond HLA donor-specific antibodies are still largely unknown. Here, we aimed at characterizing blood transcriptomic signatures prior and at the time of cABMR in order to identify non-invasive biomarkers.

Methods: We explored the transcriptome of cABMR in PBMCs (n=139) using bulk RNA-seq at different stages of the kidney graft follow-up. First, we compared gene expressions between late (time > 4 years post-transplantation) cABMR (n=35) and late stable patients (n=43). In a second step, we compared 1-year post-graft samples from patients who later experienced a cABMR (n=22) vs. those who have remained stable (n=39). The differential expression analyses were performed using linear mixed models corrected with sex, age, BMI, day at draw and graft year as covariates.

Results: cABMR was associated with an upregulation of 121 genes, notably related to the neutrophil degranulation pathway (*e.g. MMP9*, $\log_2$(FC)=2.55, padj=1.36x10^{-5}; *MMP8* and *LCN2*) and the C1q complement complex (*e.g. C1QA*; $\log_2$(FC)=0.97, padj=3.11x10^{-2}), as well as with a downregulation of 67 genes notably associated with graft tolerance (*e.g. TCL1A*; $\log_2$(FC)=-1.26, padj=1.52x10^{-2}). These data were corroborated in three independent cohorts (sample sizes: 247 stables vs. 68 ABMR; 23 stables vs. 16 ABMR; and 190 stables vs. 21 chronic rejection). Using a single-cell RNA-seq of 3 kidney transplanted patients, we highlighted the importance of the complement pathway in monocytes and the BCR signalling in naive B cells for cABMR physiopathology. Amongst the differentially expressed genes during cABMR, only *MMP9* was significantly differentially downregulated ($\log_2$(FC)=-2.78, padj=1.33x10^{-4}) at 1-year post-graft in patients who later experienced cABMR.

Conclusions: We hypothesize that *MMP9* would be a good predictive and diagnostic mRNA biomarker of cABMR in the early and late stages of renal transplantation, respectively. We plan to further validate these results in an independent cohort in order to establish a risk score and better stratify patients.

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Transplant immunology & immunosuppression

PP_417 INVESTIGATING THE ROLE OF SODIUM ON ALLOIMMUNE RESPONSES

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Background: Salt (sodium chloride; NaCl) impacts the function of both innate and adaptive immune cells, including cells involved in alloimmune responses to foreign human leucocyte antigens (HLA). Inflammatory T cell (e.g. Th17 cell) responses play an important role in this process. The impact of sodium on immune responses to foreign HLA is unknown. Hence, we investigated the effect of altering extracellular sodium on T cell responses to non-specific and HLA stimulation in vitro.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy controls and mixed lymphocyte reactions (MLRs) were performed. Responder cells were stained with the proliferation marker CFSE and stimulated with anti-CD3/28, and by incubation with allogenic (donor) PBMCs irradiated at 40G, for 3 and 5 days respectively. The proportion of proliferating live cells and the expression of IFNg and IL-17 were determined with FACS; supernatant cytokine concentrations were measured with ELISA. Experiments were undertaken in standard conditions, and in media supplemented with additional +20mM and +40mM NaCl.

Results: Sodium decreased proliferation in response to anti-CD3/28 stimulation in a dose dependent manner (**Fig. 1a and b**), an effect not consistently seen in response to foreign HLA (**Fig. 1c**). Under both stimulating conditions, sodium altered the pattern of cytokine expression with the ratio of IL17/IFNg increasing in a dose dependent manner under stimulation with both anti-CD3/28 (**Fig. 1d, e and f**) and foreign HLA (**Fig 1g**). This was supported by supernatant cytokine concentrations where an increase in IL17/IFNg ratio (**Fig 1h**) was observed with additional sodium in a dose-dependent manner under stimulation with anti-CD3/28.

Conclusions: Extracellular sodium altered cytokine responses to non-specific and foreign HLA stimulation, favouring IL-17 responses in healthy control cells. Whether this effect is seen in kidney transplant recipients and its clinical relevance in vivo is to be determined.

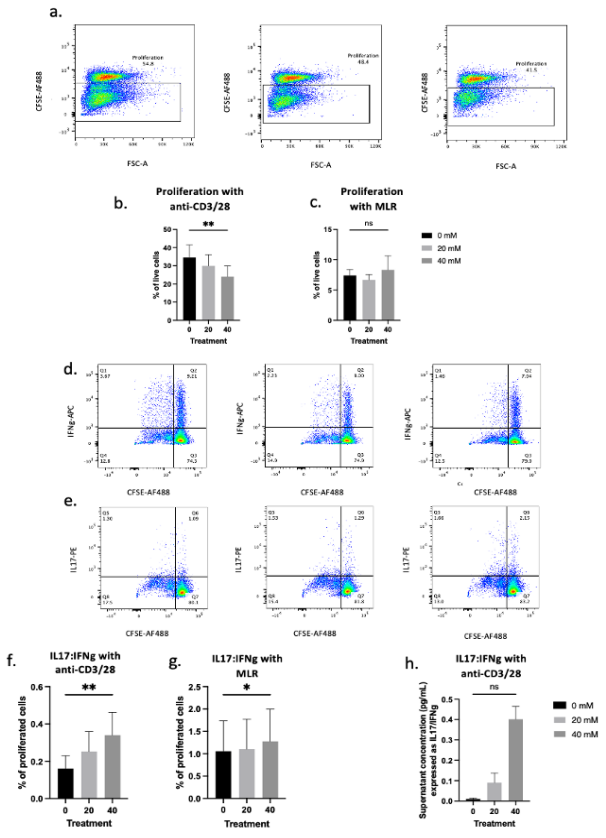

Figure 1: (a) FACS dot plots and (b) bar graphs of proliferating cells (CFSE-ve) under anti-CD3/28 stimulation and (c) MLR. Representative FACS plots of (d) IL17 and (e)IFNg expression under 0, 20 and 40 mM in proliferating cells after stimulation with anti-CD3/28. Ratio of IL17/IFNg in proliferating cells under three different salt conditions when stimulated with (f) anti-CD3/28 and (g) MLR. (h) Supernatant concentrations (pg/mL) expressed as IL17/IFNg. Groups are compared with a Kruskal–Wallis test with Dunn's multiple comparison testing (shown with significance bars). Error bars represent mean + SEM.

PP_418 VALIDATION OF TACROLIMUS AND CREATININE MONITORING FROM DRIED BLOOD SPOTS IN ADULT KIDNEY TRANSPLANT RECIPIENTS

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Background: Due to its narrow therapeutic window, therapeutic drug monitoring (TDM) of Tacrolimus levels is crucial in kidney transplant recipients (KTR) to prevent rejection and toxic drug effects. Additionally, creatinine is the most important parameter in post-transplant care to assess kidney function. To improve TDM and post-transplant care, creatinine and Tacrolimus level measurement from dried blood spots (DBS) was developed in a collaboration with the department of toxicology of Labor Berlin GmbH.

Methods: For validation of the DBS method, capillary blood was obtained from the fingertip using a lancet within 10 minutes following routine venous blood collection for Tacrolimus trough level and creatinine measurement. One to four drops of blood (20µl each) were applied to the AutoCollect™ DBS card using a minivette. The samples were left to dry at room temperature for ≥4 hours and pseudonymized before being sent to Labor Berlin. Extracts were obtained using the CAMAG DBS-500 Autosampler and analyzed by LC-MS/MS on a Sciex 6500 QTRAP. Tacrolimus levels in the venous blood samples were measured using ECLIA on a COBAS 8000. Statistical analysis of method comparison was performed using Passing-Bablok regression and Bland-Altman plot.

Results: 78 samples from 78 KTR were collected during routine visits at the transplant outpatient clinic and analyzed for tacrolimus levels. A subset of 53 was additionally analyzed for creatinine. The Passing-Bablok regression yielded the equation y = 1.38x - 0.93 (95% CI slope 1.18 – 1.61; 95% CI Intercept -2,28 – 0,35; Pearson's r= 0.852) for Tacrolimus and y= 0.86x - 0,14 (95% CI slope 0,72 – 1,02; 95%; CI Intercept -0,34 – 0,07; Pearson's r=0.822) for creatinine. The average Tacrolimus level (ng/ml) in venous blood samples was 6,91, compared to 8,42 for the DBS measurement. Therefore, the Bland-Altman plot showed a mean difference of +1,51 ng/ml (Mean ± 1.96*SD: -3.59 - 6.61). Mean creatinine levels (mg/dl) were 1,49 in whole blood, compared to 1,14 in DBS samples (Mean Difference -0,35, Mean ± 1.96*SD: -0,87- 0.18).

Conclusions: Following method improvement and potential introduction of a corrector, Tacrolimus TDM and creatinine measurements through DBS could become a valuable component of enhanced patient home monitoring providing flexible and self-managed post-transplant care.

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Transplant immunology & immunosuppression

PP_422 IMPORTANCE OF THE DONOR CYP3A5 GENOTYPE IN TACROLIMUS EXPOSURE IN LIVER TRANSPLANT PATIENTS

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Background: Improved guidance of initial immediate-release tacrolimus (Tac-IR) doses to achieve therapeutic target concentrations in liver transplant patients is critical to prevent graft rejection and adverse effects. The present study aimed to develop a Population Pharmacokinetic (PopPK) model identifying the genetic factors and clinical variables that explain the pharmacokinetic variability and allow to estimate the optimal tailored initial dose of tacrolimus.

Methods: A total of 504 blood tacrolimus concentrations from 63 liver transplant patients were intensively sampled for 24 h on the first two weeks after transplantation from September 2022 to October 2023. Tacrolimus daily doses and genetic and demographic characteristics were retrieved prospectively from medical files. A cohort of 55 de novo liver transplant patients on Tac-IR treatment was included in the final model and concentration data was collected at the following times: Pre-dose, 0.5, 1, 2, 4, 8, 12 and 24 h following Tac-IR administration. Initial doses were given as 0.05 mg/kg twice daily with mycophenolate mofetil (MMF) and steroids as concomitant therapy. A PopPK analysis was carried out using the non-linear mixed-effects approach using NONMEM 7.5 software.

Results: A two-compartment model with delayed absorption best described the tacrolimus pharmacokinetics. Tacrolimus concentrations standardized to a haematocrit value of 45% significantly improved the model ($p < 0.001$). The effect of the CYP3A5 donor genotype was statistically ($p < 0.001$) and clinically significant on CL/F. Transplant recipients with CYP3A5*1-carrying donors (high metabolizers) showed 1.28-fold higher clearance than CYP3A5*1 non-carriers (Figure 1).

Conclusions: Our study describes the first PopPK model with the Tac-IR formulation in de novo adult liver transplant patients. The donor, more than the recipient, CYP3A5 genotype should be considered for the starting dose of Tac-IR in liver transplantation to achieve therapeutic target levels.

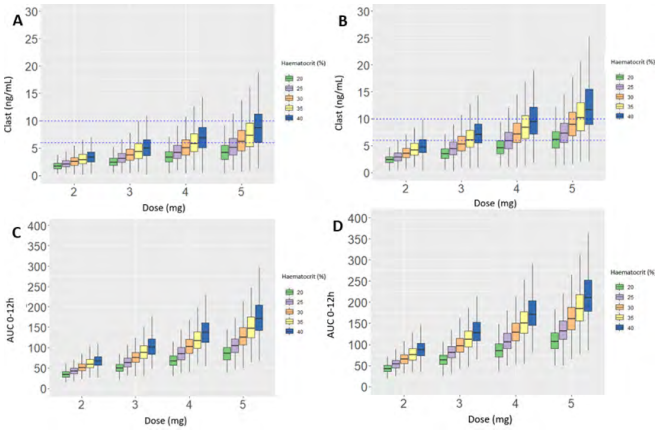

Figure 1: Simulated patient final tacrolimus concentrations (Clast) and AUC values. Figures A and C present Clast and AUC values for transplant patients with CYP3A5*1/*1 and CYP3A5*1/*3 -carrying donors. Figures B and D present these results for patients with a CYP3A5*3/*3 donor phenotype.

PP_423 MULTI-OMICS ANALYSIS IDENTIFIED CHI3L1 AS A POTENTIAL MEDIATOR OF IMMUNE-DISTURBANCE IN CAMR

***Simona Granata*[1], Francesca Leone[2], Maurizio Bruschi[3], Paola Pontrelli[4], Giovanni Candiano[5], Michele Provenzano[6], Loreto Gesualdo[7], Giuseppe Grandaliano[8], Gianluigi Zaza[9]**

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Background: Although in the last two decades many studies have defined the clinical fingerprints of the chronic antibody mediated rejection (CAMR), the leading cause of long-term kidney allograft failure, the biological machinery associated with this complex condition is still largely undefined. Omics technologies, analyzing thousands of biological factors at the same time, may contribute to filling this gap.

Methods: This study integrated mass spectrometry-based proteomic profiling of serum samples from 19 patients with clinical and histological evidence of CAMR and 26 kidney transplant recipients with normal graft function and histology (CTR) with transcriptomic analysis of peripheral blood mononuclear cells (PBMCs) from an independent cohort of 10 CAMR and 8 CTR patients. Data analysis was conducted using unsupervised hierarchical clustering and Spearman's correlation test. Partial least squares discriminant analysis (PLS-DA) with k-means and variable importance in projection (VIP) score identified key proteins differentiating CAMR from CTR. ELISA was used to validate omics results.

Results: Proteomic analysis identified 18 proteins that significantly differentiated CAMR from CTR ($p<0.01$): five were more abundant (CHI3L1, LYZ, PRSS2, CPQ, IGLV3-32), while 13 were less abundant (SERPINA5, SERPING1, KNG1, CAMP, VNN1, BTD, WDR1, PON3, AHNAK2, MELTF, CA1, CD44, CUL1). Transcriptomic profiling revealed 6 downregulated and 33 upregulated genes in CAMR versus CTR ($p<0.01$). Notably, CHI3L1, a organ damage-related protein, resulted significantly up-regulated in CAMR in both transcriptomics and proteomics. ELISA of CHI3L1 validated omics results and ROC curve showed a good discrimination power between CAMR and CTR (AUC of ROC curve of 0.81).

Conclusions: Our data revealed new systemic biological elements involved in the CAMR pathogenesis and identified CHI3L1 as a new potential biomarker and/or therapeutic target for this important clinical complication.

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Transplant immunology & immunosuppression

PP_424 METABOLIC REPROGRAMMING IN MARCOPHAGES: PP2A'S CRUCIAL ROLE IN KIDNEY TRANSPLANT REJECTION DYNAMIC

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Background: This study aims to investigate the role and mechanism of Protein Phosphatase 2A (PP2A) in antibody-mediated rejection (ABMR) of renal allogeneic transplantation.

Methods: Conditional macrophage PP2A knockout mice were employed to establish a mouse model of acute ABMR. Various techniques, including histological staining, immunohistochemistry, flow cytometry, immunofluorescence staining, quantitative reverse transcription polymerase chain reaction (qRT-PCR), and Western blotting, were utilized to assess renal transplantation injury, macrophage polarization markers, glycolysis markers, and fatty acid synthesis markers in ABMR mice. Additionally, magnetic beads facilitated RNA sequencing classification of macrophages infiltrating the transplanted kidney to elucidate the molecular mechanism by which PP2A regulates macrophage metabolic reprogramming in ABMR.

Results: Our findings revealed that both macrophage infiltration and pro-inflammatory macrophage polarization were significantly elevated in the renal tissues of ABMR patients and animal models. We subsequently generated conditional macrophage PP2A knockout mice and established an acute ABMR model using these mice. Compared to the control group, gene knockout enhanced the polarization of pro-inflammatory macrophages and exacerbated the pathological damage to renal grafts. Furthermore, PP2A deficiency in primary bone marrow-derived macrophages (BMDMs) promoted pro-inflammatory macrophage polarization, stimulated macrophage glycolysis, and increased fatty acid synthesis. Mechanistically, PP2A may mitigate pro-inflammatory macrophage activation and ameliorate the progression of ABMR in allogeneic kidney transplantation by modulating macrophage metabolic reprogramming.

Conclusions: An acute antibody-mediated rejection (ABMR) model in mice was successfully established and characterized. Protein phosphatase 2A (PP2A) appears to mitigate pro-inflammatory macrophage activation and enhance the progression of ABMR in allogeneic kidney transplantation by modulating macrophage metabolic reprogramming. This finding may offer new insights into the PP2A pathway as a potential therapeutic target for ABMR.

PP_425 A RETROSPECTIVE ANALYSIS OF BANFF LESION SCORES AND DIAGNOSES IN KIDNEY TRANSPLANT BIOPSIES

***Lottie Bottomley*[1], Rute Cardoso De Aguiar[1], Andrew Smith[2], Naomi Simmonds[2], Terry Cook[1], Michelle Willicombe[3], Candice Roufosse[4]**

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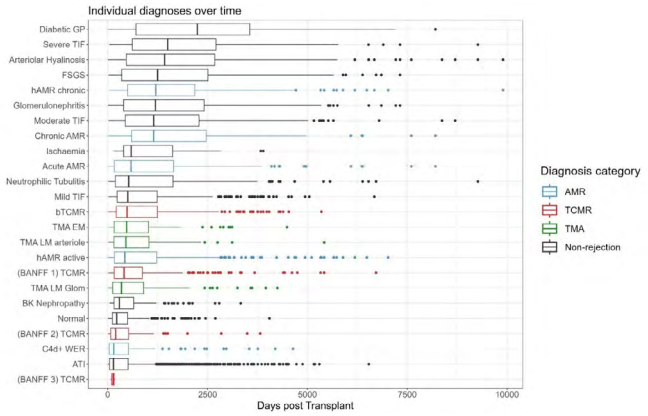
Background: Kidney transplantation remains the optimal treatment for patients with end-stage kidney disease, however transplant kidneys do not always last for a patient's lifetime, with half-life rates at 10-12 years. The Banff Classification is a complete system of diagnostic categories and lesion scores used for individual transplant patient management. In this study, we harness its additional potential to investigate population level causes of graft dysfunction and loss.

Methods: The study cohort consists of adult kidney transplant diagnostic allograft biopsies from 05.01.07-26.03.24 in our centre. 3529 biopsies from 1754 individuals were recorded according to Banff 2022 Classification. Graphic representations of diagnostic categories and Banff lesion scores over time post-transplant were derived.

Results: Recipients were 64% male, 49% non-caucasian, mean age 53.7 years. Transplants were from living donors in 42%. The most common primary diagnoses (with several diagnoses allowed per biopsy) were acute tubular injury (ATI)/mild scarring (IFTA) only (44.4%) and histology for AMR active (12.7%). Rejection was present in 34.4% of biopsies: TCMR-1 (6.5%); acute AMR (6.1%); histology for AMR chronic (5.7%), chronic AMR (3.6%); TCMR-2/3 (1.7%). Looking at mean time of diagnosis post-transplant, ATI, TCMR and C4d+ without other features of rejection were lowest whereas diabetic glomerulopathy, moderate/severe IFTA, arterial hyalinosis and chronic AMR were highest. Over time post-transplantation, Banff lesion chronicity scores (ct/ci/cv/ah/cg) increased (r = 0.619), while AMR (g/ptc) and TCMR (t/i) activity scores remained broadly stable.

Conclusions: We demonstrate that systematic recording and analysis of Banff diagnoses and lesion scores can effectively describe population level disease over time post-transplant and illustrate trends in active and chronic lesions and diagnoses. This can be used to compare effects of patient demographics and management on these findings.



Diagnosis	% total biopsies
ATI	31.07
Mild TIF	13.36
hAMR active	12.68
Arteriolar hyalinosis	12.35
Borderline TCMR	10.32
Moderate TIF	9.45
GN	9.20
FSGS	8.44
Normal	7.11
TCMR (Banff 1)	6.47
Acute AMR	6.13
Neutrophitic tubulitis	5.93
hAMR chronic	5.68
Severe TIF	5.68
Diabetic GP	4.05
BK Nephropathy	3.99
Chronic AMR	3.63
C4d+ WER	2.95
TMA LM Glom	2.67
TMA LM Arteriole	2.08
TCMR (Banff 2)	1.63
TMA EM	1.32
Ischaemia	0.45
TCMR (Banff 3)	0.08

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Transplant immunology & immunosuppression

PP_426 FACTORS INFLUENCING TORQUE TENO VIRUS VIRAL LOAD IN A SIZABLE COHORT OF LUNG AND KIDNEY TRANSPLANT RECIPIENTS

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Background: In the field of transplantation, the identification of a biomarker for immune monitoring is crucial. In this regard, interest in measuring the TTV viral load (TTV VL) has been steadily increasing. However, no consensus exists regarding the thresholds for assessing the risk of under- or over-immunosuppression.

Methods: TTV VL was measured in 779 lung (LTR) and kidney transplant recipients (KTR) at Strasbourg University Hospital. The aim of the study was to identify factors influencing TTV VL to better interpret its variations.

Results: 717 patients (93%) had a positive TTV VL, including 240 LTR and 485 KTR (KTR), with an average of 4.65 (±1.95) $\log_{10}$ cp/ml. In the overall cohort, the mean post-transplant time was 6.78 years (± 6.75), which independently and negatively influenced the TTV VL ($r = -0.318$, $p < 0.0001$). In univariate analysis, numerous patient and transplant-related characteristics were significantly associated with TTV VL. In multivariate analysis, female gender and a history of coronary artery disease positively influenced TTV VL, while the eGFR (CKD-EPI) and neutrophil count negatively influenced TTV VL. Regarding immunosuppression, tacrolimus-based triple immunosuppressive therapy was associated with a significant increase TTV VL compared to cyclosporine (5.13 vs 4.01 $\log_{10}$ cp/ml $p < 0.0001$, respectively). Furthermore, triple therapy with corticosteroids significantly increased TTV VL compared to a similar dual therapy without corticosteroids (5.13 $\log_{10}$ cp/ml vs 4.19 $\log_{10}$ cp/ml for Tacrolimus-MMF ± corticosteroids, $p < 0.01$). Therapeutic drug monitoring (TDM) data, such as tacrolimus dosage and trough levels, showed a weak correlation with TTV VL ($r = 0.309$, $p < 0.001$ and $r = 0.208$, $p < 0.001$, respectively). In multivariate analysis, the absence of induction within the first year and cyclosporine use negatively influenced TTV VL, while rituximab treatment, corticosteroid use, tacrolimus dosage, MMF dosage/body weight, and tacrolimus trough levels positively influenced TTV VL.

Conclusions: In this cohort, TTV VL was influenced by post-transplant time, comorbidities, and immunosuppressive therapy. TDM alone is insufficient for immune monitoring, highlighting the need for a new test integrating all factors influencing transplant immunosuppression

PP_428 NATURAL KILLER CELLS-DRIVEN MICROVASCULAR INFLAMMATION: THE ROLE OF MISSING SELF

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Background: Antibody-mediated rejection (AMR) remains the leading cause of late allograft failure. Notably, microvascular inflammation (MVI; g+ptc≥2), can occur without detectable donor-specific antibodies (DSA), suggesting alternative pathophysiology, potentially driven by natural killer cells.

Methods: In this retrospective study 165 kidney transplant recipients were stratified based on clinical biopsy findings and DSA status at time of biopsy into three diagnostic categories: (1) AMR (DSA+/MVI+, n=91), (2) DSA-negative, C4d-negative MVI (DSA-/C4d-/MVI+, n=35) and (3) DSA-positive controls without MVI (DSA+/MVI-, n=39). The median time to allograft biopsy was 74, 5 and 44 months for categories 1, 2 and 3, respectively. Killer-cell immunoglobulin-like receptor typing was performed, and "missing self" was calculated for each patient. Finally, we analyzed the impact of missing self on the probability of reaching one of the 3 diagnostic categories based on the DSA-status and MVI-occurrence in the biopsy.

Results: In the DSA+/MVI+ category missing self didn´t have any significant impact on diagnosis (HR=0.73, 95% CI: 0.48 – 1.11, p = 0.13). In the DSA-/C4d-/MVI+ category, missing self was associated with a higher probability to get diagnosed with the category (HR=1.37, 95%CI: 0.70–2.71, p=0.36), however didn´t reach statistical significance. In contrast, we found a significant inverse relationship between missing self (HR = 0.52, 95% CI: 0.27–0.98, p = 0.044) and the category of DSA+/MVI- biopsies. A formal test comparing these hazard ratios indicated a notable difference (HR interaction term=2.25, p=0.09) between DSA-/MVI+ and DSA+/MVI- categories, suggesting that missing self may contribute to DSA-/MVI+ category.

Conclusions: Our findings suggest a potential role of missing self in early-post-transplant DSA-/MVI+, indicating NK-cell-involvement in this novel phenotype.

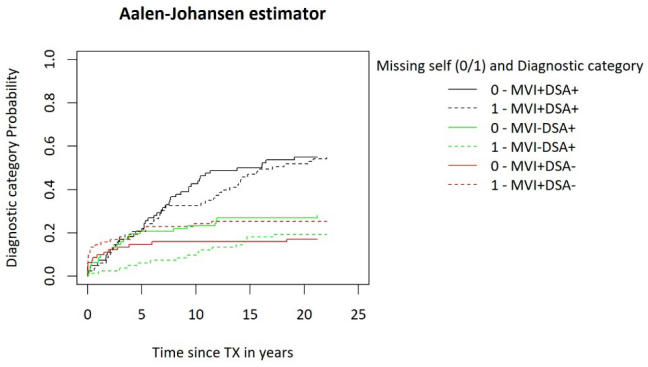

Figure 1 Ahlen-Johansen estimator for event probability based on missing self

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PP_429 TRANSFORMING KIDNEY TRANSPLANT DIAGNOSTICS: QUANTIFIABLE INDICES FROM AUTOMATED IMAGE ANALYSIS

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Background: The current Banff classification of kidney transplant biopsies is subject to three major limitations: 1) artificial dichotomizations of the continuous rejection process, 2) inter-observer variability and 3) low granularity in lesion scoring. To address these issues, we evaluated the discriminative power of continuous indices derived from automated whole-slide images (WSIs) analyses in differentiating the main Banff categories.

Methods: Two datasets of kidney transplant biopsies were used: Leuven (N=3675) and Leiden (N=517). All biopsies were scored by expert pathologists and classified according to the Banff 22 classification. The histological AMR, TCMR, activity and chronicity indices were computed as previously described. WSIs were analyzed with BanffNET, a weakly supervised deep-learning framework developed at LUMC that predicts Banff lesion scores from the integration of patch-level estimates on WSIs. The BanffNET indices were computed using the formulas of histological indices with BanffNET lesion scores re-scaled. The following lesions scores were directly retrieved from BanffNET outputs: g, ptc, i, t, v, cg, cv and IFTA. As not available from BanffNET, ci and ct were replaced by BanffNET IFTA, and C4d from traditional histology staining. The correlation between histological and BanffNET indices was measured with Pearson correlation and the discrimination of the indices with the main Banff categories by AUC.

Results: The distribution of indices amongst the Banff categories were in line with the underlying rejection continuum: no rejection - intermediate - fully inflamed phenotypes (Fig. 1). The correlation between the histological and BanffNET indices ranged from 0.68 to 0.91 (Table 1). The BanffNET AMR index discriminated AMR from No AMR with AUC of 0.90 and 0.90 in the Leuven and Leiden datasets, respectively (Table 1). BanffNET TCMR index had AUC of 0.90 and 0.86 (TCMR vs No TCMR); BanffNET Activity index had AUC of 0.90 and 0.92 (No rejection vs any rejection) and 0.96 and 0.93 (Mixed rejection vs no Mixed rejection).

Conclusions: Quantifiable indices from automated WSIs analyses demonstrated excellent discriminative performance on the main Banff categories while modeling the continuous spectrum of rejection with enhanced granularity.

1. doi.org/10.1101/2024.12.10.24318058

Fig. 1 Distribution of the BanffNET indices amongst the relevant Banff diagnostic categories in the combined dataset (N=4192 biopsies)

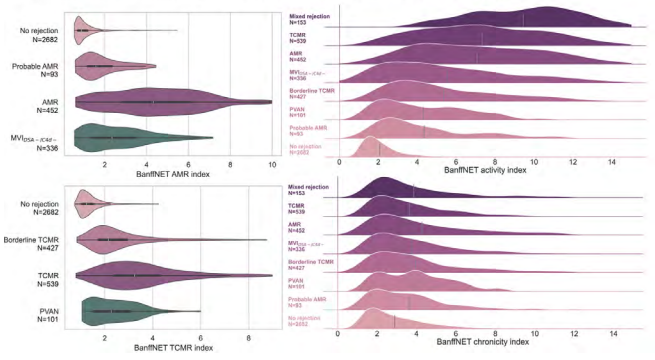

Table 1 Discrimination performance measured by AUC of the indices and the relevant Banff categories (95% confidence interval) AMR: Antibody-mediated rejection, MVI: DSA-negative, C4d-negative microvascular inflammation, PVAN: polyomavirus-associated nephropathy, TCMR: T cell-mediated rejection

	Leuven dataset (N=3675)	Leiden dataset (N=517)
CORRELATION		
Histological vs BanffNET index		
AMR index	0.76 (p<0.001)	0.91 (p<0.001)
TCMR index	0.68 (p<0.001)	0.88 (p<0.001)
Activity index	0.70 (p<0.001)	0.91 (p<0.001)
Chronicity index	0.79 (p<0.001)	0.88 (p<0.001)
DISCRIMINATION AUC (95% CI)		
BanffNET AMR index		
AMR vs no AMR	0.90 (0.88-0.92)	0.90 (0.87-0.92)
$MVI_{DSA-/C4d-}$ /AMR vs no $MVI_{DSA-/C4d-}$ /AMR	0.84 (0.82-0.86)	0.92 (0.89-0.94)
BanffNET TCMR index		
TCMR vs no TCMR	0.90 (0.88-0.92)	0.86 (0.83-0.89)
PVAN vs no PVAN	0.76 (0.72-0.80)	0.56 (0.37-0.75)
BanffNET Activity index		
No Rejection vs any Rejection	0.86 (0.84 - 0.87)	0.87 (0.83-0.90)
Mixed vs no Mixed	0.96 (0.95-0.97)	0.93 (0.90-0.96)

PP_430 MOLECULAR DIAGNOSTIC CLASSIFICATION OF HEART ALLOGRAFT REJECTION: A CALIBRATED AND VALIDATED SYSTEM

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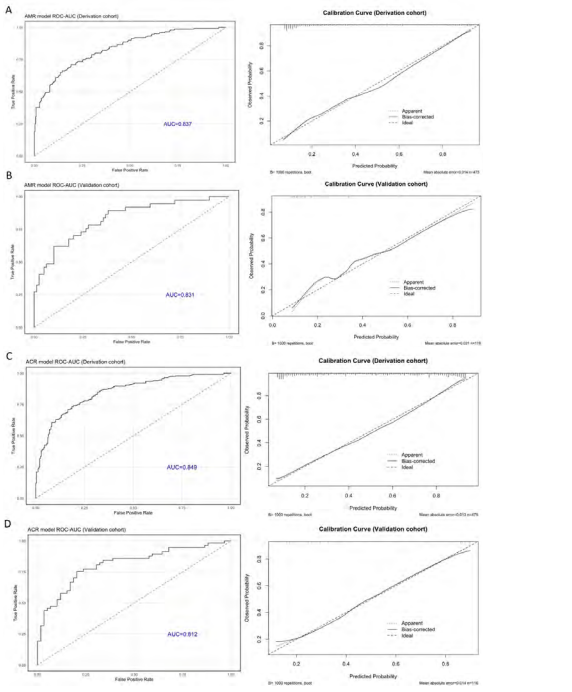
Background: Endomyocardial biopsies (EMB) gene expression profiling is a promising companion tool for rejection diagnosis. However, novel molecular diagnostic systems need to be properly tested and validated to support diagnosis post heart transplantation.

Methods: We performed a multicenter, retrospective study (NCT06436027), collecting 591 FFPE-EMBs between 2011 and 2021 representative of the landscape of rejection (antibody-mediated rejection-AMR, n=188; acute cellular rejection-ACR, n=289; non-rejection, n=114). Tissue gene expression was analyzed using the consensus Banff Human Organ Transplant gene panel. Molecular classifiers for AMR and ACR were built using a supervised model, assessing thoroughly the performance. Models' calibration was optimized, and discrepancies were analyzed in derivation and validation set.

Results: In the validation cohort (n=116), the molecular classifiers demonstrated strong diagnostic performance: AMR detection achieved an accuracy of 81.89% (ROC-AUC=0.831, Brier score=0.143, F1 score=0.70), while ACR detection achieved 77.58% accuracy (ROC-AUC=0.812, Brier score=0.176, F1 score=0.76). Models' stabilization was reached around 400 samples, confirming sufficient statistical power for reliable predictions. Calibration curves resulted adequate for AMR and ACR models sets, reflecting the reliability of the probabilistic predictions (**Figure**). In the derivation cohort, the predicted probabilities closely followed the ideal trend for both rejection-specifics models, indicating minimal bias. In the validation cohort, the mean absolute error was 0.031 for the AMR model and 0.014 for the ACR model respectively, suggesting excellent calibration. Minor deviations from the ideal line were observed at sub-clinical probability levels. Overall, the calibration curves support the reliability of the models for predicting rejection events in both cohorts.

Conclusions: The molecular diagnostic system demonstrated robustness and reliability in identifying cardiac rejection events. This system can complement standard pathology, reduce diagnostic uncertainty, and serve as a practical companion tool in the clinical management of heart transplant patients.



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Transplant immunology & immunosuppression

PP_431 IMMUNOGENICITY OF MISMATCHED HLA EPITOPES INFORMS RISK OF DONOR SPECIFIC ANTIBODIES IN ADDITION TO EPITOPE MISMATCH LOAD

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Background: Data has shown the added value of determining HLA mismatch at the epitope level (EpMM) to inform risk of alloimmune injury in organ transplant recipients. Only a few studies have investigated the clinical relevance of immunogenic epitopes. The aim of this study is to investigate whether the presence of an immunogenic mismatched epitope (iEpMM) helps predict outcomes independently from EpMM load.

Methods: 466 low immunological risk kidney transplant recipients receiving a steroid sparing immunosuppression protocol were investigated. All donors and recipients were HLA typed by high-resolution NGS using GenDx MX6-1 HLA kits. HLA-Matchmaker algorithm was used for epitope analysis. Protocolised testing for DSA was undertaken at 3 and 12 months, and at times of graft dysfunction using LABScreen SAB. Immunogenicity was determined by analysis of DSA using the HLA-Matchmaker antibody analysis program, and calculating high reaction frequencies to mismatched epitopes (>5%).

Results: 64 (13.7%) patients developed DSA, with a DSA free survival at 3 and 12 months of 89.0% and 86.6% respectively. The mean HLA EpMM was 19.9±7.4, and HLA EpMM was independently associated with DSA development, HR:1.08 (1.04-11.1), p<0.0001. Nine high frequency epitopes were identified, with 58 (87.5%) of DSA occurring in patients with an iEpMM. Only 131 (28.1%) patients had no iEPMM. There was a predictable correlation between the EpMM and iEpMM, the median EpMM in patients with and without an iEpMM was 21 (16-25) and 14 (10-18) respectively, p<0.001. DSA were significantly more likely to occur in high EpMM patients with an iEpMM, p<0.001 (**Figure 1**). Patients with an iEpMM were also more likely to experience rejection, HighEpMM+iEpMM (p=0.028) and LowEpMM+iEpMM (p=0.04), whilst HighEpMM-iEpMM were not (p=0.53).

Conclusions: Whilst HLA EpMM load may predict risk of DSA, consideration of immunogenicity enables further stratification of the risk. Preferential avoidance of mismatched iEpMM may help improve outcomes.

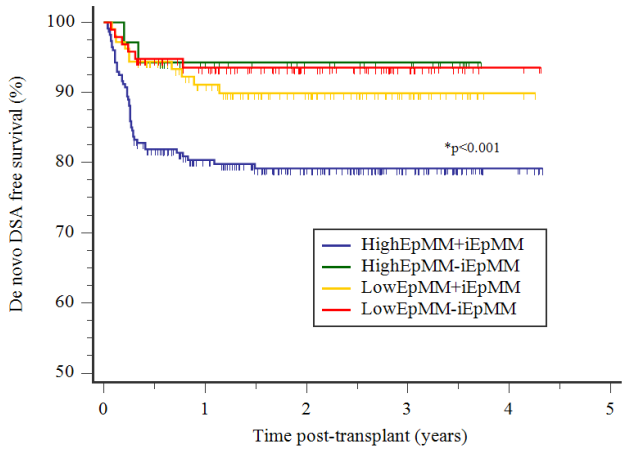

Figure 1. De novo DSA free survival by molecular mismatch load and immunogenicity

PP_432 PREFORMED DONOR-SPECIFIC ANTIBODIES AND THEIR ROLE IN KIDNEY TRANSPLANTATION: INSIGHTS FROM A SINGLE-CENTER STUDY

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Background: The impact of preformed HLA donor-specific antibodies (preDSAs), detected using sensitive solid-phase assays in deceased-donor (DD) kidney transplantation (KT) remains unclear. This study aimed to evaluate the short- and long-term posttransplant outcomes in patients with preDSAs.

Methods: A retrospective, matched 1:1, cohort analysis of 142 DD recipients, between 2011 and 2023 was conducted. In total, 71 patients (median age: 52 years, 55% females) with preDSAs at the time of KT, were matched for demographics, cold ischemia time (CIT) and time on dialysis with 71 patients without preDSAs (controls). The blood samples were analyzed for IgG DSAs using a SAB assay (One Lambda). Mean Fluorescence Intensity (MFI) values >1000 were considered positive for DSAs. All patients were transplanted with negative CDC and T/B Flow Crossmatch (FCM). The median follow-up period was 60 [IQR: 86] months.

Results: Detected HLA-DSAs were class I, with a median MFI of 1855 (IQR: 1209) in 38 patients (52%), class II, with a median MFI of 2651 (IQR: 2566) in 32 patients (44%), while 1 patient had class I & II. Twenty-three (32%) patients with preDSAs had cPRA>85%. There were no significant differences in immunosuppression regimens between the two groups, whereas 35/71 patients with preDSAs received Rituximab. Patients with preDSAs had increased risk of DGF (OR: 3.1, p=0.001), regardless of donor, recipient characteristics, and CIT. Biopsy-proven acute rejection (BPAR) was more common in patients with preDSAs (18% vs 11%, p=0.2), mainly acute cellular rejection (ACR) (54%), while 23% had antibody-mediated rejection (AMR) and 23% mixed ACR/AMR. Only those with MFI>3000 had a significantly increased probability for BPAR (OR: 6.4, p=0.006). Although *de novo* DSAs increased the risk of BPAR (OR: 2.8, p=0.09), there was no significant difference in *de novo* DSAs development between the groups (8.3% vs 5.5%, p=0.74). The eGFR was comparable in both groups in months 1, 6, 12, and at the end of follow-up (p>0.05). Death-censored graft survival rates and patient survival rates were not significantly different between the groups.

Conclusions: KT recipients with circulating preDSAs exhibit an elevated risk of adverse outcomes (DGF, BPAR) in the early posttransplant period; however, this does not appear to affect the long-term outcomes.

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Transplant immunology & immunosuppression

PP_433

MOLECULAR DIAGNOSTIC CLASSIFICATION FOR HEART ALLOGRAFT REJECTION: A VALIDATED AND AUTOMATED SYSTEM

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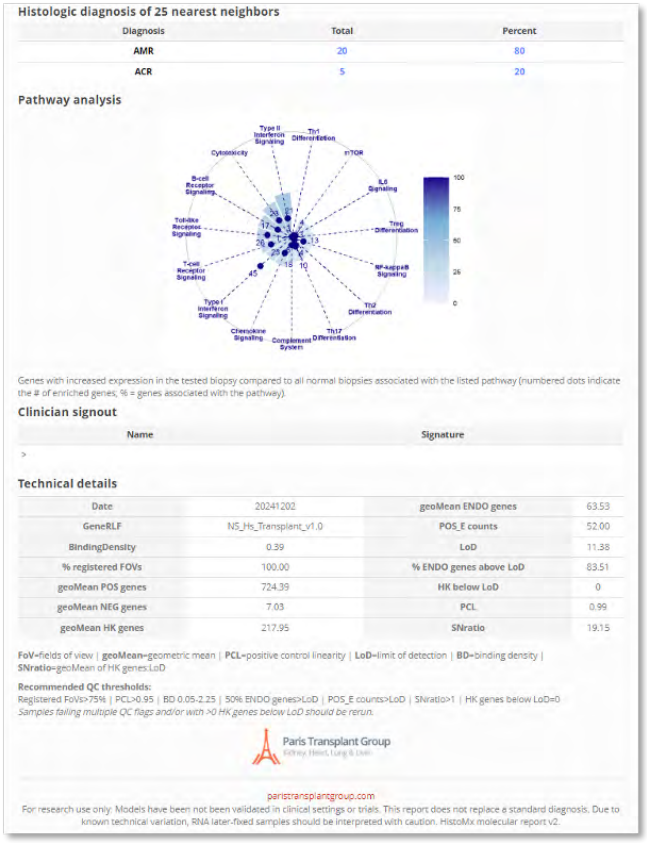
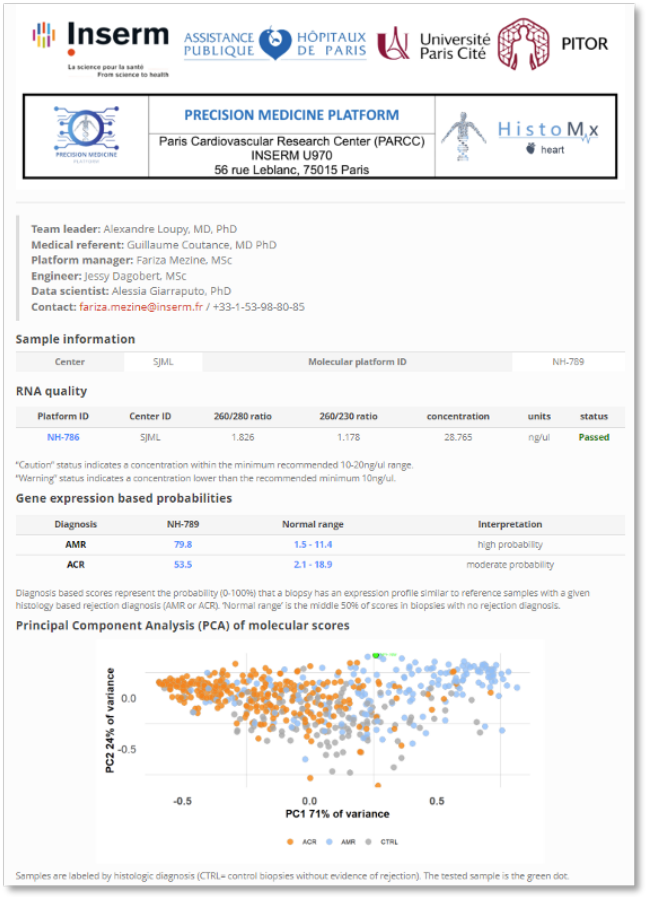
Background: Endomyocardial biopsies (EMB) gene expression profiling is a promising companion tool for rejection diagnosis. However, novel molecular diagnostic systems need to be validated and designed accessible for routine application in clinical practice to support diagnosis post heart transplantation.

Methods: We performed a multicenter, retrospective study (NCT06436027), collecting 591 FFPE-EMBs between 2011 and 2021 representative of the landscape of rejection (antibody-mediated rejection-AMR, n=188; acute cellular rejection-ACR, n=289; non-rejection, n=114). Tissue gene expression was analyzed using the Banff Human Organ Transplant gene panel. Molecular classifiers for AMR and ACR were built using a supervised model, assessing thoroughly the performance. An automated molecular report was developed to provide a comprehensive visualization for clinical use.

Results: In the validation cohort (n=116), the molecular classifiers demonstrated strong diagnostic performance: AMR detection achieved an accuracy of 81.89% (ROC-AUC=0.831, Brier score=0.143), while ACR detection achieved 77.58% accuracy (ROC-AUC=0.812, Brier score=0.176). The molecular report provided real-time assessment of molecular-based rejection scores, while allowing to contextualize a novel biopsy within the reference set rejection landscape. In addition to delivering quantitative scores for AMR and ACR, clinical and biological information are recapitulated in each report, correlating the molecular findings with the pathophysiological insights from primary molecular pathways involved. This tool captured subtle molecular signals in cases of early or sub-clinical rejection, offering insights into potential risks even when histology was inconclusive. The automated nature of the report minimizes variability and considerably reduces turnaround time, seamlessly integrating into clinical workflows.

Conclusions: The molecular diagnostic system, validated and supported by an automated report, demonstrated high reproducibility and reliability in identifying cardiac rejection. This system can complement standard pathology, reduce diagnostic uncertainty, and serve as a practical companion tool in the clinical management of heart transplant patients, ensuring timely and accurate diagnosis.





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Transplant immunology & immunosuppression

PP_434 CRYOPRESERVED T REGULATORY CELLS MAINTAIN FUNCTIONALITY AND RED BLOOD CELL LYSIS ENHANCES MEMORY T CELL FUNCTION

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Background: T regulatory cells (Tregs) separated from peripheral blood mononuclear cells (PBMCs) can be used for the adaptive transfer to solid organ transplant recipients to induce donor-specific tolerance. Such cell therapies have shown promising results in reducing immunosuppression after organ transplantation. These cells can be used immediately after preparation or cryopreserved for later use, the latter making tolerance studies more feasible. The effect of cryopreservation on the immunomodulatory function is still unclear. This study investigated the effect of cryopreservation on the immunomodulatory functions of PBMCs with or without pretreatment with the red blood cell (RBC) lysing buffer ammonium-chloride-potassium (ACK).

Methods: PBMCs from buffy coats from healthy human blood donors were treated with/without ACK, and a part of these cells were cryopreserved with 10% DMSO. Cell samples were examined for phenotype, functionality, and relative gene expression by flow cytometry, ELISpot, and qPCR respectively. The immunosuppressive effects of Tregs were assessed by % inhibition of proliferation with anti-CD3/CD28 antibody-activated PBMCs.

Results: ACK-treated PBMCs exhibited higher numbers of IFN-γ producing cells both spontaneously and in stimulation with viral peptides than non-treated PBMC. Cryopreservation reduced contamination of RBCs and granulocytes and led to a lower cell yield and viability. Cryopreserved PBMCs maintained the Treg population and its ability to suppress responder cell proliferation. The relative gene expression of IL-1β increased, but FoxP3 decreased after cryopreservation. IFN-γ ELISpot assays indicated that memory $CD8^+$ T cell activities against virus peptides increased after cryopreservation.

Conclusions: Memory T cell responses improved after RBC lysate. Cryopreservation improves PBMC purity but reduces cell yield and viability. T regulatory cells maintained suppressive capacity after cryopreservation. Thus, cryopreservation may be suggested as an option in tolerance induction studies as it can simplify logistics.

PP_435 TORQUE TENO VIRUS RELATES TO REJECTION AND INFECTION AFTER LUNG TRANSPLANTATION, BUT NOT WITH EXPOSURE TO IMMUNOSUPPRESSIVE DRUGS

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Background: Lung transplant (LTx) recipients are at high risk of both infection and rejection. Measurement of Torque Teno virus (TTV) load has been developed as a method to monitor the net immunosuppression status of solid organ transplant recipients. Hence, TTV monitoring has been proposed as a method to guide immunosuppressive therapy. However, the relationship between TTV viral load and exposure to immunosuppressive drugs in LTx has not been extensively studied.

Methods: We performed a prospective study including all LTx recipients carried out in our center from January 2021 to April 2023 who were willing to participate. Blood TTV load was measured by an in-house PCR at the time of entry onto the waiting list and at the first- and third-months post-transplant. We calculated the tacrolimus (Tac) coefficient of variability (CV), time in therapeutic range (TTR), concentration/dose ratio (C/D) and area under the curve of the trough concentrations of Tac (AUC-Tac) up to months 1 and 3, and the MPA-area under the curve (AUC-MPA) at the third month.

Results: 53 LTx recipients were included. Mean TTV load values increased from pretransplant levels (1.5 ± 0.2 log10 copies/mL) to month 1 (2.7 ± 0.4 log10 copies/mL, $p < 0.001$) and decreased to month 3 (2.3 ± 0.3 log10 copies/mL, $p < 0.001$). 18 patients with early acute rejection exhibited lower levels of TTV load at month 1 (8.5 ± 2.8 vs. 6.9 ± 2.1 log10 copies/mL, $p = 0.035$) and 3 (10.5 ± 1.9 vs. 8.8 ± 2.6 log10 copies/mL, $p = 0.007$). Patients with a TTV load in the fourth quartile at month 1 exhibited a reduced rate of acute rejection (43% vs. 8%, $p = 0.021$) and a higher rate of opportunistic infections (3% vs. 23%, $p = 0.015$) from month 3 to 6. TTV viral load at months 1 and 3 did not correlate with Tac-blood levels, CV, TTR, C/D, AUC-Tac and AUC-MPA.

Conclusions: We found a relationship between blood TTV load and the risk of infection and rejection in our population of LTx recipients. This suggests that TTV can be a useful tool for monitoring the immunosuppression status of LTx recipients. However, our findings did not reveal a relationship between TTV load and exposure to maintenance immunosuppressive drugs. Before considering the use of TTV load monitoring for lung transplant patients, it would be important to analyse the impact of variables not related to immunosuppressive therapy on TTV burden.

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PP_436 SEX DIFFERENCE FOR ABMR RISK AND GRAFT FAILURE IN HIGHLY SENSITIZED KIDNEY RECIPIENTS

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Background: Highly sensitized (HS) kidney transplant recipients (KTR) have an increased risk for antibody-mediated rejection (ABMR), particularly in those with preformed donor-specific antibodies (DSAs). ABMR is a major cause of graft failure. Sex-based differences in immune responses are well-documented. Sexual hormones also play a significant role in immune responses. The aim of this study was to analyze sex-based differences for risk factors of ABMR during the first year posttransplant, and graft failure in a cohort of HS KTR.

Methods: We conducted a retrospective multicenter study including highly sensitized KTR (calculated panel reactive antibody [cPRA] ≥90%) who received a kidney transplant in any of the six transplant centers from Catalonia, Spain, between July 2015 and December 2021. Patients with primary graft failure (<48h) were excluded from the analysis.

Results: A total of 438 patients were included for analysis. Pre-formed DSAs were present in 26.5% (n=116). Estimated death-censured graft survival at 1 year and 5 years was of 96.9 and 81.6%, respectively. Seventy-five patients (17.1%) presented an acute rejection during the first year post-transplant (68% ABMR). In a multivariate analysis, men (HR=9.9, p=0.03), preformed DSA mean fluorescence intensity (MFI) (HR=4.3, p=0.006), and verified HLA-DQB eplet mismatches (OR= 5.2, p=0.003) were associated with an increased risk for ABMR during the first year. The causes of graft failure showed a significant difference between sexes. Immunological causes predominated in both sexes, but were more frequent in men while infections were notably more prevalent in women. A sex-stratified analysis showed a six-fold higher ABMR risk for men with a preformed DSA, regardless of number of transplants (1st vs any retransplant), or age (<50yo vs ≥50yo). Among women, the risk fro ABMR was found to be increased in they under <50 yo (when compared to older women ≥50yo), particularly when there is a verified HLA-DQB1 eplet mismatch >2.

Conclusions: Herein we highlight sex-specific differences in the risk for ABMR in a large cohort of highly sensitized kidney transplant recipients. The increased risk for ABMR observed in men advocates for the need of further investigation on the impact of testosterone in immune response post-transplant.

PP_437 IMPACT OF AUTOLOGOUS TOLEROGENIC DENDRITIC CELLS ON FULL MISMATCH KIDNEY TRANSPLANTATION RAT MODEL

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Background: Highly sensitized kidney transplant recipients' present an increased risk for acute rejection. Tolerogenic dendritic Cells (TolDCs) skew immune responses towards a regulatory. We conducted a preclinical study to explore the ability of autologous TolDCs to improve graft outcomes in a rat model of kidney transplantation.

Methods: Tolerogenic profile of bone marrow-derived dendritic cells (BM-DCs) was induced *in vitro* with dexamethasone. TolDCs phenotype was characterized by flow cytometry and cytokine secretion by ELISA. Autologous (Lewis) TolDCs were then administered at day of kidney transplantation in a rat model of full mismatch kidney transplant (Dark-Agouti–Lewis) treated transiently with tacrolimus (D0-D+4). Recipient rats were sacrificed at day +7 (D7) to evaluate immunomodulatory properties of TolDCs when compared to untreated rats or rats treated with mature dendritic cells (mDCs).

Results: *In vitro* generated autologous TolDCs present significantly lower expression of cell surface markers CD86, CD83, and MHC II when compared to mature DCs (mDCs). These cells were less prone towards a maturation differentiation and produce lower levels of inflammatory cytokines. In a rat model of full mismatch kidney transplant we observed that rats treated with TolDCs presented an improved renal function at D7 post-transplant, when compared to untreated or mDCs treated rats.

Conclusions: Data demonstrate for the first time, in a rat model of kidney transplant, the feasibility for the use of autologous TolDCs in deceased donor kidney transplantation. Furthermore, it postulates a potential benefit in the improvement of renal function in this full mismatch kidney transplant model.

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Transplant immunology & immunosuppression

PP_438 LYMPHOCYTE POPULATION DIFFERENCES BETWEEN TRIPLE IMMUNOSUPPRESSION AND EVEROLIMUS/ TACROLIMUS REGIMENS

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Background: triple immunosuppression with tacrolimus, mycophenolate, and corticosteroids strongly suppresses B cells, monocytes, and vaccine responses, effectively reducing the risk of antibody-mediated rejection (AMR). In contrast, everolimus/tacrolimus regimens allow for residual B cell and monocyte activity, enhancing vaccine responses and increasing the risk of donor-specific antibody (DSA) formation. This study is a post-hoc analysis of B and T lymphocyte subpopulations based on immunosuppression and time post-transplant in SARS-CoV-2 vaccinated patients (doi.org/10.3389/fimmu.2023.1202630)

Methods: This multicenter prospective study assessed immune responses in kidney transplant recipients (KTRs). Peripheral blood samples were obtained 30 days after administering SARS-CoV-2 vaccine boosters. Lymphocyte subsets were analyzed using the EuroFlow PID Orientation Tube (PIDOT) and automated analysis. Patients were stratified into two groups based on their immunosuppressive regimen: triple immunosuppression (tacrolimus, mycophenolate, corticosteroids) or everolimus/tacrolimus (everolimus, tacrolimus, with or without prednisone).

Results: Out of 110 patients initially enrolled, 13 were excluded due to receiving alternative immunosuppressive regimens. Table 1 shows the absolute count of lymphocyte subpopulations according to the type of immunosuppression. The percentages of CD4 T cells, effector memory CD4 T cells, neutrophils, and monocytes differed between the two groups. The number of monocytes after the first-year post-transplant and in subsequent years is lower in the triple immunosuppression group compared to the tacrolimus/everolimus group, as shown in Figure 1.

Conclusions: Monocyte levels were significantly higher in the everolimus/ tacrolimus group across all post-transplant times. Subtle, non-significant increases were observed in switched memory B cells, CD4+ T cells, effector memory CD4+ T cells, and NK cells, suggesting immunological distinctions between the regimens. Further studies are needed to evaluate the clinical implications of these differences.

Subpopulation	Triple IS	Eve/Tac	p-value
n	57	17	
B cells, cell/ul, median (IQR)	67 (9-123)	70 (34-108)	0.587
Unswitched MBC, cell/ul, median (IQR)	10 (5-16)	9 (5-15)	0.792
Switched MBC, cell/ul, median (IQR)	13 (8-29)	24 (14-23)	0.118
CD4 T cells, cell/ul, median (IQR)	516 (321-798)	729 (559-963)	0.065
Naïve CD4 T cells, cell/ul, median (IQR)	98 (38-190)	154 (100-271)	0.112
CM/TM CD4 T cells, cell/ul, median (IQR)	255 (176-380)	340(301-403)	0.131
Effector memory CD4 T cells, cell/ul, median (IQR)	19 (6-46)	31 (20-89)	0.060
CD8 T cells, cell/ul, median (IQR)	529 (321-861)	672 (464-787)	0.201
Naïve CD8 T cells, cell/ul, median (IQR)	37 (23-97)	70 (29-156)	0.235
Effector memory CD8 T cells, cell/ul, median (IQR)	41 (19-75)	67 (34-119=	0.422
Double negatve T cells, cell/ul, median (IQR)	73 (43-127)	86 (63-201)	0.225
NK cells, cell/ul, median (IQR)	29 (12-56)	42 (22-100)	0.128
Monocytes, cell/ul, median (IQR)	583 (409-698)	775 (580-946)	0.009
Plasmocytoid DC, cell/ul, median (IQR)	9 (6-14)	6 (3-13)	0.077
Neutrophils, cell/ul, median (IQR)	4944 (4004-5996)	3771 (3306-5621)	0.220

Table 1. Lymphocyte subpopulations according to immunosuppression. GC : germinal center, MBC : memory B cells, CM: central memory, TC: transitional memory, TD: terminally differentiated, DC: dendritic cell.

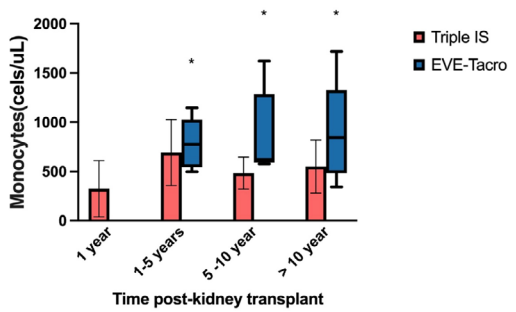

Figure 1. Monocyte Count Over Time Post-Transplant in Triple Immunosuppression vs Tacrolimus/Everolimus Group. Triple IS: triple immunosuppression. Eve-Tacro: everolimus/ tacrolimus regimen.

PP_439 M1 MACROPHAGE-DERIVED EXOSOME MEDIATES ENDOTHELIAL INJURY IN ABMR AFTER KIDNEY TRAMNSPLANTATION

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Background: M1 polarized macrophage, which is recruited in ABMR after kidney transplantation, has recently been shown to participate in the immune response of acute kidney allograft rejection. Exosomes are important intermediates of intercellular communication through their nucleic acid components, which are widely studied.

Methods: In this study, we extracted bone marrow-derived macrophages (BMDMs) from mice and induced M1 polarization in vitro for high-throughput sequencing and exosome proteomics analysis to identify differentially expressed proteins. A macrophage and endothelial cell co-culture model was established in vitro, and endothelial cell inflammation markers were detected. Transcriptomic and proteomic sequencing were performed to identify potential inflammatory pathways in endothelial cells. In a conditional knockout mouse model of acute rejection following kidney transplantation, vascular injury levels were assessed by immunohistochemistry, and Syk expression in vascular endothelial cells and macrophages was analyzed.

Results: In the macrophage-endothelial cell co-culture model in vitro, M1-polarized macrophages increase the expression of inflammatory injury-associated protein in endothelial cells, which can be reduced by pretreatment of M1-polarized macrophages with exosome inhibitors. By intervening Syk knockout endothelial cells with M1-polarized macrophage exosomes, we found that exosome-derived Syk was associated with elevated inflammatory injury markers in endothelial cells by binding to NLRP3 inflammsomes. In vivo adoptive transfer experiments demonstrated that M1 exosomes exacerbated endothelial inflammatory injury in transplanted kidneys. Immunofluorescence confirmed high expression of Syk, accompanied by activation of the NLRP3 pathway. In contrast, endothelial damage caused by exosomes from Syk-knockdown M1 macrophages was relatively reduced.

Conclusions: Syk, which can be detected in M1 polarized macrophage-derived exosomes, mediates vascular endothelial injury in ABMR after kidney transplantation via NLRP3 pathway. Further research may provide a potentially prognostic biomarker and therapeutic target for kidney transplantation.

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PP_440 IMPACT OF EARLY VERSUS DELAYED TACROLIMUS INITIATION ON CLINICAL OUTCOMES IN KIDNEY TRANSPLANTATION WITH THYMOGLOBULIN

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Background: In kidney transplant recipients (KTRs), thymoglobulin has been shown to be beneficial by delaying the exposure to tacrolimus with nephrotoxicity in patients with delayed recovery of allograft function after kidney transplantation (KT). However, delaying tacrolimus may negatively affect transplant outcomes. This study aims to evaluate the impact of early versus delayed tacrolimus initiation on clinical outcomes in KT with thymoglobulin.

Methods: We analyzed 155 KTRs who received thymoglobulin among 395 KTRs from 2013 to 2020. We divided them into two groups: early tacrolimus initiation (n=50) and delayed tacrolimus initiation (n=105) based on the impact of tacrolimus timing on these outcomes. We investigated allograft function after KT, the rate of slow or delayed recovery of graft function (SGF or DGF) after KT, acute rejection within 1 year after KT, infection, death-censored graft survival, and patient survival.

Results: The baseline characteristics were not different between the groups. There were no significant differences between the groups in the number of HLA mismatches, the proportion of patients with panel reactive antibody > 50%, or the presence of preformed donor-specific antibody (DSA). The delayed initiation group had a higher incidence of SGF and DGF compared to the early initiation group. Allograft function was significantly better in the early initiation group than in the delayed group at the early post-transplant period, but this difference disappeared in the later post-transplant period. Delayed initiation group showed a higher frequency of acute rejection within 1 year after KT, and the development of de novo DSA, and lower death-censored graft survival rate compared to the delayed initiation group. There were no significant differences in the development of infection like cytomegalovirus or BK virus, and patient survival rate between them.

Conclusions: Delayed tacrolimus initiation in KTRs treated with thymoglobulin resulted in better allograft function during the only early post-transplant period compared to early initiation. However, delayed tacrolimus initiation was associated with higher rates of acute rejection and reduced graft survival. Therefore, early use of tacrolimus in KTRs with thymoglobulin may have a positive effect on the clinical outcomes of KTRs.

PP_441 BEYOND STABLE RENAL FUNCTION: UNVEILING SUBCLINICAL ISSUES IN KIDNEY TRANSPLANT RECIPIENTS AT 12 MONTHS

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Background: The first year after kidney transplantation (KT) is crucial for achieving a favorable long-term prognosis. Maintaining a stable balance of immunosuppression during this period significantly influences the sustained function of the transplanted kidney. However, relying solely on parameters such as creatinine, eGFR, tacrolimus trough levels, and viral markers may not sufficiently detect subtle changes in kidney status. Although transplant kidney biopsies are performed, their effectiveness remains controversial.

Methods: We investigated the association between transplant outcomes and the pathological changes of a 12-month protocol biopsy in kidney transplant recipients (KTRs) with stable allograft function between 2017 and 2023.

Results: A 12-month protocol biopsy was performed in 86 KTRs (48 from living and 38 from deceased donors). The causes of end-stage renal disease were glomerulonephritis (45), hypertension (7), diabetes (23), polycystic kidney disease (5), and unknown (6). Among them, 43 (50.0%) were considered as nonspecific change, 6 (7.0%), borderline, 4 (4.7%), acute T-cell mediated rejection (TCMR), 3 (3.5%), chronic active TCMR, 10 (11.6%), acute antibody-mediated rejection (ABMR), 1 (1.2%), chronic active ABMR, 4 (4.7%), de novo glomerulopathy/recurrence of primary disease, 4 (4.7%) calcineurin inhibitor toxicity, 10 (11.6%), interstitial fibrosis and tubular atrophy, and, 1 (1.2%), BK virus nephropathy. There was no significant difference of baseline characteristics according to the biopsy findings. There was also no significant association between the occurrence of donor specific antibody (DSA) and subclinical ABMR. The mean eGFR at the time of the biopsy was 79.3 ± 25.2 mL/min/1.73 m^2, which meant that the most of the findings were subclinical.

Conclusions: In this study, the 12-month protocol biopsy revealed a range of pathological findings despite stable kidney function. Notably, subclinical rejection was observed in 21% of cases, while chronic allograft nephropathy was identified in 11.6% of patients 12-months post-transplantation. These findings highlight the importance of careful monitoring, even when kidney function appears stable, to account for potential pathological changes.

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PP_442 DIFFERENCES IN INTESTINAL FLORA BETWEEN MICE WITH ABMR AFTER RENAL TRANSPLANT USING 16S RNA SEQUENCING

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Background: To explore differences in intestinal flora between mice with antibody-mediated rejection after renal transplantation and syngeneic mice.

Methods: 5 male 6-8 weeks old BALB/c^{H2d} and 5 male 6-8 weeks old C57BL/6^{H2b} mice were used as experimental mice and randomly divided into following two groups: 1. Syngeneic control group (SYN): only C57BL/6^{H2b} to C57BL/6^{H2b} kidney transplantation was conducted, the transplanted kidney was removed 5 days later; 2. Antibody-mediated rejection group (ABMR): full-thickness back skin transplantation was performed on C57BL/6 mice for 5 days(BALB/C^{H2d}→C-57BL/6^{H2b}), followed by BALB/c^{H2d} to C57BL/6^{H2b} kidney transplantation, the transplanted kidney was removed 5 days later. Faecal samples were collected from two groups of mice and 16S rRNA gene sequencing was performed to analyse diversity and differences in the distribution of the flora.

Results: ANCOM analyses showed that abundance of *Desulfovibrionaceae*, *[Clostridium]_methylpentosum_group* differed significantly between SYN and ABMR. Kruskal Wallis analyses showed that abundance of *Clostridia_UCG_014*, *Akkermansia*, *Eubacterium_siraeum_group* and *Candidatus_Saccharimonas* were significantly less abundant in ABMR group compared to SYN group (P<0.05). LEfSe analyses showed that *Helicobacter* and *Parabacteroides* were biomarkers in ABMR group, with higher abundance in ABMR group, *Eubacterium_siraeum_group*, *Clostridia_UCG_014* and *Candidatus_Saccharimonas* were biomarkers in SYN group, with higher abundance in SYN group. Phylogenetic analyses showed that groups that differed between ABMR and SYN groups included *[Clostridium]_methylpentosum_group*, *Desulfovibrio*, *Parabacteroides and Mucispirillum*, which were significantly elevated in ABMR group, *Muribaculum*, *Muribaculaceae*, *Candidatus_Saccharimonas*, *Lachnospirales*, *Oscillospirales* and *Parvibacter*, which were significantly elevated in SYN group.

Conclusions: Differences in intestinal flora between mice with antibody-mediated rejection after renal transplantation and syngeneic mice exist and improvements of intestinal flora may be helpful in treating antibody-mediated rejection after renal transplantation.

PP_443 NEUTROPHILS IN THE IMMUNE MICROENVIROMENT OF TRANSPLANTED KIDNEY INDUCE METABOLIC REPROGRAMMING VIA OSM-LIFR

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Background: Chronic allograft dysfunction (CAD) induced by kidney interstitial fibrosis is the main cause of allograft failure in kidney transplantation. However, the mechanisms of interstitial fibrosis in transplanted kidneys remain unclear. In this study, we aim to identify and validate novel mechanisms leading to interstitial fibrosis in kidney allograft based on single-cell sequencing results from a mouse model of CAD.

Methods: We constructed a mouse model of CAD at 16 weeks and utilized single-cell sequencing to analyze transcriptomic changes in various cell types within the CAD grafts compared to syngenetic grafts. Immunohistochemistry and Western blotting were utilized to validate sequencing results in both mouse and human tissues. Cytokine levels were assessed in mouse and human peripheral blood using a cytokine array. In vitro co-culture of human neutrophils and renal tubular epithelial cells utilized to further explore relevant mechanisms. Additionally the conditional gene knockout mice were used to validate the relevant molecular mechanisms in vivo experiments.

Results: The results of pseudo-time analysis suggest that the trans-differentiation of renal tubular epithelial cells is the primary cause of interstitial fibrosis in transplanted kidneys. Cellular communication analysis indicates the significant role of interactions between neutrophils and renal tubular epithelial cells in the immune cells. Neutrophils within the immune microenvironment of allograft induced metabolic reprogramming of ATP, ribose phosphate and purine ribonucleotide metabolic in renal tubular epithelial cells through OSM-LIFR, promoting the trans-differentiation. However, in peripheral blood, there were no significant differences observed in the quantity of neutrophils or the secretion levels of OSM.

Conclusions: Neutrophils in the immune microenvironment of kidney allograft induced the metabolic reprogramming of renal tubular epithelial cells via OSM/LIFR and promoting interstitial fibrosis in CAD.

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PP_444 EXPLORING THE IMMUNE LANDSCAPE OF SUBCLINICAL BORDERLINE CHANGES IN KIDNEY TRANSPLANT RECIPIENTS AT A SINGLE-CELL LEVEL

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Background: Kidney transplantation (KT) significantly improves survival and quality of life in patients with end-stage renal disease (ESRD). However, the clinical implications and optimal management of subclinical borderline changes (SBCs) detected in protocol biopsies remain unclear. This study investigates the immunological characteristics of SBCs to develop strategies for improving KT outcomes

Methods: Eleven kidney transplant recipients under 60 years old were analyzed, comprising six patients without acute rejection (No Rej) and five patients with SBCs. Single-cell RNA sequencing (scRNA-seq) was performed on peripheral blood mononuclear cells (PBMCs) obtained from 1-year protocol biopsies to delineate immune profiles

Results: Whole cluster analysis revealed a significant increase in T cells, particularly naïve T cells, in the SBCs group. While the proportions of proliferating T cells and $CDKN1A^{+}CD4^{+}$ T_{EM} cells decreased, $GZMH^{+}CD8^{+}$ T_{EM} cells markedly elevated. Additionally, regulatory T cells (Tregs) in the SBCs group showed reduced activation and decreased FOXP3 expression.

Conclusions: SBCs are characterized by enhanced cytotoxic T cell activity and impaired Treg functionality, indicating an increased risk of acute rejection. These findings emphasize the importance of precise immune monitoring and timely intervention to enhance long-term transplant outcomes.

PP_445 A SINGLE-CENTER EXPERIENCE WITH DONOR-DERIVED CELL-FREE DNA IN KIDNEY TRANSPLANT RECIPIENT ON REDUCED IMMUNOSUPPRESSION

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Background: This study evaluated the utility of serial dd-cfDNA testing for early rejection detection in high-risk renal transplant recipients on reduced immunosuppressive therapy due to infections or medication-related side effects.

Methods: This single-center, prospective, nonrandomized study included deceased donor kidney transplant recipients from 2020–2022, with final follow-up in July 2023. Inclusion criteria: reduced immunosuppression >1 month, >1 month post-transplant, and <2 years post-transplant. The primary objective was to assess dd-cfDNA's role in predicting rejection; the secondary objective evaluated its relationship with BK viremia (BKV). dd-cfDNA testing was performed, with follow-up at 4-week intervals if initial results were <1%. Levels >1% prompted biopsy and donor-specific antibody (DSA) testing. Protocol biopsies were performed at 4, 12, and 24 months.

Results: 64 subjects on reduced immunosuppression were enrolled. 53 subjects had an initial dd-cfDNA <1% and underwent 4-week testing intervals. Reduced immunosuppression was due to infections (e.g., CMV, BK, COVID-19, Nocardia) or side effects (e.g., gastrointestinal intolerance, leukopenia, malignancies). Mean time from transplantation to dd-cfDNA testing was 281 days (SD 171 days). Among the 53, 27 had reduced immunosuppression due to BKV. At 8 weeks, 2 patients developed dd-cfDNA >1%, confirmed by biopsy as acute rejection, both associated with BKV. dd-cfDNA performance for detecting rejection under reduced immunosuppression was 100%. One patient with dd-cfDNA, 1.36%, had glomerulitis (C4d-negative), and another with 6.56% had Banff grade 2A acute cellular rejection (DSA-negative). Sensitivity and NPV for detecting biopsy-proven rejection were 100%. Spearman correlation for dd-cfDNA and BKV was 0.65 (p=0.0001). In patients with detectable BKV, the PPV and NPV of dd-cfDNA for rejection were 44.4% and 81.5%, respectively. The test demonstrated high specificity and good NPV, particularly for ruling out rejection when dd-cfDNA was negative.

Conclusions: In renal transplant recipients on reduced immunosuppression, serial dd-cfDNA monitoring effectively detected acute rejection, offering clinical value in high-risk settings.

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PP_446 RETROSPECTIVE COMPARISON OF LOW DOSE ALEMTUZUMAB- BASED INDUCTION THERAPY WITH CONVENTIONAL INDUCTION THERAPY

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Background: Alemtuzumab (Az) is a lymphocyte-depleting induction agent. This study compared the renal transplantation (RT) outcomes of patients (Pts) who received low-dose Az with those who received conventional induction, anti-thymocyte globulin (ATG) or basiliximab (IL2R).

Methods: Between 2006 and 2014, pts who received 10mg of subcutaneous Az pre-transplant (Gp I) were compared with those who received ATG or IL2R as an induction agent (Gp II). The follow-up beyond 5 yrs post-transplant ending 2019. Patients with missing data or inadequate follow-up were excluded. Immediate transplant outcomes, infections, maintenance immunosuppressant doses, and metabolic and malignancy complications were compared. Statistical significance was analysed.

Results: Group I included 75 patients, and Group II included 102 patients (Table 1). There was no significant difference between the two groups in terms of acute rejection, death with a functioning graft, incidence of infection, malignancy, or post-transplant diabetes. Tacrolimus monotherapy was used in 29% of patients in Group I compared to none in Group II ($p<0.05$). Group II patients required triple-drug immunosuppression more frequently (92%, $p<0.05$) than Group I. The incidence of dyslipidemia, high blood pressure requiring more than two antihypertensive drugs, and graft failure beyond five years was significantly higher in Group II ($p<0.05$). The induction cost was less than 500 USD in Group I compared to more than 1000 USD in Group II.

Conclusions: Low-dose Az as an induction agent is cost-effective, offering similar or better graft survival with additional benefits regarding metabolic side effects and lower post-operative maintenance immunosuppressant doses.

Variable	Gp I	Gp II	P Value
Patient number	75	102	
M:F	50:25	75:27	
Acute Rejection	2	8	>0.05
Graft loss	2	4	1
Only Tac and steroid < 7.5mg	22	0	<0.05
Tac and MMF	40	8	<0.05
TAC MMF and Steroid	13	94	<0.05
Lymphocytopenia Beyond 3mo Post Tx	65	12	<0.05
Lymphocytopenia Beyond 1 yr post Tx	12	8	>0.05
Death with functioning graft till 2019	8	12	
Malignancy	6	4	
PTDM	6	18	
Dyslipidemia	12	56	<0.05
High BP requiring > 2 Anti HBP drugs	12	82	<0.05
Graft Failure > 5Yr	3	22	<0.05
Induction cost	<500 USd	>1000USd	

Table 1 Comparison between Low dose Az induction vs Conventional Induction

PP_448 IMPACT OF TACROLIMUS TROUGH LEVELS AT DISCHARGE ON KIDNEY TRANSPLANTATION OUTCOMES: A NATIONWIDE COHORT STUDY

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Background: Tacrolimus is a cornerstone of kidney transplantation (KT) immunosuppression but requires careful monitoring due to potential toxicity. This study investigates the impact of tacrolimus trough levels (C0) at discharge on early post-transplant outcomes, including rejection and infections, using data from the Korean Organ Transplant Registry (KOTRY).

Methods: The study population consists of 5,293 KT recipients from the KOTRY database, spanning from April 2014 to December 2019. Patients were divided into three groups based on discharge C0 levels, defined by population percentiles: below 5.9 ng/mL(below the 25th percentile), 5.9–9.5 ng/mL(between the 25th and 75th percentiles), and above 9.5 ng/mL(above the 75th percentile). Outcomes assessed included serum creatinine (sCr), biopsy-proven acute rejection (BPAR), and infection rates at 6 months and 1 year. Immunologic high-risk recipients were defined as recipients who had a positive crossmatch, a panel reactive antibody (PRA) of 10% or higher, or positive DSA. Statistical analyses were conducted to evaluate group differences.

Results: The sCr levels and BPAR rates at 6 month and 1 year were no significant differences between the groups. However, the incidence of infections requiring hospitalization was significantly higher in the higher C0 groups (28.1%, $P < 0.001$). In immunologic high-risk recipients, BPAR incidence was significantly higher in the lowest C0 group (33.9%) compared to the middle (29.1%) and highest groups (26.4%, $P = 0.030$). While sCr levels at discharge and 1 year were similar among high-risk groups, variability in tacrolimus levels correlated with increased BPAR incidence (HR = 1.110, 95% CI: 1.037–1.188, $P = 0.003$)

Conclusions: Optimal C0 levels at discharge are crucial for balancing the risks of rejection and infection in KT. Specifically, in immunologic high-risk recipients, lower C0 levels at discharge were associated with an increased risk of acute rejection, emphasizing the importance of meticulous early monitoring and individualized protocols. Further research is necessary to establish regional thresholds for tacrolimus levels.

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PP_449 IMPROVED HLA MATCHING THROUGH SELECT OF RED BLOOD UNITS; A REPORT FROM A NATIONAL PILOT PROGRAMME

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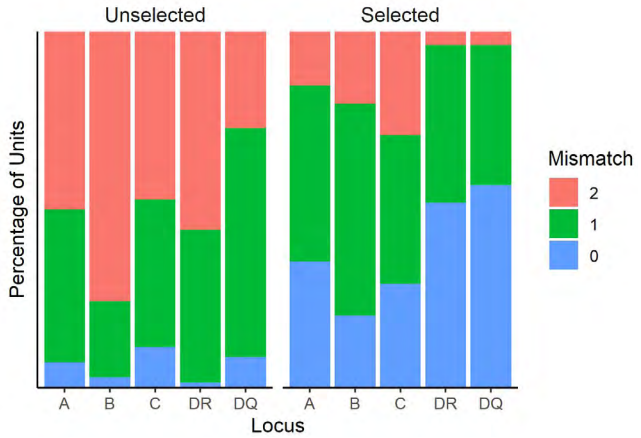
Background: Red blood cell (RBC) transfusion is an acknowledged alloimmune stimulus and transfusion avoidance is often practiced in kidney transplant candidates and patients. Where transfusion is unavoidable HLA selection of RBC units may mitigate the potential harm. The National Blood Transfusion service in the United Kingdom has undertaken a pilot programme to offer HLA selected blood units to kidney transplant candidates and recipients as a prelude to the roll out of a nationwide clinical service. Here we report on the HLA matching achieved compared with that of previously supplied random RBC units.

Methods: All clinical requests for HLA selected cells over the first 9 months of the pilot programme are included. Blood donors and recipients were typed for HLA-A, -B, -C, -DRB1 and -DQB1 using One Lambda AllType NGS and GenDx MX6-1 respectively. A historic group comprising unselected RBC units retrospectively typed were used as our controls. The split antigen level mismatch at each locus was compared, as well as the ABDR mismatch.

Results: Overall, 38 patients received 79 units of selected blood; the control group of 42 patients received 70 units of unselected blood. There were no significant differences in the age, gender or ethnicity of the two cohorts (see table). At all loci the number of antigen matched units was higher in the selected group (see figure). The median ABDR mismatch was 2 (IQR 2-3) in the selected group compared with 5 (IQR 4–5.75) in the unselected group.

Conclusions: In this study we have shown that improved HLA matching of RBC units can be achieved as an extension of current clinical practice. The influence of HLA selecting RBC units on de novo allosensitisation in this cohort is currently being investigated, with post-transfusion antibody results being analysed for reporting in the coming months. Improvements in HLA-matching are expected to reduce allosensitisation arising from blood transfusion and potentially reduce waiting time and improve organ longevity.

		Unselected (n=42)	Selected (n=38)	p
Age (mean (SD))		51.88 (14.62)	52.76 (14.80)	0.789
Gender (n(%))	Female	17 (40.5)	22 (57.9)	0.183
	Male	25 (59.5)	16 (42.1)	
Ethnicity (n(%))	Black	7 (16.7)	12 (31.6)	0.380
	Indo-Asian	16 (38.1)	12 (31.6)	
	Other	8 (19.0)	4 (10.5)	
	White	11 (26.2)	10 (26.3)	



PP_450 DONOR-SPECIFIC ANTIBODIES IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION: A MULTICENTER STUDY

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Background: Vascularized Composite Allotransplantation (VCA), including upper extremity transplantation (UET) and face transplantation, requires immunosuppression to prevent allosensitization and subsequent rejection. Donor-specific anti-HLA antibodies (DSA) are recognized contributors to vascular rejection and poorer graft outcomes in solid organ transplantation. This study evaluates the prevalence, characteristics, and clinical implications of DSA in VCA recipients.

Methods: Thirty-seven VCA recipients from six international centers were included. A total of 402 pre-transplant and follow-up sera were screened for DSA using a centralized Single Antigen Bead assay. Clinical and histological data, including rejection episodes and graft vasculopathy, were collected and analyzed.

Results: The 37 patients were grafted between 2000 and 2019: 23 upper extremity transplantations (UETs), 13 face transplantations and 1 patient with simultaneous UET and face transplantation. There were 29 men and 8 women with a median age at transplantation of 32.5 years. Thirty-one recipients were evaluable for DSA: 17 had no DSA, 2 had preformed DSA and unclassifiable de novo anti-HLA antibodies, 3 had preformed DSA only, 8 had de novo DSA, 1 had both preformed and de novo DSA. The incidence of de novo DSA did not significantly differ between UET and face recipients, with an average onset of 9 months post-transplantation. Pretransplant DSA primarily targeted class I HLA, whereas de novo DSA predominantly targeted class II HLA. Both preformed and de novo DSA displayed comparable disappearance kinetics. DSA positivity was associated with a significantly higher incidence of chronic rejection and a trend towards increased graft vasculopathy. In one face recipient who developed de novo DSA and graft vasculopathy leading to graft loss, histological analysis revealed microvascular inflammation features, including lamellation, endothelial cell swelling, and intravascular cells in capillaries and venules.

Conclusions: Humoral immunization is a common event following VCA, in both face and UET recipients, and is associated with chronic rejection and likely contributes to graft vasculopathy. However, mechanistic studies are needed to confirm the causal role of DSA in graft damage in VCA recipients.

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PP_451 INNOGRAFT, SHAPING THE FUTURE OF TRANSPLANT CARE

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Background: There is a pressing need for a safe, rapid method for continuous monitoring and early detection of graft rejection in solid organ transplant patients. In cases of graft rejection, donor DNA is released into the recipient's bloodstream, with higher levels of donor cell-free DNA (cfDNA) indicating greater graft damage. InnoGraft is a tool that targets highly variable regions of the human genome to detect and assess the proportion of circulating donor DNA (as a rejection marker) through a simple, non-invasive blood sample.

Methods: Nanopore sequencing is performed using an amplicon panel of 94 highly variable SNPs (WO2019149673A1) to analyze two human genomes (G1 and G2). To evaluate the capability of detecting and quantifying mixed genotypes, laboratory-created 'Hybrid' samples containing defined proportions of G1 and G2 (ranging from 9:1 to 6:4) were analyzed. Using G2 as a reference, we compared allelic frequencies across variants to estimate the proportional contributions of each genome in the Hybrids.

Results: The algorithm is able to estimate with high accuracy, achieving a mean absolute percentage error (MAPE) of 6.19%, with deviations remaining consistent across hybrid samples (TABLE1). We are defining the sensitivity range of the system under conditions that closely replicate cell-free DNA, with the final goal of confirming the kit's potential on patient samples. With 0.1 Gb per sample required and sequencing completed in just 20 minutes on the MiniON platform, this system is fast and cost-effective.

Conclusions: InnoGraft is a rapid, cost-effective tool for real-time graft rejection monitoring and long-term oversight. Due to its simplicity and reproducibility it can be readily applied in clinical laboratories and has the potential to become a point-of-care solution, improving patient outcomes, supporting immunosuppressive treatment adjustments, and contributing to personalized medicine, with added value for pediatric patients.

Expected RDb (Hybrid samples: G1/ G2)	Observed RDb (G1/ G2) Best score , [min – max] *	
90% / 10%	83.5% / 16.5%	[83% - 84%]
80% / 20%	76.6% / 23.4%	[76% - 77%]
70% / 30%	65.6% / 34.4%	[65% - 66%]
60% / 40%	55.8% / 44.2%	[55% - 56.5%]

* Scores computed with 3 different variant callers

TABLE1
Hybrid samples with defined G1:G2 proportions were analyzed using G2 as a reference (donor) to assess the detection and quantification of mixed genotypes by comparing allelic frequencies and estimating the proportional contributions of each genome.

PP_452 THE IMPACT OF LONGITUDINAL TACROLIMUS INTRA-PATIENT VARIABILITY BEYOND THE FIRST YEAR ON KIDNEY TRANSPLANT OUTCOMES

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Background: Intra-patient variability (IPV) of tacrolimus trough concentrations has emerged as a novel marker for predicting poor clinical outcomes in kidney transplant recipients. However, maintaining consistent long-term follow-up in kidney transplant recipients remains challenging, and there is a lack of studies investigating IPV over extended periods. This study aimed to evaluate the changes in IPV beyond one year after kidney transplantation and their impact on long-term clinical outcomes.

Methods: This retrospective single-center study included 1,942 adult kidney transplant recipients who underwent transplantation at Severance Hospital between 2006 and 2022. The study divided the post-transplant period into two intervals based on the one-year mark. The Tacrolimus IPV, measured during outpatient follow-ups, was assessed separately for each interval. Patients were then classified into four groups according to changes in their IPV: low to low, low to high, high to low, and high to high.

Results: There were no significant differences among the groups in terms of recipient age, sex, deceased donor or living donor, re-transplantation, ABO-incompatible transplantation, dialysis duration before transplantation, or the use of antithymoglobulin induction or rituximab. The patients' death-censored graft survival was highest in the low-to-low group and lowest in the high-to-high group. Furthermore, the multivariable Cox model demonstrated that the change in IPV to high-to-high acts as a risk factor for graft survival (Hazard ratio: 1.907; 95% confidence interval: 1.140–3.191; P = 0.014). De novo DSA (dnDSA) was observed to occur significantly more frequently in the low-to-high group (P = 0.002).

Conclusions: This study suggests that the group in which IPV remained low even after one year post-kidney transplantation showed better survival outcomes. By addressing various factors that increase IPV, such as medication adherence, pill burden, GI motility, and pharmacogenetics, it may be possible to maintain low tacrolimus IPV and thereby improve transplant outcomes.

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PP_453 IMMUNOSENESCENCE IN SHORT AND LONG TERM KIDNEY TRANSPLANTATION

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Background: Immunosenescence is a consequence of ageing and long standing chronic kidney disease, however, in kidney transplantation (KT) serves as an adaptive mechanism of the immune system to protect graft rejection. Aim of this cross-sectional study was to evaluate differences in immunosenescent profile between patients on hemodialysis (HD), and after short-term (ST-KT) and long-term KT (LT-KT) patients and assess possible parameters that can affect it.

Methods: Senescent T lymphocyte populations, defined as CD4+CD28null and CD8+CD28null cells, were assessed by flow cytometry in 118 ST-KT [M/F 80/38, Age 47±14yrs], 25 LT-KT (M/F 12/13, Age 56±12yrs], 101 HD [M/F 67/34, Age 48±13yrs] and 38 healthy controls (HC) [M/F 21/17, Age 52.3±15yrs].

Results: The table describes differences in immunosenescent profile between ST-KT, LT-KT, HD patients and HC. Age was similar between groups, but time between HD vintage and LT-KT was significantly different, 102(79) vs. 288(120) months, respectively, p<0.001. Previous CMV infection and CMV-IgG levels was the main parameter significantly correlated with CD4CD28null cells in HD patients (r=0.5, p<0.01). In KT, CD8CD28null(%) correlated with age (r=0.7, p<0.001), CMV-IgG levels (r=0.3, p<0.001), and eGFR at time of evaluation (r=-0.8, p=0.04).

Conclusions: Immunosenescent alterations, as a consequence to aging, time since KT and CMV infection, develop progressively after KT and may have a long term beneficial effect.

	KT		HD	HC	P (ST-KT vs. LT-KT)	P (ST-KT vs. HD)	P (LT-KT vs. HD)
	ST-KT	LT-KT					
Lymphocytes	1700(900)	2400(1100)	1200(350)	2289(900)	0.007	<0.001	<0.001
CD4(%)	45.4(16)	53(17.9)	41(11.5)	51(11.9)	0.01	0.03	<0.001
CD4(cells/μL)	815(507)	1105(786)	476(259)	999(409)	<0.001	<0.001	<0.001
CD4CD28null(%)	4.1(8.1)	12.4(25)	6.5(8.9)	3.1(5.7)	<0.001	0.1	0.005
CD4CD28null(cells/μL)	37(55.3)	125(217)	28(42.9)	35.9(66.5)	<0.001	0.3	<0.001
CD8(%)	29(13.9)	28.9(13)	25(10)	23(13)	0.5	<0.001	0.007
CD8(cells/μL)	535(353)	683(475)	311(208)	460(395)	0.08	<0.001	<0.001
CD8CD28null(%)	38.6(31)	63.3(33)	39(29)	37(25.5)	<0.001	0.9	<0.001
CD8CD28null(cells/μL)	217(250)	441(489)	122(759)	142(260)	0.003	<0.001	<0.001

PP_454 TAILORING IMMUNONOSUPPRESSION: A RISK-STRATIFIED APPROACH TO INDUCTION THERAPY IN KIDNEY TRANSPLANT OUTCOMES

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Background: Induction therapy in kidney transplantation (KTx) remains a critical area of research, particularly in patients with varying immunological risk profiles, and its role in preventing early rejection continues to be debated, especially in the context of stratified risk groups. This study investigates the efficacy and safety of tailored induction therapy in kidney transplant recipients, categorizing patients by immunological risk and assessing outcomes including graft survival, delayed graft function (DGF), infection rates, and rejection.

Methods: This prospective study involved 244 kidney transplant recipients who received deceased donor transplants at our centre between 2016 and 2021. Patients were stratified into low, intermediate, and high immunological risk groups based on factors such as PRA, HLA mismatches, age, ethnicity, DSA, AB0 incompatibility, and cold ischemia time (CIT). Five arms were established based on immunological risk and induction protocols: low-risk patients (Arm 0) received no induction; intermediate-risk patients (Arms 1 and 2) received no induction or basiliximab; high-risk patients (Arms 3 and 4) received basiliximab or rATG. All groups received maintenance therapy with tacrolimus, mycophenolate, and prednisone. Outcomes assessed included patient and graft survival, DGF, acute rejection, infection rates, and DSA development.

Results: No significant differences were observed in patient or graft survival between low- and intermediate-risk groups, regardless of induction therapy. In high-risk patients, basiliximab induction (Arm 3) resulted in superior graft survival (93.9%) compared to rATG (Arm 4, 74.3%, p = 0.0457). Infection rates were higher in Arm 4, particularly for CMV (52.5% vs. 36.4%, p = 0.0480). DGF and rejection rates were similar across all arms, highlighting the importance of aligning induction therapy with immunological risk.

Conclusions: This prospective study emphasizes the value of stratified induction therapy in optimizing kidney transplant outcomes. Basiliximab induction is preferred for high-risk patients due to superior graft survival and a lower infection burden, while low-risk patients may safely forgo induction. Further research is needed to refine immunosuppressive protocols for kidney transplantation.

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Transplant immunology & immunosuppression

PP_455 ENHANCING HLA DESENSITIZATION: SERUM DILUTION AND PLATFORM-SPECIFIC THRESHOLDS FOR KIDNEY TRANSPLANTATION SUCCESS

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Background: Kidney transplantation remains the most effective treatment for end-stage renal disease, offering significant improvements in survival and quality of life. However, highly sensitized patients face substantial barriers due to the presence of anti-HLA antibodies. This study explores advanced HLA desensitization protocols and antibody profiling to improve transplantation success rates for these patients.

Methods: This retrospective, multicenter study included 20 sensitized patients from two transplantation centers, all of whom underwent desensitization prior to kidney transplantation. The protocol involved ≥10 sessions of immunoadsorption (IA), combined with rituximab and thymoglobulin induction, and maintenance therapy with tacrolimus, mycophenolate mofetil, and prednisone. Serum samples collected at key timepoints—before desensitization, after 10 IA sessions, on the day of transplantation, and post-transplantation—were analyzed using Luminex single antigen bead (SAB) assays from Immucor and One Lambda. Serum dilution was used to address bead saturation and improve donor-specific antibody (DSA) quantification.

Results: Results showed significant antibody reductions across desensitization stages, with strong correlations (Pearson's r > 0.8) between pre- and post-desensitization timepoints. Diluted serum measurements consistently outperformed undiluted in predicting AMR risk, with area under the curve (AUC) values reaching 0.857. However, inter-platform variability in mean fluorescence intensity (MFI) highlighted the need for platform-specific thresholds, as Immucor and One Lambda assays demonstrated differences in sensitivity and calibration. Post-desensitization MFI levels were the strongest predictors of AMR, reinforcing the importance of precise antibody profiling.

Conclusions: This study demonstrates the critical role of serum dilution and platform-specific calibration in refining HLA desensitization protocols. It underscores the necessity of harmonized standards for antibody measurement and risk assessment to enhance transplantation access and outcomes for highly sensitized patients, thereby mitigating immunological barriers to successful kidney transplantation.

PP_456 IMPACT OF LOW TACROLIMUS LEVEL OF GRAFT REJECTION, SURVIVAL, AND HEPATOCELLULAR CARCINOMA RECURRENCE

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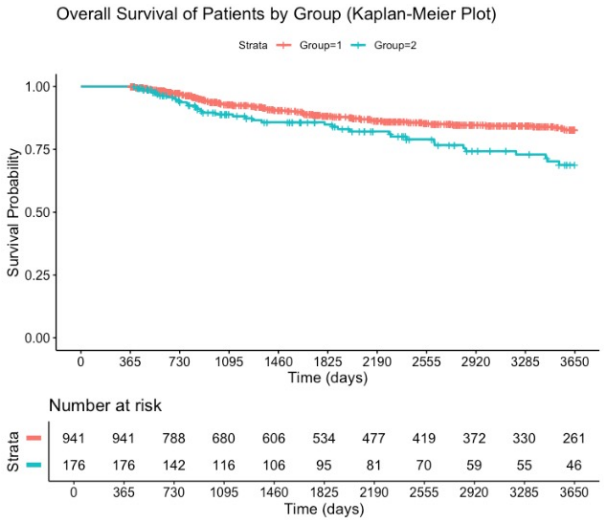
Background: Tacrolimus is a cornerstone immunosuppressant following liver transplantation. Although guideline-based trough levels are typically maintained at 4–10ng/mL, concerns about nephrotoxicity, metabolic complications, and malignancies have prompted interest in tacrolimus minimization strategies. However, whether lowering tacrolimus trough levels increases the risk of graft rejection or confers benefits in reducing hepatocellular carcinoma (HCC) recurrence remains controversial.

Methods: We conducted a single-center, retrospective study of adult patients (≥19 years) who underwent living donor liver transplantation at our institution between Jan 2000 and Dec 2021. Patients were categorized into two groups based on tacrolimus trough levels (measured between one and two years post-transplant): a low FK group (<6 ng/mL) and a high FK group (≥6 ng/mL). We analyzed overall survival and biopsy-proven rejection-free survival in all recipients, and HCC recurrence-free survival among those transplanted for HCC. Cox proportional hazards regression was used to identify independent predictors of mortality, rejection, and HCC recurrence.

Results: A total of 1,117 recipients were included, with 941 in the low FK group and 176 in the high FK group. In the overall population, the low FK group showed higher 10-year overall survival (82.8% vs. 68.8%, p=0.002) and higher rejection-free survival (86.7% vs. 72.8%, p<0.001) than the high FK group. Cox regression confirmed that higher tacrolimus trough levels were an independent predictor of increased mortality (adjusted HR=1.98, 95% CI 1.35–2.89; p<0.001) and rejection (adjusted HR=2.20, 95% CI 1.48–3.27; p<0.001). Among the 614 patients transplanted for HCC, there was no statistically significant difference in recurrence-free survival (77.7% vs. 81.2%, p=0.483), and tacrolimus levels were not independently associated with HCC recurrence in multivariable analysis.

Conclusions: In this single-center, retrospective study, maintaining tacrolimus trough levels below 6 ng/mL did not appear to increase the risk of graft rejection or worsen overall survival. However, no significant reduction in HCC recurrence was observed in the low FK group. These findings suggest that careful tacrolimus dose minimization may be feasible in selected patients.



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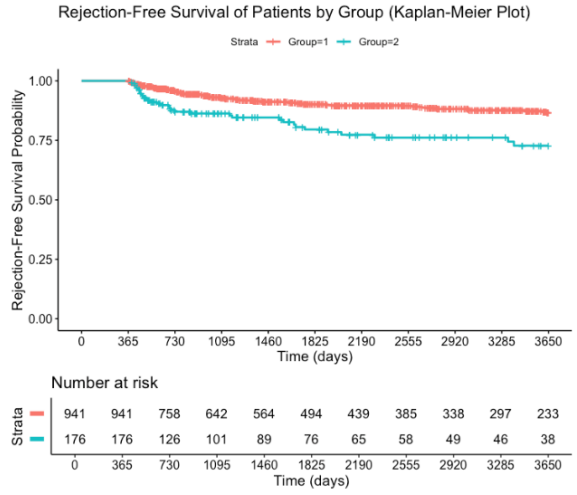

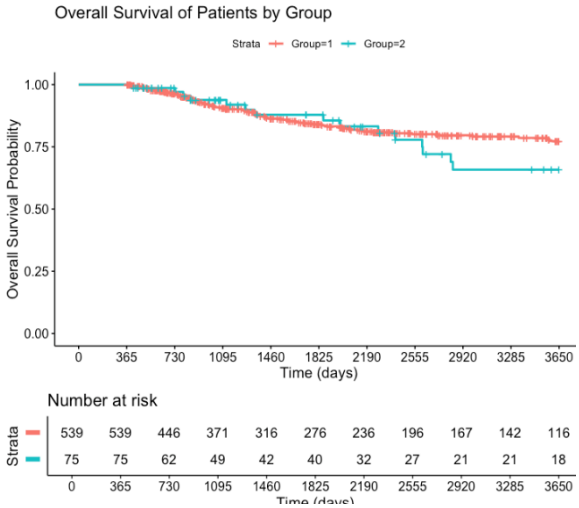

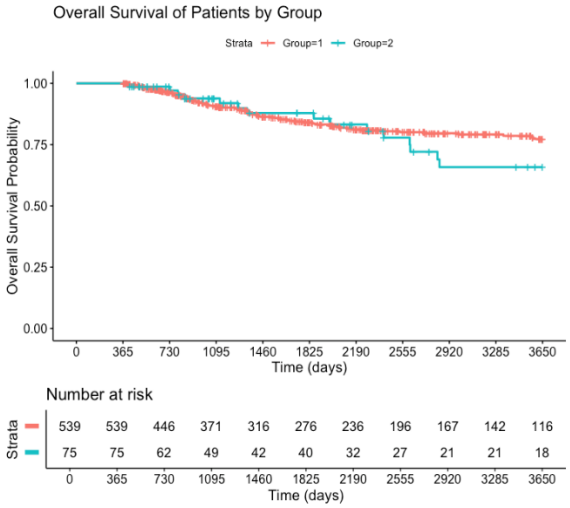

PP_457 SAFETY AND EFFICACY OF BASILIXIMAB INDUCTION WITH DELAYED CNI IN LIVER TRANSPLANT RECIPIENTS WITH RENAL IMPAIRMENT

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Background: Calcineurin inhibitors (CNI) are essential for immunosuppression in liver transplantation, but their nephrotoxic effects are particularly concerning in patients with pre-existing renal insufficiency. This study evaluates the safety and efficacy of combining Basiliximab induction therapy with delayed CNI initiation in liver transplant recipients with mild preoperative renal insufficiency (eGFR 30–60 mL/min/1.72m²). The aim is to assess its impact on renal complications, graft recovery, and long-term survival outcomes.

Methods: This retrospective analysis included 85 adult liver transplant recipients treated at Policlinico Tor Vergata, Rome, from 2009 to 2020. Patients were divided into two groups: 55 in Group 0 received immediate post-transplant CNI starting on Day 1, while 30 in Group 1 received Basiliximab induction followed by delayed CNI introduction on Day 7. Data collected included demographic details, comorbidities, MELD-Na scores, donor characteristics, and organ function parameters such as eGFR, AST, and ALT. Long-term survival outcomes were assessed using Kaplan-Meier analysis, with statistical significance determined via ANOVA, Bonferroni post-hoc tests, and Chi-square analyses.

Results: Basiliximab induction with delayed CNI initiation showed significant benefits. Group 1 had better renal function at Day 30, with an average eGFR of 108.5±12.4 mL/min/1.72m² compared to 85.5±10.7 mL/min/1.72m² in Group 0 ($p<0.001$). Hepatic recovery was faster in Group 1, with lower AST and ALT on Days 1 and 3. The five-year survival rate in Group 1 was significantly higher at 91% compared to 82% in Group 0 (hazard ratio 0.48; $p=0.03$). Additionally, Group 1 had a lower incidence of acute kidney injury (18.4% vs. 35.5%) and required less renal replacement therapy (3.3% vs. 11.1%).

Conclusions: Basiliximab induction with delayed CNI initiation in liver transplant recipients with preoperative renal insufficiency offers clear advantages. This strategy reduces nephrotoxicity, enhances graft recovery, and improves long-term survival. These findings support the integration of this approach in clinical practice to optimize transplant outcomes and improve patient quality of life.

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Transplant immunology & immunosuppression

PP_458 THICK ASCENDING LIMB INJURY CRITICALLY PREDICTS KIDNEY ALLOGRAFT SURVIVAL AFTER T-CELL-MEDIATED REJECTION

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Background: T-cell mediated rejection (TCMR) remains a significant challenge after kidney transplantation and is associated with reduced allograft outcome. Previous research highlighted the critical role of TCMR-induced renal epithelial injury. Yet, the detailed cellular origin of these injury responses and the associated clinical implications remain poorly understood.

Methods: To induce acute TCMR, we used mouse models of allogeneic (C57BL/6 to BALB/c and BALB/c to C57BL/6) kidney transplantation and syngeneic controls (C57BL/6 to C57BL/6 and BALB/c to BALB/c). Molecular changes were analyzed 7 days post-transplant using single-nucleus RNA sequencing and spatial transcriptomics. Results were compared with snRNA-seq data from three human TCMR biopsies and three stable allografts without rejection. The clinical impact of TCMR-induced epithelial injury was evaluated using marker gene sets on bulk transcriptomic data from 1292 kidney allografts, including 95 TCMR samples, with allograft outcome.

Results: Mouse kidneys from allogeneic transplants exhibited all hallmark histological features of TCMR. Single-nucleus RNA sequencing revealed TCMR-induced injured cell states and significant gene expression changes particularly in proximal tubules (PT) and thick ascending limbs (TAL). Spatial transcriptomics showed a heterogeneous spatial distribution of these injured cell states and proximity to leukocytes. Cross-species analysis confirmed similar injured PT and TAL cell states in human TCMR. Signatures of a severely injured TCMR-induced TAL cell state correlated strongly with allograft survival in a large kidney transplant cohort specifically after TCMR.

Conclusion: This is the first study showing kidney allograft outcome with distinct injured epithelial cell states. We found a particularly strong correlation between kidney allograft survival and TAL injury in TCMR, which occurred with reduced proximity to leukocytes, suggesting potential epithelial injury driven by non-immune mechanisms.

PP_459 ADRENOMEDULLIN AS A NOVEL BIOMARKER OF GRAFT DYSFUNCTION IN LIVER TRANSPLANTATION: PRELIMINARY RESULTS OF A PILOT STUDY

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Background: Mid-Regional Pro-Adrenomedullin (MR-proADM), a stable fragment of the ADM precursor, reflective of endothelial damage, has emerged as a valuable non-invasive biomarker for risk stratification and mortality prediction in sepsis and multi-organ failure in ICU Units. Likewise, MR-proADM has been demonstrated as a prognostic factor in patients affected by chronic cirrhotic and non-cirrhotic liver damage. To date, the role of MR-proADM has not been explored in liver transplant patients.

Methods: This is a prospective, single-center pilot study aimed at evaluating the course of MR-proADM levels in liver transplant patients in correlation with graft functional recovery, particularly in Early Allograft Dysfunction (EAD) and Primary Non-Function (PNF). A secondary objective was to assess MR-proADM levels in post-transplant surgical or infectious complications. We included all adult patients who underwent liver transplantation at our Center from October 2023, with a minimum 3 months follow-up. Recipients with autoimmune liver diseases or undergoing re-transplantation were excluded. MR-proADM levels were assessed pre-transplant, on postoperative day (POD) 1, 3, 5, and 15, at 1, 3, 6, 9, and 12 months and in cases of suspected complications and/or acute rejection (AR).

Results: Between October 2023 and September 2024 31 patients were enrolled (mean age: 63 years [35-74]). No cases of PNF were observed. Patients with defined EAD (n=13, 41.9%) showed significantly higher MR-proADM levels in POD 1 (5.21 [1.65-11.25] vs 2.39 [1.85-3.98] p=0.02) compared to patients who did not develop EAD (n=18, 58.1%). MR-proADM stayed consistently higher in POD 3 (4.28 [1.11-10.65] vs 3.44 [1.81-2.76] p=0.17), POD 5 (4.22 [1.27-9.89] vs 2.51 [1.74-2.98] p=0.19) and POD 15 (2.52 [0.77-7.86] vs 1.87 [0.81-3.72] p=0.44) in the EAD group. In the 6 (19.4%) patients who developed a post-operative complication (n=1 hemorrhage, n=1 bowel perforation, n=4 pneumonia) MR-proADM showed a peak increase near the day of the event.

Conclusions: Levels of MR-proADM on POD 1 are consistent with the development of Early Allograft Dysfunction after liver transplantation and may serve as an indicator of graft functional recovery and development of post-operative complications.

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PP_461 CROSSMATCH IN PIG-TO-HUMAN XENOTRANSPLANTATION

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Background: Histocompatibility testing in Xenotransplantation (XTx) is essential, to identify pre-formed natural antibodies against porcine antigens and exclude cross-reactivity between human sera and swine leucocyte antigens (SLA).

Methods: Therefore, we aim to establish a complement-dependent cytotoxicity (CDC) and flow-cytometry cross-match (FCXM) using porcine peripheral blood mononuclear cells (pPBMCs) to detect cross-reactive human IgM and IgG in sera. The assay included pPBMC from genetically modified (GM) Auckland pigs knocked out for GGTA1 (no αGal antigen expression) and wild type (WT). To define positive and negative controls, pooled sera from either HLA-negative tested platelet donors, HLA-negative tested animal farm workers, or donors with known broad HLA immunization and commercial anti-HLA-A2 and HLA-B7 specific serum were tested. In all cases, the sera were immunoadsorbed (IA) or not (nonIA) with red blood cells from WT animals.

Results: All nonIA sera showed strong positive cross-matching results (IgM and IgG) with WT pPBMCs. With GM pPBMCs, reactivity of nonIA sera was clearly reduced, but still positive. After IA, this cross-reactivity could be reduced to weakly positive, but not completely negative in WT and GM. Reactivity of sera after IA tested against WT and pPBMCs was stronger in sera from HLA-sensitized donors, followed by HLA-negatively tested platelet donors' and animal farm workers. Finding possible explained by pro-zone effect. While commercial sera from HLA-sensitized patients to HLA-A2 and -B7 showed almost negative reactions to WT and GM pPBMCs.

Conclusions: These preliminary results showed that the elimination of the αGal antigen was not sufficient to eliminate natural antibody binding to pPBMCs supporting the notion that triple-KO animals are essential in XTx.

PP_462 UNLOCKING PRECISION IN IMMUNOSUPPRESSIVE MINIMIZATION: INSIGHTS FROM AI-DRIVEN ANALYSIS OF LIVER FUNCTION PARAMETERS

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[1]Medical University of Warsaw; Immunology, Transplantology and Internal Diseases,; Immunology Transplantology and Internal Diseases, [2]Medical University of Warsaw; Department of Transplantology, Immunology, Nephrology and Internal Medicine, [3]Clinical Center of the Medical University of Warsaw; Immunology, Transplantology and Internal Diseases,, [4]Cliniques Universitaires Saint-Luc, [5]University of Białystok; Institue of Computer Science

Background: Using artificial intelligence (AI) in transplantology could transform patient care by enabling rejection diagnosis based on noninvasive markers and personalized immunosuppressive (IS) regimens. The minimization of IS in liver transplant (LTx) recipients has showed to be a safe method of reducing the burden of IS deleterious side effects. Liver function tests obtained during ambulatory visits of LTx recipients who underwent IS minimization were analyzed using AI. The analysis focused on identifying which parameters are most susceptible to changes during minimization of IS and secondly, on building a model to predict the patients response to a dose reduction.

Methods: Liver function parameters of 96 LTx from 14 ambulatory visits were normalized as a percentage of a baseline which was calculated individually from four initial visits prior to IS minimization. All visits, except the first and last, were treated as individual events. Each event included parameter values from the previous, current, and next visits, along with their differences. From each event two decision were generated for each event: A binary prediction of the patient's respond to dose reduction. A dosage adjustment decision: decrease (-1), no change (0) or increase (1). The analysis used the Boruta algorithm for feature selection and Random Forest to build classifiers.

Results: The binary decision models performed no better than random. However, weak but statistically significant classifiers were developed for binary prediction of patient response and for the tri-state dosage adjustment decision. Odds ratios for -1, 0, and 1 decisions were 1.7, 1.7, and 7, respectively (only 46 cases in the +1 class). Joint analysis suggested greater importance for gamma-glutamyltransferase (previous visit) and aspartate transaminase (current visit) in decision-making.

Conclusions: Liver function parameters alone cannot fully explain physicians' decisions or patient responses to IS reduction. However, AI can help identify key parameters to monitor closely for guiding IS minimization.

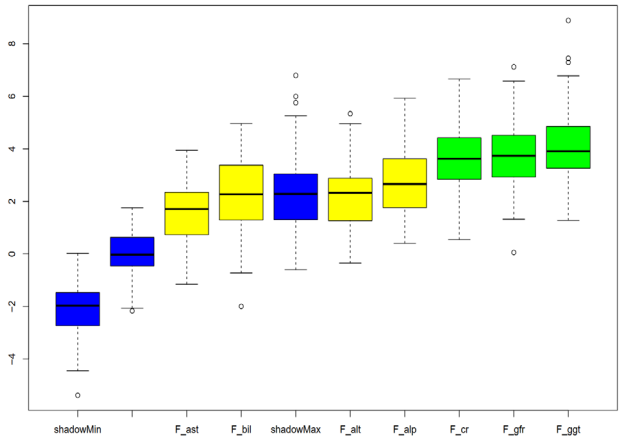

Figure 13: Importance of variables for deduction of previous decision (binary model).

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Transplant immunology & immunosuppression

PP_463 EX-VIVO-GENERATED IMMUNOMODULATORY CELLS REDUCE PROINFLAMMATORY MACROPHAGE (M1) POLARIZATION

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[1]Karolinska Institute; Transplantatin Surgery; Clintec, [2]Karolinska Institutet; Department of Clinical Sciences, Intervention and Technology; Division of Transplantation Surgery, [3]Karolinska Institutet, [4]Karolinska University Hospital Huddinge; Transplantation Surgery; Me Transplantation, [5]Karolinska Institutet; Clintec, [6]Karolinska Institutet; Transplantation Surgery; Clintec, Transplantation Surgery

Background: In clinical liver transplantation, adoptive transfer of donor-specific immunomodulatory cells (DSIMC) has been shown to result in the early withdrawal of general immunosuppression. Donor-specific immunomodulatory cells (DSIMCs) are generated ex vivo by culturing recipients' peripheral mononuclear cells (PBMC) and irradiated donor PBMC with co-stimulation blockers such as anti-CD80/86 antibodies or CTLA4Ig (Belatacept). Macrophages could be an important factor in maintaining tolerance. Here, we examine whether DSIMCs are able to act in an anti-inflammatory capacity to reduce M1 macrophage polarization in vitro in a donor-specific fashion.

Methods: PBMCs were separated from buffy coats of healthy volunteers and used either to generate DSIMC or to differentiate macrophages. DSIMC or donor-specific activated cells (DSAC) were generated by co-culturing responder PBMC with irradiated stimulator PBMC with or without belatacept. These cells were harvested on day 10. For macrophage differentiation, CD14+ cells were separated and cultured with a macrophage medium. On day 10, M1 polarization was performed with LPS and IFN-γ for six hours, and different amounts of DSIMC or DSAC were added. After 20 hours of incubation, cytokine profiles and macrophage polarization markers were examined.

Results: DSIMC, but not DSAC, suppressed M1 macrophage marker expressions such as CD64 and CD80 in a dose-dependent manner. Similar results were found in all groups, i.e., autologous macrophages, stimulator macrophages, and 3rd party macrophages. TGF-β production increased by co-culturing with all types of macrophages. IL-10 production also increased in DSIMC co-cultured with stimulator macrophages.

Conclusions: Our findings suggest that DSIMCs have a donor non-specific anti-M1 polarization capacity. This anti-inflammatory function could be important in maintaining tolerance of transplanted liver grafts.

PP_464 SEVEN YEARS LONGITUDINAL MEASUREMENTS OF TTV IN LUNG TRANSPLANT RECIPIENTS

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Background: Torque tenovirus (TTV) is a DNA virus which causes no known human disease, and which is endemic with up to 90% - 100% of tested subjects having detectable TTV in blood. From studies in solid organ transplantation (SOT), it has become accepted that an elevated TTV viral load is an indication of over-immunosuppression, while a low TTV viral load is an indication the patient is under-immunosuppressed. So far no long term longitudinal studies exist investigating TTV loads for longer than 3 years after SOT. In this study we retrospectively examine TTV dynamics in lung transplantation recipients (LTR), over a period of up to 7 years. We further analyze the relationship between TTV, all-cause mortality, acute and chronic lung allograft dysfunction (CLAD), and infectious risk.

Methods: 88 patients that received a lung transplantation between January 2015 and December 2017 were included. Plasma was taken within 2 weeks after transplantation, and at routine outpatient visits, approximately every 3 months during the first year, every 6 months during the second and third year, and once per year thereafter. All samples were stored at −80 ◦C, until analysis. DNA was extracted from thawed plasma samples using the eMAG Nucleic Acid Extraction System, and tested for TTV using the RGene kit (bioMérieux, France). Data analyses were performed using SPSS 23.0.

Results: Following transplantation a rapid increase in TTV load was observed in nearly all patients, reaching a peak TTV load of 7.7 log (+/-2.77) in 90 % of cases. Peak levels occurred between 90 and 120 days after transplantation and was followed by a gradual decrease. During the study period, 23 patients died, of whom 13 died of infections, and 26 developed CLAD. Both death and CLAD occurred significantly more in patients whose TTV load was above the mean value for that time after transplantation during their most recent out-patient visit (fig.1).

Conclusions: This retrospective study, which investigates TTV loads over a period of 7 years after lung transplantation, suggests that sustained high TTV loads are associated with increased mortality and allograft dysfunction.

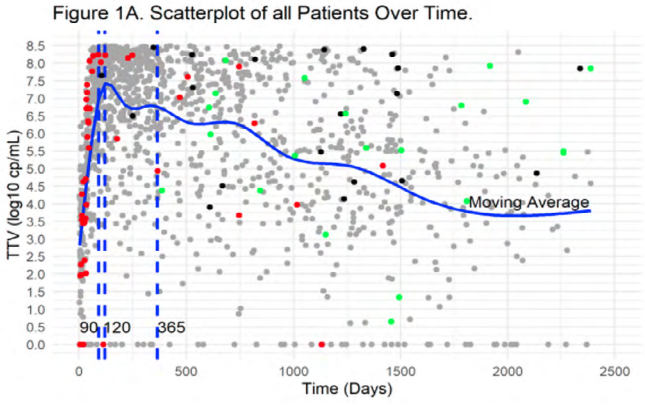

Figure 1: Scatterplot of all TTV measurements. TTV measurement immediately prior to death (black dots), acute rejection episodes (red dots), and diagnosis of CLAD (green dots) are indicated.

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Transplant immunology & immunosuppression

PP_465 THE MOLECULAR DIAGNOSIS IN DISCREPANT KIDNEY ALLOGRAFT BIOPSY FINDINGS: INSIGHTS FROM KIDNEY TRANSPLANT CENTER LJUBLJANA

Neva Bezeljak[1], Miha Arnol[2], Nika Kojc[3], Manca Oblak[1], Gregor Mlinšek[1], Anja Ponikvar Ležaič[1], Željka Večerić Haler[4]

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Background: To improve the diagnostic accuracy of kidney transplant biopsies, the Alberta Transplant Applied Genomics Center developed the Molecular Microscope® Diagnostic System (MMDx). This system utilizes gene expression analysis and machine learning to identify post-transplant pathologies.

Methods: We retrospectively analyzed 200 kidney allograft biopsies performed at Kidney Transplant Center Ljubljana since 2020. Biopsies underwent histological evaluation and MMDx analysis, including both indication and surveillance samples.

Results: MMDx demonstrated significant utility in borderline diagnoses (e.g., C4d-negative and borderline rejection), cases with insufficient tissue, or overlapping histological features. It often corroborated histology findings and clarified diagnostic ambiguities. Notably, most of our histological borderline biopsies lacked molecular evidence of T cell mediated rejection. Discrepancies between histology and MMDx were observed in 20% of biopsies, influencing therapeutic decisions in half of these cases. Negative MMDx results occurred in 30% of indication biopsies classified as rejection by histology. Patients were treated based on histology and clinical information showed improved renal function during follow-up. Positive MMDx findings indicating rejection, when histology concluded no rejection, were rare but concerning, as they highlighted potential overlooked conditions. Subsequent clinicopathological correlations and histological reevaluations in these cases revealed alternative diagnoses, including pyelonephritis and BK virus nephropathy.

Conclusions: The integration of MMDx with histology and clinical assessment has mitigated the limitations of traditional biopsy diagnostics, improving accuracy and patient outcomes. Nevertheless, robust histological and clinical evidence remains crucial for determining treatment strategies.

PP_466 IMPACT OF ATG INDUCTION ON GRAFT AND PATIENT SURVIVAL IN LIVING DONOR KIDNEY TRANSPLANTS: LARGEST SINGLE CENTER STUDY

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Background: Kidney transplantation (KT) is the preferred therapy for end-stage renal disease (ESRD), offering a better quality of life and survival than dialysis. Anti-thymocyte globulin (ATG) induction therapy remains a cornerstone in KT. However, its benefits in living-related donor KT, particularly regarding long-term graft and patient survival, remain debated. This study, the largest single-center experience to date, examines the impact of ATG induction versus no induction on graft survival, patient survival, and rejection rates in living donor KT.

Methods: This retrospective single-center study analyzed living donor kidney transplants (LDKT) performed between September 2008 and December 2022. A low-dose ATG induction protocol (1 mg/kg/day for three days) was implemented for unrelated LDKT with high-risk recipients (e.g., sensitization, prior transplantation, or mismatched donor-recipient HLA). In contrast, no ATG induction therapy was used for related LDKT in low-risk recipients, characterized by no sensitization and a donor-recipient HLA match of ≥3/6.

Results: In the analysis of 2,248 LDKTs, 48.57% of kidney transplant recipients (KTRs) received ATG induction. This group included older KTRs, more unrelated donors, and longer pre-transplant dialysis periods. Despite these factors, ATG induction significantly improved short- and long-term allograft function and graft survival, with a notably reduced rejection rate (Table). However, patient survival was comparable between groups during a mean follow-up of 61.86±44.91 months (Figure). KTRs lost to follow-up, accounting for less than 10% of the cohort, were excluded from the final analysis.

Conclusion: This study provides compelling evidence that ATG induction significantly enhances allograft function, improves survival, and reduces rejection rates in LDKT, underscoring its crucial role in optimizing transplantation outcomes and supporting its continued use in clinical practice.

Parameters	KTR without ATG Induction (n=1156) (51.42%)	KTR with ATG Induction (n= 1092) (48.57%)	P-value
Recipient and Donor Characteristics			
KTR Age (yrs)	29.92 ± 9.69	39.99 ± 10.35	<0.001
KTR Sex (Male/Female)	953/203 (82.4%/17.6%)	928/ 164 (85 %/15 %)	0.110
KTR weight (kg)	53.39 ± 11.09	56.90 ± 10.80	<0.001
Donor Age (yrs.)	46.51 ± 10.50	40.44 ± 9.50	<0.001
Donor Sex (Male/Female)	379/775 (32.8%/67.2%)	194 /895 (17.8%/ 82.2%)	<0.001
Donor weight (kg)	60.30 ± 7.38	60.07 ± 9.21	0.552
Related/Unrelated	1128/27 (97.7%/2.3%)	121/969 (9.7%/ 88.9%)	<0.001
Pretransplant Dialysis Duration (months)	11.44 ± 10.56	14.06 ± 15.94	<0.001
Surgical Details			
Laparoscopic Donor Nephrectomy (right vs left)	1027/107 (90.6%/9.4%)	965/98 (90.8%/9.2%)	0.883
Donor Surgery (Min)	198.60 ± 47.16	195.11 ± 49.37	0.022
Warm ischemia time (WIT) Min	4.75 ± 1.39	4.67 ± 1.45	0.127
Cold Ischemia time (CIT) Min	89.50 ± 73.10	92.69 ± 71.92	0.048
Post-Operative Outcomes			
Immediate graft function	790 (68.3%)	826 (75.6%)	<0.001
Slow graft function-1 (SGF-1= Scr >1.5 mg/dl past one-week post-KT)	243 (21%)	184 (16.8%)	0.013
Slow graft function-2 (SGF-2= Scr >1.5 mg/dl past two-week post-KT), including DGF	123 (10.6%)	80 (7.3%)	0.006
Delayed Graft Function (DGF)	33 (2.85%)	36 (3.29%)	0.544
Scr Day 1(mg/dl)	3.05 ±1.63	2.99 ± 1.60	.392
Scr Discharge (mg/dl)	1.74 ± 1.11	1.58 ± .96	<0.001
Recipient Hospital Stay (days)	9.85 ± 7.22	9.39 ±7.12	0.028
Scr 1 Month(mg/dl)	1.36 ± .48	1.26± .46	<0.001
eGFR- 1 Month	66.90 ± 26.30	68.62 ± 25.49	0.007
Scr 3 Month (mg/dl)	1.33 ± .43	1.21 ± .38	<0.001
Long term outcome			
Biopsy-proven Acute Rejection	361 (32%)	135 (12.4%)	<0.001
Scr one year (mg/dl)	1.37 ± .74	1.23 ±.45	<0.001
eGFR one year	67.85 ± 24.12	69.83 ± 21.51	0.008
Scr Current (mg/dl)	1.96 ± 1.54	1.60 ± 1.21	<0.001
eGFR current	53.76 ± 26.28	60.71 ± 26.67	<0.001
Renal Allograft loss	91 (7.9%)	56 (5.1%)	0.010
KTR mortality	81 (7%)	80 (7.3%)	0.806

eGFR= Estimated Glomerular Filtration Rate, KTR- Kidney Transplant Recipients, Scr- Serum creatinine

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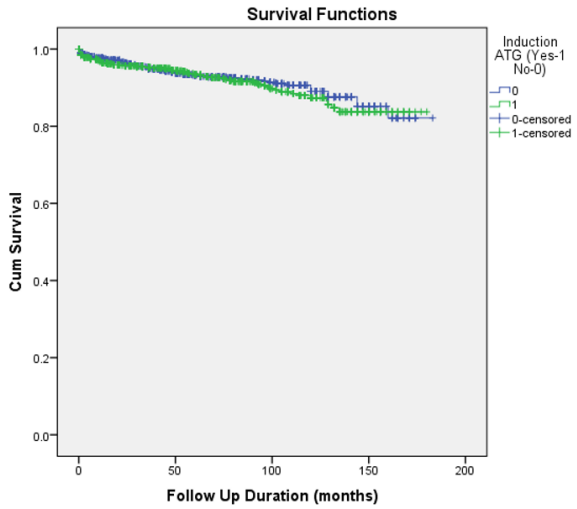
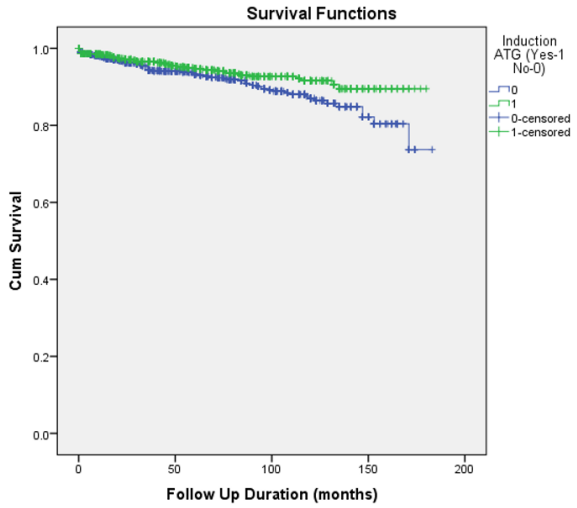
Patient Survival (P=0.528)



Death-Censored Graft Survival (P=0.026)



PP_467 LOWER REFERENCE TACROLIMUS TROUGH TARGETS FOR SIMULTANEOUS PANCREAS KIDNEY TRANSPLANT RECIPIENTS IN FIRST YEAR

Armin Gelinck[1], Jasper Kamp[1], Soufian Meziyerh[2], Siebe Spijker[1], Paul van der Boog[3], Hanneke Bouwsma[4], Maryam Lyousoufi[1], Teun Van Gelder[5], Jesse Swen[1], Amar Levens[1], Volkert Huurman[6], Dirk Jan Moes[3], Aiko de Vries[7]

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Background: Tacrolimus (Tac) targets in simultaneous pancreas-kidney transplant recipients (SPK) are often extrapolated from the kidney transplant recipient (KT) population as evidence is scarce. We aimed to demonstrate how differences in Tac pharmacokinetics affect the lower Tac trough concentration (C_0) limit for rejection in SPK during the first year post-transplant.

Methods: In this cohort study, we included 183 SPK and 1239 KT transplanted between 2011-2023, started on Tac during the first year. We assessed Tac exposure using trough concentration (C_0), area under the curve (AUC), and AUC/C_0 ratio. We used a limited sampling strategy to assess the AUC at 3 time intervals: 0–6 weeks (samples obtained at 1, 2, 3, 4, 5, and 6 hours), 6–26 weeks, and 26–52 weeks (samples obtained at 1, 2, and 3 hours). Pancreas rejection was diagnosed using enzyme levels and imaging, while kidney rejection was diagnosed by biopsy. The difference in AUC_{0-12h}/C_0 was estimated using linear mixed models to address all exposure measurements over time. Age, BMI, sex, and CYP3A5 status were included as covariates. Albumin, hematocrit, and creatinine were assessed as mediators. The dose-response relationship between C_0 and rejection in SPK was modeled using a joint modeling framework that included all C_0 measurements, sex, antigen mismatch, and PRA scores. The lower C_0 threshold was explored by comparing SPK with and without rejection.

Results: Compared to non-diabetic KT, SPK obtained a covariate-adjusted -8.4% [-11.8 to -4.9%; P < 0.001] lower AUC_{0-12h} for the same C_0 at 0–6 weeks. This difference decreased over time (Table 1). The adjusted hazard ratio for every 1 ng/ml increase in Tac-C_0 was 0.81 [95% CI: 0.67–0.93, P = 0.009]. In contrast to a Tac target of 5-7 ng/ml suggested by previous studies for KT, we found that the lower C_0 limit during the first year after transplantation was between 6–8 ng/ml for SPK (Fig. 1).

Conclusions: SPK obtained a lower AUC for the same C_0 as KT. The difference diminished by the end of the first year. Future guidelines should account for the need for a 10% higher C_0 threshold in SPK compared to KT to confer optimal protection during the first year post-transplantation.

	Unadjusted		Confounder adjusted	
Period	% Difference (95% CI)	*P* value	% Difference (95% CI)	*P* value
Weeks 0 - 6	-6.68% (-10.06 to -3.30%)	*<0.001*	-8.39% (-11.80 to -4.97%)	*<0.001*
Weeks 6 - 26	-3.82% (-7.32 to -0.32%)	*0.03*	-4.77% (-8.35 to -1.19%)	*0.009*
Weeks 26 - 52	-1.90% (-5.95 to 2.15%)	0.35	-2.27% (-6.90 to 2.15%)	0.18

Table 1

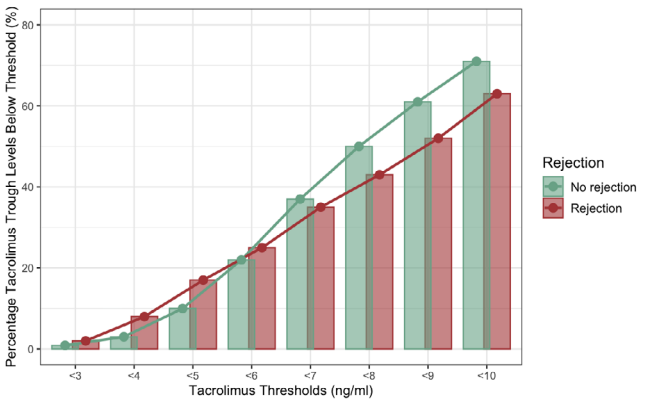

Figure 1

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Transplant immunology & immunosuppression

PP_469 INITIAL EXPERIENCE OF VIRTUAL CROSSMATCH IMPLEMENTATION IN GERMANY

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Background: Virtual crossmatch (vXM) started in all Eurotransplant (ET) member states on 2023-01-23 for kidney and kidney-pancreas allocation. This required organisational and technical changes: Due to ambiguity resulting from technical limitations in HLA typing, all laboratories upload in an HML-File to ET all possible HLA-alleles identified in a donor (A, B, C, DRB1, DRB3, DRB4, DRB5, DQB1, DQA1, DPB1, DPA1). ET converts this into 2-field-typing respecting CIWD 3.0 catalogue and 18th HLA nomenclature workshop definitions. Laboratories check correctness of the automatic conversion and adjust in case of unexpected deviations in phenotypes. Hereafter all kidney, pancreas and intestine waiting list candidates with unacceptable antigens or alleles against the donor are deselected from the allocation for this donor. The vXM is complemented by a physical crossmatch (LCT) prospectively performed for immunized recipients and retrospectively for all others.

Methods: For all German organ donors from 2023-4-24 to 2025-01-14 (1) HLA-HML-file uploads were analyzed to identify any technical limitations and (2) results of vXM and LCT were compared to identify any inconsistencies.

Results: (1) For 1768 donors 1814 HML-files were uploaded. 1662 files (92%) required no major correction, 136 files (7%) needed manual adjustment due to complex HLA issues. Switch to manual backup occurred in 16 cases (1%). Mean duration for completing vXM was 6 min. (including all manual work). (2) 2880 LCT tests were performed for allocated recipients with negative vXM. In 33 cases (1.2%) a positive result occurred (see table).

Conclusions: Since implementation of vXM the quality of donor HLA-typing improved and is standardized. For LCT an excellent prediction of results exists by vXM. Further quality control is necessary about future indication for LCT tests and its' results.

unacceptable antigens not entered by user	4
recipient added manually to match-list (bypass of vXM)	1
unacceptable alleles not entered (IT issue in AM program)	1
immunization-event not investigated (e.g. transfusion)	2
autoimmune disease or infect in recipient etc.	10
pending investigation	4
not HLA-antibodies (false positive)	10
interaction by HLA epitopes cannot be excluded	1

Table: Reasons for discrepancy between positive LCT-XM test and negative vXM:

PP_471 LONG-TERM OUTCOMES IN HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS: A PROPENSITY SCORE-MATCHED ANALYSIS

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[1]Hôpital Necker Paris France; Pitor, [2]Necker Enfants Malades; Necker Hospital; Kidney Transplant Department, [3]Necker-Enfants Malades Hospital; Necker Hospital; Pathology Department, [4]Necker - Enfants Malades Hospital; Necker Hospital; Pathology, [5]Hôpital Necker Enfants Malades; Necker Hospital, [6]Hôpital Necker Enfants Malades, [7]Hôpital Necker Enfants Malades - Ap-Hp; Department of Adult Nephrology and Transplantation; Department of Adult Nephrology and Transplantation, [8]Necker Hospital; Assistance Publique–hôpitaux de Paris, Hôpital Necker, Service des Maladies du Rein et du Métabolisme, [9]Necker Hospital; Transplantation Unit; Nephrology and Renal Transplantation, [10]Hopital Necker; Hôpital Necker & Université Paris Cité; Chef de Service de Nephrologie A1 et Transplantation Adultes, [11]Necker Hospital; Necker Hospital; -

Background: Highly sensitized kidney transplant recipients are at higher risk for antibody-mediated rejection (AMR) and graft failure due to preformed donor-specific antibodies (DSAs). Despite these challenges, recent advances in desensitization protocols provide new hope for sensitized patients. This study assesses graft and patient survival over a 15-year period, comparing highly sensitized patients to a matched cohort of non-sensitized recipients.

Methods: This retrospective study includes 95 highly sensitized patients, defined by DSA levels (MFI > 3000), and managed with intensive immunosuppressive regimens. Using propensity score matching, 82 of these patients were matched to 261 non-sensitized recipients based on age, sex, transplant year, cold ischemia time, and other clinical factors. Outcomes included long-term allograft and patient survivals and the impact of immunologic sensitization.

Results: The mean follow-up after transplantation was 11.9 ± 5.6 years. Among the matched patients, kidney allograft survival rates after transplantation at 5, 10, and 15 years were 86.4%, 75.5%, and 69.5% for the matched patients without preformed DSA and 83.1%, 59.4%, and 49.5% for the matched highly sensitized patients, respectively (p=0.006) (**Figure 1A**). The patient survival rates after transplantation at 5, 10, and 15 years were 88.1%, 70.4%, and 57.3% for the matched patients without preformed DSA and 86.6%, 72.8%, and 46.9 %for the matched highly sensitized patients, respectively (p=0.200) (**Figure 1B**). More AMR occurred in the highly sensitized group (p=0.003) while there was no significant difference for TCMR (p=0.715).

Conclusions: Although sensitized patients have a higher risk of graft loss, their long-term survival is comparable to non-sensitized recipients, supporting the use of intensive immunosuppression in this population.

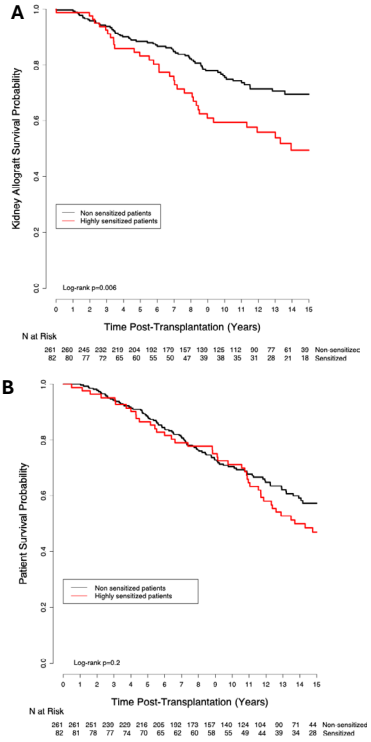

Figure 1. Kaplan-Meier curves of allograft and patient survival rates for highly sensitized patients and non-sensitized patients.

Panel A correspond to kidney allograft survival and Panel B corresponds to patient survival.

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Transplant immunology & immunosuppression

PP_472 TACROSAFE, AN AGENTIC AI-DRIVEN PERSONALIZED TACROLIMUS MANAGEMENT APPLICATION FOR KIDNEY TRANSPLATE PATIENTS.

Ala Elcircevi[1]

[1]*Florence Nightingale Hastanesi; Kidney Transplant*

Background: Tacrolimus, a cornerstone immunosuppressant in kidney transplantation, is vital for preventing allograft rejection but presents challenges due to its narrow therapeutic range. Achieving and maintaining optimal Tacrolimus levels require precise dose adjustments tailored to dynamic patient-specific factors, such as drug interactions, renal function, and concurrent therapies. Agentic AI—an advanced paradigm that actively engages in decision-making and problem-solving—has been harnessed to develop "TacroSafe" a personalized Tacrolimus management application. Acting as a dynamic, self-improving system, this application analyzes patient data, adapts recommendations based on evolving clinical parameters.

Methods: TacroSafe, An agentic AI-powered application was developed to facilitate personalized Tacrolimus dose optimization. The platform leverages patient-specific clinical data, including Tacrolimus blood levels, markers of infection, drug interaction profiles, renal function indicators (e.g., creatinine levels), and the immunotherapy regimen. By integrating these parameters, the application employs predictive analytics to recommend appropriate dose adjustments in real time. It also communicates dosage changes directly to patients and healthcare providers to ensure timely interventions and adherence.

Results: While the application is currently under development, preliminary testing on simulated patient datasets has shown promising potential in maintaining therapeutic Tacrolimus levels between 8-10 ng/mL. Expected outcomes include reduced incidences of Tacrolimus toxicity, improved graft survival rates, and enhanced patient quality of life. Prospective clinical trials are planned to validate these findings in a real-world setting.

Conclusions: This innovative AI application represents a significant advancement in personalized medicine for kidney transplant patients. By automating and optimizing Tacrolimus dose management, the platform aims to mitigate risks associated with traditional dosing methods, ensuring better long-term outcomes for transplant recipients. This tool has the potential to become an integral part of post-transplant care, providing both patients and clinicians with a robust decision-support system.

PP_473 ROLE OF ALLOREACTIVE ADAPTIVE NATURAL KILLER CELLS IN RENAL ALLOGRAFT MICROVASCULAR INFLAMMATION

Elisenda Alari-Pahissa[1], **Judith Federico-Vega[1], Michelle Ataya[2], Anna Buxeda[3], Víctor Bello-Rico[4], Javier Gimeno[5], José Yélamos[6], Mireia Altadill[7], Sara Sanz-Ureña[1], Marta Riera[1], Carla Burballa[3], Betty Chamoun[3], María José Pérez-Sáez[3], Dolores Redondo-Pachón[8], Carlos Vilches[4], Miguel López-Botet[7], Marta Crespo[9]**

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Background: Inhibitory Killer-cell immunoglobulin-like receptors (iKIR) are randomly expressed by Natural Killer (NK) cell subsets and recognize motifs shared by HLA class-I allotypes. Such interactions prevent NK cell autoreactivity while enhancing their response against cells lacking those HLA-I molecules (missing self), a situation defined in transplantation as iKIR-HLA-I mismatch (iKIR-MM), whose genotypic prediction has been associated with microvascular inflammation (MVI).

Methods: Herein we compared iKIR-MM in kidney transplant recipients (KTR) with MVI≥2 (n=21) and controls with MVI≤1 (n=41). In parallel to genetic analysis of iKIR-MM, putative alloreactive iKIR-MM NK cells were defined by flow cytometry as NKG2A- cells bearing self-specific but lacking donor-specific iKIR.

Results: Genetic iKIR-MM was more frequent in MVI≥2 patients. Although iKIR-MM NK cells were detected in both groups, their pretransplant numbers were higher in MVI≥2 patients (median=9.31, IQR=0-55.26 vs median=0, IQR=0-4.79), correlated with MVI grade and were associated to decreased MVI≥2-free graft survival (HR=1.018, p=0.004) independently of posttransplant donor-specific antibodies (DSA) or C4d. A subset of MVI≥2 patients showed pretransplant high proportions and numbers of oligoclonal iKIR-MM NK cells, which displayed an NKG2C+ adaptive phenotype associated with cytomegalovirus infection.

Conclusions: This pilot study provides a novel perspective on the contribution of iKIR-MM NK cells to MVI, with potential practical implications.

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PP_474 A RETROSPECTIVE ANALYSIS OF BASILIXIMAB VERSUS ANTI-THYMOCYTE GLOBULIN IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Background: Pediatric kidney transplant recipients present unique immunological challenges that necessitate tailored induction therapy. The efficacy of monoclonal anti-IL2 receptor antibody basiliximab compared to polyclonal anti-thymocyte globulin (rATG) remains inadequately explored in this population. This study aims to compare the short- and long-term outcomes of basiliximab versus rATG in pediatric kidney transplant recipients, focusing on patient and graft survival, infection rates, and complications related to immunosuppression.

Methods: A retrospective cohort study was conducted using data from the Organ Transplant Centre of Excellence registry at King Faisal Specialist Hospital, Riyadh. Pediatric patients (<18 years) who received basiliximab or rATG from January 2010 to December 2023 were included. Key demographic, clinical, and transplant-related variables were analyzed. Outcomes were assessed using Kaplan-Meier survival curves and multivariable Cox proportional hazards models.

Results: Among 474 pediatric recipients, basiliximab-treated patients demonstrated superior composite outcome-free survival compared to those receiving rATG (85% vs. 68% at one year, P < 0.001). The rATG group exhibited significantly higher rates of delayed graft function (12% vs. 2.7%, P < 0.001) and acute rejection episodes. Multivariable analysis confirmed that rATG recipients faced nearly twice the risk of adverse outcomes compared to their basiliximab counterparts (HR: 1.63, 95% CI: 1.05–2.54).

Conclusions: The findings highlight the clinical advantages of basiliximab over rATG in pediatric kidney transplantation, particularly in improving graft longevity and minimizing complications. This emphasizes the need for tailored induction therapy based on immunologic risk profiles, positioning basiliximab as a safer and more effective option for pediatric patients.

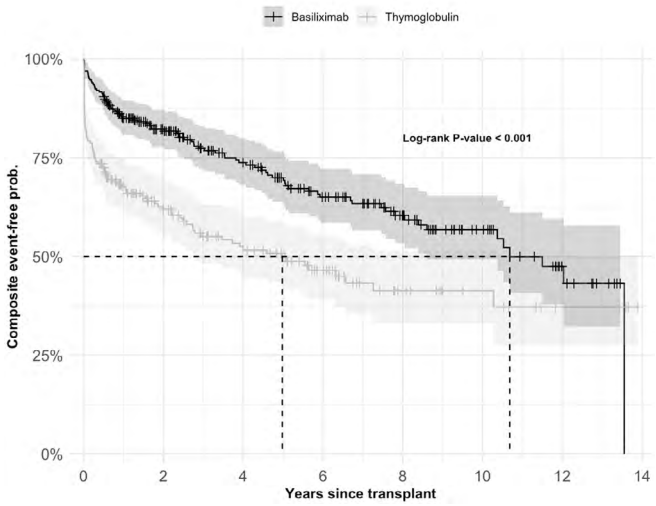

Figure 1: Composite-outcome free Kaplan-Meier Curve for induction groups.

	Composite outcome adjusted HR (95% CI)		
	Adjusted for demographics	Adjusted for disease etiology	Adjusted for transplant characteristics
Basiliximab	Reference	Reference	Reference
Thymoglobulin	1.94 (1.45-2.59)	1.83 (1.33-2.53)	1.63 (1.05-2.54)

Table 1: Multivariable modeling examining induction type and composite outcome

PP_475 "ON-DEMAND" TACROLIMUS-LOADED DRUG DELIVERY EXTENDS GRAFT SURVIVAL IN A VCA LARGE ANIMAL MODEL

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Background: Vascularized Composite Allotransplantation (VCA) has revolutionized the restoration of complex tissue loss. However, the lack of immunosuppressive regimens with fewer side effects has hindered widespread clinical use. Traditional systemic immunosuppression carries significant risks, highlighting the need for targeted, localized drug delivery approaches. This study aims to improve graft survival by employing an on-demand, localized tacrolimus-loaded drug delivery system (TAC-DDS) that could potentially reduce off-target effects and maintain graft survival.

Methods: SLA-mismatched pigs underwent a osteomyocutaneous flap as a representative VCA model. Animals were divided into three groups: 1) Untreated controls, 2) those receiving a single dose of TAC-DDS, and 3) those receiving multiple TAC-DDS administrations. After surgery, animals were monitored regularly until either grade III rejection or post-operative day (POD) 90. Blood and tissue samples were collected at predefined intervals to assess the distribution of TAC in the graft and markers of systemic toxicity, such as liver and kidney function.

Results: As expected, untreated pigs in group 1 exhibited grade IV rejection within 8 days. In contrast, group 2 animals showed significantly prolonged graft survival, with a median survival time of 45 days (range: 34-60 days). Most notably, all animals in group 3 survived up to POD90. Tissue analysis confirmed that TAC levels were higher in the graft than in contralateral tissue, indicating successful localized drug delivery. Kidney and liver function markers remained stable in group 2, while group 3 showed a slight increase in creatinine. However, this elevation was not associated with histological evidence of kidney or liver toxicity.

Conclusions: This study demonstrates that a single administration of a tacrolimus-loaded DDS can significantly extend graft survival in a porcine VCA model. Repeated DDS administration maintained graft survival through the study's endpoint. The sustained survival may be due to higher localized concentrations of TAC within the graft. These findings suggest that on-demand, localized immunosuppression may be a promising alternative to conventional systemic approaches in VCA, potentially reducing systemic toxicity while maintaining graft function.

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PP_476 GENE EXPRESSION PROFILE IN PANCREAS TRANSPLANTATION

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Background: Blood based molecular biomarkers present good accuracy to predict short-term outcomes in kidney transplantation. We explored the ability of gene expression profile (GEP) to correlate with short-term pancreas transplant outcomes or to predict pancreas graft rejection.

Methods: In a cross-sectional study, we analyzed blood gene expression profile (GEP) in 75 pancreas biopsy-matched plasma samples from pancreas transplant recipients using Trugraf. In a subset of 38 paraffin embedded samples we correlated plasma GEP with graft transcript gene signatures using the Banff Human Organ Transplant (B-HOT) NanoString panel.

Results: Blood GEP overall sensitivity for the diagnosis of P-BPAR was 74.1%, with a specificity of 83.3%, and a negative predictive value (NPV) of 86.7%. GEP performance improved in biopsies performed for cause (NPV 91%) and for the diagnosis of pancreas subclinical rejection (specificity 86.1%). There were no differences in GEP result according to type of rejection (Indeterminate, TCMR, or ABMR) or the location of inflammation within the graft (ducts, septal, or acinar area). Graft transcripts analysis demonstrated an overexpression of interferon gamma (IFN-γ) superfamily, IL7R, SERPINE1, LN2, and TNFRSF17, in patients with a positive Trugraf (No-TX). Gene enrichment analyzes highlighted an increase of genes associated with TCR signaling, CD28 family activation, IFN-γ signaling, and phagosome pathway in patients with No-TX. Furthermore, a positive Trugraf was associated with an overexpression of immune cell-related genes, namely CD8+ T cells, macrophages, and plasma cells ($p<0.05$). Tissue common response module (tCRM) score was higher in patients with a positive GEP result. Conversely, Trugraf predicted grafts' tCRM score, with an AUC of 0.71 (95% CI 0.55-0.88; p=0.02).

Conclusions: These results unveil the utility of blood GEP as a noninvasive alternative to tissue biopsy for diagnosis of pancreas graft rejection, and its ability to depict pancreas inflammatory activity. Blood GEP may be useful for the identification of subclinical and T-cell mediated rejections and to help individualize immunosuppression therapy.

PP_478 STRATEGIES TO MANAGE DONOR-SPECIFIC ANTIBODIES IN DECEASED-DONOR KIDNEY TRANSPLANT: DELISTING AND DESENSITIZATION

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Background: Delisting and post-transplant desensitization are strategies implemented to improve access to deceased donor kidney transplants, for patients with high immunological risk.

Methods: We studied patients with high immunological risk (cPRA ≥ 98%) with preformed donor-specific antibodies (DSAs), and analyzed the results of patients who underwent post-transplant desensitization vs. patients who did not require desensitization. Thymoglobulin and Methylprednisolone were used for induction, plus maintenance therapy with Tacrolimus, mycophenolic acid derivatives and Prednisone. Post-transplant desensitization was performed in patients with two or more DSA, with MFI > 1500; or a single DSA, with MFI > 3000. The desensitization protocol consisted of Plasmapheresis (PF), Immunoglobulin (IVG) post-plasmapheresis, and Rituximab 375 mg/m2.

Results: We studied 46 patients with high immunological risk. Sixteen of them presented positive preformed DSA, with negative CDC crossmatch; and 7 required post-transplant desensitization. The cPRA was higher in the desensitization group with 99.71 ± 0.49 vs. 99.22 ± 1.30 in the non-desensitized group (p=0.22), as well as the MFI mean of preformed DSAs with 6011.71 ± 2838.56 vs. 2125 ± 1404.84 (p=0.055) respectively. The staying period at the hospital was longer for the desensitization group, with a mean of 42 ± 24 days vs. 25 ± 16 days (p=0.33).Two cases of Acute Rejection were observed in the desensitization group (1 case of Mixed Acute Rejection and 1 case of Antibody-mediated Rejection) vs. 3 cases of Antibody-mediated Acute Rejection in the non-desensitization group (p= 0.608). All patients with acute rejection had a favorable response to treatment. The mean creatinine at 3 months was slightly lower in the desensitization group (Cr 1.45 ± 0.44 versus 1.72 ± 0.39) (p=0.79); proteinuria was similar in both groups (p=0.36). No significant differences were found for infections such as CMV or BK. Two patients required surgical re-intervention in the desensitization group, versus 1 case in the other group (p=0.4).

Conclusions: Delisting and desensitization of patients with preformed DSA are feasible options to improve access to renal transplantation for hyperimmunized patients, with acceptable results despite the immunological and infectious risks.

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PP_479 DECODING EARLY TRANSPLANT GRAFT BIOPSIES - A TRANSCRIPTOMIC ANALYSIS OF EARLY PANCREAS ACUTE REJECTION

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Background: Pancreas transplantation presents one of the highest acute rejection incidences among abdominal solid organ transplants. Acute rejection is most frequent during the first year post-transplant. The underlying mechanisms driving this phenomenon remain poorly understood in pancreas transplantation. Herein we aimed to investigate the molecular characteristics of early pancreas graft rejection

Methods: We conducted a transcriptomic analysis of formalin-fixed, paraffin-embedded (FFPE) pancreatic biopsies collected within 60 days post-transplant (n = 20). Samples were categorized into two groups based on histological assessment: acute rejection group (n=13) - T cell-mediated rejection (TCMR) n=9; antibody-mediated rejection (ABMR) n=2, and undetermined for rejection type (ND) n=2; and a no-rejection group (n=7). Transcriptomic profiling was performed using the NanoString Banff-Human Organ Transplant (B-HOT) panel. Data were analyzed using nSolver Analysis Software.

Results: In an unsupervised analysis most acute rejection samples were clustered separately to no rejection. A total of 117 genes were found to be significantly differentially expressed between the two study groups. Among these, 86 genes, including CCL18, IL7R, CD163, KLRK1, and CD3D, were overexpressed in the rejection group. In contrast, 31 genes, such as RORC, ALDH3A2, and RASIP1, were underexpressed in this group. Pathway analysis revealed heightened activity of adaptive and innate immune system pathways in the rejection group compared to the no-rejection group. Tissue common rejection model (tCRM) gene score was higher in acute rejection group. Additionally, increased activity was observed in cytotoxicity and T cell receptor signalling pathways. Rejection samples demonstrated a higher presence of B cells and T cells, particularly CD8+ T cells, along with other cytotoxic cells and macrophages.

Conclusions: These findings highlight distinct molecular and cellular features associated with early pancreas graft rejection, characterized by increased immune pathway activity and the presence of cytotoxic and immune effector cells. Gene expression analysis in early graft biopsies may aid in the refinement of diagnostic criteria between ischemia-reperfusion injury and acute rejection.

PP_480 WHY GIVE TWO, WHEN ONE WILL DO- BASILIXIMAB, IS THERE A NEED FOR A SECOND?

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Background: Induction therapy with the IL2- receptor antagonist (IL-2RA) Basiliximab (BXB) with reduced, delayed introduction of tacrolimus (Tac) is associated with a beneficial effect in both mid and long-term (12 month) renal function (RF) and recommended in patients (pts) with pre- liver transplant (LT) renal dysfunction. The relatively high cost of this Novartis agent, combined with manufacturing shortages emphasises the importance of ensuring pt cohorts are appropriately selected. A retrospective audit of BXB in pts undergoing LT against Leeds Liver Unit guidelines: • *Combined liver and kidney recipients (SLK).* • *Baseline eGFR ≤50 or Creatinine ≥150umol/L Consider also in pts (versus delaying introduction of tac to day 2).* - *Rise of creatinine of 50 µmol/l from baseline in the 1st 24 hours Oliguria <0.5mls/kg/hr, unresponsive to fluid challenge.* • *Second dose (day 4) BXB was indicated if RF had not improved.* • *Not recommended in pts on CVVHd post LT.* Tac introduction from day 5 is recommended post BXB and switching Azathioprine (AZA) to Mycophenolate Mofetil (MMF).

Methods: All BXB use between 01.09.22 and 31.08.24 were reviewed. Data was collected from the hospital electronic patient record and compared against the guidance above.

Results: Data was collected on 224 LT. 86 pts (38.3%) received BXB; 20/86 received IL2RA whilst on CVVHd. 26/66 (39.39%) received 1 dose, 4/26(15.38%) did not meet criteria for induction. 40-pts received 2 doses; all met criteria for 1st dose but 25/40(62.5%) did not meet the criteria for 2nd dose. AZA to MMF switch occurred in 77% of patients receiving 1 dose and 75% receiving 2 doses BXB. Table demonstrates the post op day (POD) that tac was introduced vs no. of doses of BXB.

Conclusions: Our audit suggests overuse of BXB in LT pts. There was poor compliance with the guideline regarding use of the 2nd dose. In pts receiving 2 doses, tac was introduced in 37 pts prior to POD 7, with tac introduced in 15 pts prior to dose 2 been given, suggesting BXB is not being used appropriately with regards to enabling a delayed introduction of tac. These results warrant discussion about the use of BXB from a waste reduction perspective especially due to its relatively high-cost burden.

Doses of BXB	Tac introduced					
	POD 2	POD 3	POD 4	POD 5	POD 6	POD 7
1	5(19.2%)	14(53.8%)	3(11.5%)	3(11.5%)	1(3.8%)	-
2	-	2(5%)	13(32.5%)	18(45%)	4(10%)	3(7.5%)

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PP_481 IMPACT OF NATIVE LUNG DISEASE AND TORQUE TENO VIRUS (TTV) ON POST-LUNG TRANSPLANTATION OUTCOMES: A RETROSPECTIVE REVIEW

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Background: Torque Teno Virus (TTV) is a common viral infection that has been implicated in monitoring immunosuppression after solid organ transplantation. However, the potential influence of native lung disease on TTV levels and their impact on post-lung transplantation outcomes remains unclear.

Methods: We conducted a retrospective review of 364 lung transplant recipients who received alemtuzumab induction and calcineurin inhibitor-based immunosuppression between January 2018 and December 2022. TTV viral loads were routinely monitored during follow-up (average 2-3 times per month), and transplant outcomes were tracked until April 2024. Data were analyzed to assess the relationship between native lung disease, TTV levels, and post-transplant outcomes.

Results: Mean TTV levels varied by underlying lung disease. Patients with obstructive lung disease had a mean TTV of 1.025 × 10^9 copies/mL (95% CI: 7.397 × 10^8 - 1.421 × 10^9, N = 155), while those with restrictive LD had 6.527 × 10^8 copies/mL (95% CI: 4.491 × 10^8 - 9.486 × 10^8, N = 111). Cystic fibrosis patients had 7.631 × 10^8 copies/mL (95% CI: 4.470 × 10^8 - 1.303 × 10^9, N = 35), and pulmonary hypertension (PH) had the lowest at 4.511 × 10^8 copies/mL (95% CI: 7.457 × 10^7 - 2.729 × 10^9, N = 10). The highest TTV levels were seen in acute respiratory distress syndrome (ARDS), with a mean of 3.032 × 10^9 copies/mL (95% CI: 1.722 × 10^9 - 5.340 × 10^9, N = 24). No significant differences in TTV levels were observed in patients with COPD, lung fibrosis, or bronchiectasis.

Conclusions: Native lung disease does not appear to significantly influence TTV viral load or post-transplant outcomes, except in ARDS patients, who exhibit elevated TTV levels during the early post-transplant period. This suggests that ARDS may impact the immunological environment in lung transplant recipients over time. Further prospective studies are needed to clarify the role of TTV in guiding post-transplant management and its potential as a prognostic biomarker.

PP_482 THE CHALLENGE OF RENAL TRANSPLANTATION IN THE PRESENCE OF ANTI-CD36 ANTIBODIES

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Background: A highly sensitised 48-year-old African male (calculated reaction frequency, 94% following two previous kidney transplants and transfusions) received multiple deceased kidney donor offers with unexpected strong positive flow cytometry (FC) crossmatch (XM) results in the absence of HLA donor-specific antibodies (DSA). Additional testing identified anti-CD36 antibodies.

Methods: The Luminex-based Pak Lx Assay (Werfen) (PLX) and the Monoclonal Antibody Immobilisation of Platelet Antigen (MAIPA) assay were used to test selected patient samples and assess anti-CD36 antibody titre. FC was used to evaluate CD36 expression. Next Generation Sequencing (NGS) of the CD36 gene for the patient and two previous donors was performed. The patient had a trial of 3 high-volume double filtration plasmapheresis (DFPP) sessions with CD36 antibody levels monitored using PLX.

Results: Genetic testing and FC expression analysis confirmed the patient has Type I CD36 deficiency. FCXM using third-party T and B lymphocytes with confirmed CD36 expression, correlated with previous deceased donor xm results. Figure 1 illustrates the patients CD36 antibody profile at selected time points, with a marked increase following the second kidney transplant. The antibody titre in September 2024 was > 1:256. DFPP treatment did not result in any marked decrease in antibody MFI.

Conclusions: The unexpected positive FCXM results were due to the high titre anti-CD36 antibody, in the patient who is CD36 deficient. CD36 is a transmembrane glycoprotein receptor expressed on a variety of cells, including lymphocytes, platelets and renal endothelial cells. CD36 antibodies are implicated in several clinical conditions including immune-mediated thrombocytopenia. The significance in renal transplantation is unknown; to our knowledge there are no publications of CD36 antibodies in kidney transplant recipients. The high antibody titre and trial of DFPP has shown that it is unlikely that antibody removal would achieve a negative FCXM. CD36 deficiency varies by ethnic groups, with higher prevalence in Asians (up to 6.8%) and Africans (4.8%) compared to Caucasians (0.3%). Given the deceased donor population in the UK, this makes the likelihood of a CD36 negative donor offer extremely low.

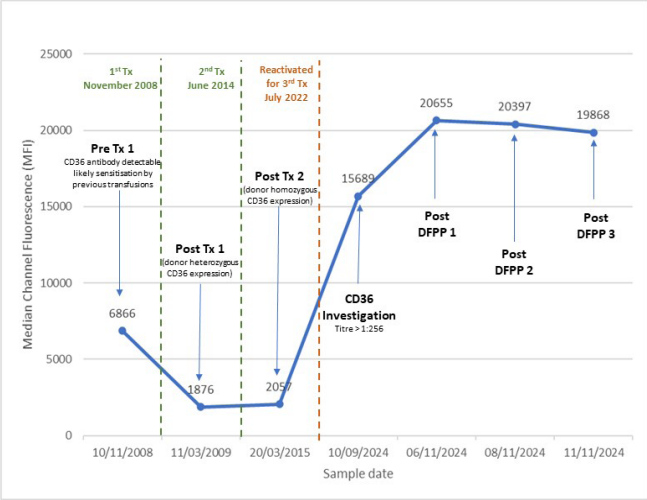

Figure 1: Results of CD36 antibody testing using the Luminex based Pak-LX assay, at selected time points pre and post transplantation (tx), and following three double filtration plasmapheresis (DFPP) sessions

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Transplant immunology & immunosuppression

PP_483 DECODING ACUTE REJECTION-INDUCED ISLET INJURY IN PANCREAS TRANSPLANTATION

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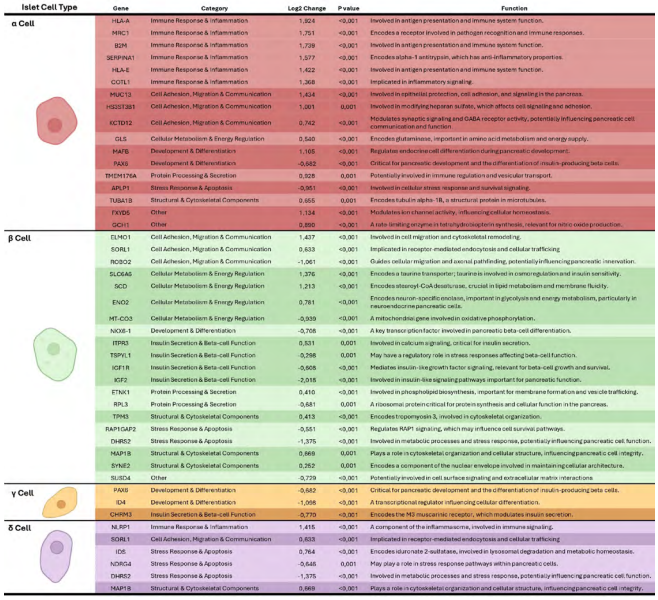
Background: Acute rejection in pancreas transplantation is associated with a reduction in long-term graft survival. At the histological evaluation, endocrine pancreas (islets) inflammation is seldom observed, but islet cell damage, and occasional islet necrosis may occur in T cell mediated rejection (TCMR) and antibody mediated rejection (ABMR). In this study, we leveraged to explore the relation between acute rejection and islet injury through molecular analysis.

Methods: Bulk RNA sequencing was performed from 33 pancreas graft biopsies (No rejection: n=11; T cell-mediated rejection: n=22), including both for-cause and surveillance biopsies. Whole tissue RNA was extracted from formalin-fixed paraffin-embedded (FFPE). Non-coding genes were excluded from the analysis. Differentially expressed islet-specific genes were cross-referenced with a predefined islet α, β, γ, and δ cell-specific geneset (n=260 genes, scPancMeta).

Results: Of the 16,743 coding genes sequenced, 247 aligned with the pancreas-specific geneset, and 80 were significantly differentially expressed across islet cell types. In α cells, overexpression of cell adhesion and communication genes (MUC13, KCTD12, HS3ST3B1), while underexpression of developmental and stress response genes (PAX6, APLP1) suggested disruptions in adhesion and differentiation. β cells displayed underexpression of insulin signaling genes (IGF1R, ITPR3), critical for insulin secretion, and overexpression of stress response genes (DHR52, RAP1GAP2), reflecting adaptation to stress. δ cells showed most prominently underexpression of stress response genes (DHRS2, NDRG4) and overexpression of structural genes (MAP1B), highlighting structural vulnerability.

Conclusions: These findings unveil a prominent islet injury phenotype during pancreas T cell mediated rejection. Further studies are warranted to understand the pathways involved in islet-induced injury and its impact on graft survival.



Islet Cell Type	Gene	Category	Log2 Change	P value	Function
α Cell	HLA-A	Immune Response & Inflammation	1,924	<0,001	Involved in antigen presentation and immune system function.
	MRC1	Immune Response & Inflammation	1,751	<0,001	Encodes a receptor involved in pathogen recognition and immune responses.
	B2M	Immune Response & Inflammation	1,739	<0,001	Involved in antigen presentation and immune system function.
	SERPINA1	Immune Response & Inflammation	1,577	<0,001	Encodes alpha-1 antitrypsin, which has anti-inflammatory properties.
	HLA-E	Immune Response & Inflammation	1,422	<0,001	Involved in antigen presentation and immune system function.
	CCTL1	Immune Response & Inflammation	1,368	<0,001	Implicated in inflammatory signaling.
	MUC13	Cell Adhesion, Migration & Communication	1,424	<0,001	Involved in epithelial protection, cell adhesion, and signaling in the pancreas.
	HS3ST3B1	Cell Adhesion, Migration & Communication	1,001	0,001	Involved in modifying heparan sulfates, which affects cell signaling and adhesion.
	KCTD12	Cell Adhesion, Migration & Communication	0,742	<0,001	Modulates synaptic signaling and GABA receptor activity, potentially influencing pancreatic cell communication and function.
	GLS	Cellular Metabolism & Energy Regulation	0,540	<0,001	Encodes glutaminase, important in amino acid metabolism and energy supply.
	MAFB	Development & Differentiation	1,105	<0,001	Regulates endocrine cell differentiation during pancreatic development.
	PAX6	Development & Differentiation	-0,662	<0,001	Critical for pancreatic development and the differentiation of insulin-producing beta cells.
	TMEM176A	Protein Processing & Secretion	0,928	0,001	Potentially involved in immune regulation and vesicular transport.
	APLP1	Stress Response & Apoptosis	-0,951	<0,001	Involved in cellular stress response and survival signaling.
	TUBA1B	Structural & Cytoskeletal Components	0,655	0,001	Encodes tubulin alpha-1B, a structural protein in microtubules.
	FXYD5	Other	1,134	<0,001	Modulates ion channel activity, influencing cellular homeostasis.
	GCH1	Other	0,890	<0,001	A rate-limiting enzyme in tetrahydrobiopterin synthesis, relevant for nitric oxide production.
β Cell	ELMO1	Cell Adhesion, Migration & Communication	1,437	<0,001	Involved in cell migration and cytoskeletal remodeling.
	SORL1	Cell Adhesion, Migration & Communication	0,633	<0,001	Implicated in receptor-mediated endocytosis and cellular trafficking.
	ROBO2	Cell Adhesion, Migration & Communication	-1,061	<0,001	Guides cellular migration and axonal pathfinding, potentially influencing pancreatic innervation.
	SLC6A6	Cellular Metabolism & Energy Regulation	1,376	<0,001	Encodes a taurine transporter; taurine is involved in osmoregulation and insulin sensitivity.
	SCD	Cellular Metabolism & Energy Regulation	1,213	<0,001	Encodes stearoyl-CoA desaturase, crucial in lipid metabolism and membrane fluidity.
	ENO2	Cellular Metabolism & Energy Regulation	0,781	<0,001	Encodes neuron-specific enolase, important in glycolysis and energy metabolism, particularly in neuroendocrine pancreatic cells.
	MT-CO3	Cellular Metabolism & Energy Regulation	-0,939	<0,001	A mitochondrial gene involved in oxidative phosphorylation.
	NKX6-1	Development & Differentiation	-0,708	<0,001	A key transcription factor involved in pancreatic beta-cell differentiation.
	ITPR3	Insulin Secretion & Beta-cell Function	0,531	0,001	Involved in calcium signaling, critical for insulin secretion.
	TSPYL1	Insulin Secretion & Beta-cell Function	-0,298	0,001	May have a regulatory role in stress responses affecting beta-cell function.
	IGF1R	Insulin Secretion & Beta-cell Function	-0,608	<0,001	Mediates insulin-like growth factor signaling, relevant for beta-cell growth and survival.
	IGF2	Insulin Secretion & Beta-cell Function	-2,015	<0,001	Involved in insulin-like signaling pathways important for pancreatic function.
	ETNK1	Protein Processing & Secretion	0,410	<0,001	Involved in phospholipid biosynthesis, important for membrane formation and vesicle trafficking.
	RPL3	Protein Processing & Secretion	0,681	0,001	A ribosomal protein critical for protein synthesis and cellular function in the pancreas.
	TPM3	Structural & Cytoskeletal Components	0,413	<0,001	Encodes tropomyosin 3, involved in cytoskeletal organization.
	RAP1GAP2	Stress Response & Apoptosis	-0,551	<0,001	Regulates RAP1 signaling, which may influence cell survival pathways.
	DHRS2	Stress Response & Apoptosis	-1,375	<0,001	Involved in metabolic processes and stress response, potentially influencing pancreatic cell function.
	MAP1B	Structural & Cytoskeletal Components	0,669	0,001	Plays a role in cytoskeletal organization and cellular structure, influencing pancreatic cell integrity.
	SYNE2	Structural & Cytoskeletal Components	0,252	0,001	Encodes a component of the nuclear envelope involved in maintaining cellular architecture.
	SLISD4	Other	-0,729	<0,001	Potentially involved in cell surface signaling and extracellular matrix interactions.
γ Cell	PAX6	Development & Differentiation	-0,662	<0,001	Critical for pancreatic development and the differentiation of insulin-producing beta cells.
	ID4	Development & Differentiation	-1,066	<0,001	A transcriptional regulator influencing cellular differentiation.
	CHRM3	Insulin Secretion & Beta-cell Function	-0,770	<0,001	Encodes the M3 muscarinic receptor, which modulates insulin secretion.
δ Cell	NLRP1	Immune Response & Inflammation	1,415	<0,001	A component of the inflammasome, involved in immune signaling.
	SORL1	Cell Adhesion, Migration & Communication	0,633	<0,001	Implicated in receptor-mediated endocytosis and cellular trafficking.
	IDS	Stress Response & Apoptosis	0,764	<0,001	Encodes iduronate 2-sulfatase, involved in lysosomal degradation and metabolic homeostasis.
	NDRG4	Stress Response & Apoptosis	-0,646	0,001	May play a role in stress response pathways within pancreatic cells.
	DHRS2	Stress Response & Apoptosis	-1,375	<0,001	Involved in metabolic processes and stress response, potentially influencing pancreatic cell function.
	MAP1B	Structural & Cytoskeletal Components	0,669	<0,001	Plays a role in cytoskeletal organization and cellular structure, influencing pancreatic cell integrity.

PP_484 LEVELS OF CIRCULATING MICROVESICLES IN PATIENTS WITH CARDIAC TRANSPLANT REJECTION

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Background: Endomyocardial biopsy (EMB) is the "gold" standard for diagnosing cardiac allograft rejection. There is a high demand for non-invasive methods to exclude rejection. The aim was to determine the relationship between the level and composition of microvesicles (MVs) and the presence of rejection.

Methods: From January 2022 to December 2024 43 heart transplant patients (74%, n=32 - male) were enrolled in the study and based on the EMB results they were divided into 2 groups: group №1 – without rejection (47%, n=20), group №2 – with acute rejection (53%, n=23). Recipients from the 1st group were 47±12-year-old and were 1429 [726;1967] days after heart transplantation (HTx), p>0.05. Those included in the group №2 were 53±11-year-old with 1651 [604; 2418] days after HTx. Standard immunosuppressive therapy was prescribed to all of them: Tacrolimus, Mycophenolic acid and steroids; in long-term Mycophenolic acid was switched to Everolimus in case of developing complications (i.e. allograft vasculopathy and cancer development). Peripheral blood sampling for MVs analysis was performed in all patients, the size and concentration of extracellular vesicles in the blood plasma were assessed by nanoparticle trajectory analysis on a NanoSight NS3000 device (Malvern, UK), and phenotyping was performed using fluorescently labeled antibodies and highly sensitive flow laser cytometry on a Cytoflex S flow laser cytometer (Beckman Coulter, USA). The study was supported by a grant from the RSF № 24-15-20016 and by a grant from the SPbSF (№ 24-15-20016 by 24 May 2024).

Results: Both groups did not differ significantly in age, sex, causes of heart failure and time of follow-up after heart transplantation, comorbidities, results of biochemical blood test parameters and transthoracic echocardiography. When assessing MVs positive for tetraspanin, platelet and endothelial markers, a significant increase (p=0.009) in the level of CD90+ MVs was revealed in the group №1 compared to the 2nd: 2017.5 [8.0; 14225.0] events/ml and 3.4 [0.5; 181.1] events/ml, respectively.

Conclusion: Long-term after HTx high levels of CD90+ MVs in the peripheral blood of heart recipients are associated with the absence of allograft rejection. The level of CD90+ MVs may be a potential marker for non-invasive assessment of acute heart transplant rejection.

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PP_485 EXTENDING REJECTION-FREE SURVIVAL IN VCA WITH COMBINATION B AND T CELL DEPLETING INDUCTION IMMUNOSUPPRESSION

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Background: Face VCA transplantation has become a transformative option for patients with severe facial disfigurement. Graft rejection remains a significant challenge in maintaining long-term transplant success. In this study, we seek to evaluate the validity of our institutional immunosuppressive protocols, the efficacy of our rescue immunosuppression, and the need for long-term monitoring of key hematologic immune markers, with the goal of elucidating mechanisms of acute rejection (AR) in our patient cohort.

Methods: This retrospective study included 4 patients who underwent face containing VCA with rituximab induction at NYU Langone Health from 2015 to 2024. All patients received both T-Cell and B-cell depletion with thymoglobulin and rituximab, followed by standard triple maintenance immunosuppression. Rejection was monitored via clinical assessment, histopathology, blood sampling, and donor-specific antibody (DSA) levels, with data analyzed using a linear mixed-effects model.

Results: Median time to initial rejection in our cohort was 536 days. AR related transient DSA was seen at POD 1465 for patient 1, POD 450 for patient 2, and none for patients 3 and 4. Statistical significance was not found between clinically treated episodes of rejection and DSA levels on linear effects modeling. Further stratification with postoperative day and tacrolimus as a random effectors demonstrated that none of the previously mentioned DSA subsets were significantly upregulated during rejection. 1 pt has been free of rejection at 18 months, 1 pt has had a single AR in 7 yrs, 1 pt with 2 AR in 9 yrs, and 1 with multiple AR in 4.5yrs.

Conclusions: Our median time to first rejection is 1.5yrs. This is significantly longer than the typical time to first rejection in VCA, 85% of which typically occur within 6-12 months. These results suggest that our institutional combination T and B-cell depleting induction regimen delays the time to first rejection episode as well as overall number of rejections. De novo DSA was not associated with most rejection episodes in our cohort. Resident donor mature B lymphocytes may play a role in acute rejection episodes in skin containing VCA, especially in the early post-transplant period. Further studies are needed to assess the efficacy of our immunosuppression in differing transplant scenarios.

PP_486 MACHINE LEARNING APPROACHES TO IDENTIFY KEY TIME-POINTS MEASUREMENT OF HLA-DSA FOLLOWING AIT

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Background: In HLAi transplantation, monitoring donor-specific antibodies (DSA) post-transplantation aids decision-making and managing antibody mediated rejection (AMR). However, when, and how often this is required is not well established leading to huge variation in practice and usually unnecessary testing adding pressure on resources and is often unsustainable. In our previous work, using unsupervised clustering experiment, we defined five dynamic patterns from regular posttransplant DSA monitoring (up to 50 time points) and linked to the outcome and AMR (Phillpott, et al. 2022). Using this dataset, predicting DSA dynamics from a minimum number of tests would contribute to effective DSA monitoring practice is described in this paper.

Methods: 88 patients who underwent HLA-incompatible kidney transplantation who had their HLA-DSA monitored frequently up to 50 days following transplantation were included. A machine learning classification algorithm based on dynamic time wrapping () was utilized to predict the DSA patterns. The algorithm systematically tested various single-day measurement and their combinations. The combinations of days yielding the highest prediction accuracy were considered critical for DSA monitoring. We also compared the current regimen reported in literature.

Results: DSAs measured on days 1, 10, and 26 (or 34) predict the dynamic pattern with 93.7% accuracy; keeping both days (26 and 34) improved accuracy to 96.9%. Testing beyond day 34 did not yield any additional improvement. Various regimens commonly reported in clinical practice (Table 1, A-F) were also assessed and our setting (G, H) outperformed all.

Conclusions: DSA dynamic group can be accurately predicted with three monitoring points (days 1, 10, 26, or 34), optimizing DSA monitoring and improving post-transplant care. This will allow more sustainable approach in safe monitoring and evaluation of such high risk cases.

Reported regimen	monitoring days	Prediction accuracy %
A	3,7,14,28	84.4
B	1to14,17,18,20,22,27,30	95.3
C	1,8,15,22	84.4
D	1,7,30	87.5
E	4,7,14,30	84.4
F	1-3,7,14,21,28	92.2
G	1,10,26 or 34	93.7
H	1,10,26,34	96.9

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PP_487 IS LOW SERUM C3 A RELIABLE BIOMARKER FOR SUSPECTED COMPLEMENT-MEDIATED TMA IN KIDNEY TRANSPLANTS?

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Background: Recently, a growing number of transplant candidates with unknown causes of end-stage kidney disease (ESKD) and with unclear medical history and genetic abnormalities are regarded as suspicious cases of complement-mediated thrombotic microangiopathy (S-cTMA) that may recur post-transplantation. In such instances, isolated low serum C3 with normal serum C4 (LowC3) is often used as biomarker for S-cTMA diagnosis and for S-cTMA post-transplant monitoring. At our center, serum C3/C4 is part of the standard work-up for wait-listing and post-transplant monitoring. We, therefore, performed a retrospective study to test whether LowC3 is a useful biomarker in this setting.

Methods: We retrospectively followed-up all transplant candidates and recipients who had available C3/C4 data at Parma University Hospital, Parma, Italy, between Sep 2022 and Feb 2024. We divided them into LowC3 and Others. In transplant candidates, we examined cross-sectional associations with principal component analysis (PCA), biplots and two-sample tests. In transplant recipients, we used mixed-effects random-coefficients models to compare differences in the post-transplant time trend of graft function (eGFR) and other relevant lab data.

Results: Among 216 candidates, 61 (28.2%) belonged to the LowC3 group. Neither group showed any significant association of C3 levels with Hb, PTL count, or elevated LDH (**Figure 1A**). In contrast, regardless of group membership, serum C3 correlated with serum C4 (P=0.002). In the 116 patients who underwent kidney transplantation, 46 (39%) were LowC3. In longitudinal analyses, there was no difference between the two groups in the change of eGFR, Hb, LDH, PLT count, serum C3, macrohematuria or proteinuria (interaction test between time and laboratory variable, P > 0.05) (eGFR and Hb in **Figure 1B**).

Conclusions: Low serum C3 is not a reliable biomarker for transplant candidates or recipients with suspicious cTMA.

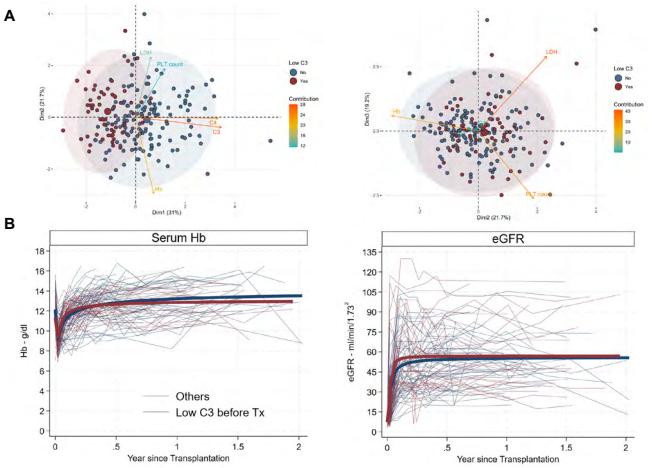

Figure 1 (A-B).

PP_488 IMPACT OF IMMEDIATE-RELEASE VS. EXTENDED-RELEASE TACROLIMUS ON TREMOR SEVERITY IN LUNG TRANSPLANT RECIPIENTS: AN RCT

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Background: Tremor is a common dose-dependent side effect of tacrolimus in lung transplant recipients (LTR) and is associated with a lower health-related quality of life. We hypothesized that a once-daily extended-release (LCP) tacrolimus preparation, with its lower peak concentration, may cause less severe tremor over time compared to twice-daily immediate-release (IR) tacrolimus.

Methods: This prospective randomized controlled trial (NCT05001074) had a follow up of 2 years. Clinically stable lung transplant recipients >1 year after transplantation who were on a stable dose of IR tacrolimus were randomized to continue IR tacrolimus or to switch to LCP tacrolimus. Tremor severity was objectively assessed with the Fahn-Tolosa-Marin Tremor Rating Scale Part B (TRS-B) and subjectively with a visual analogue scale (VAS), both resulting in a unitless score, where a higher score indicates more severe tremor. Repeated measures generalized estimating equation (GEE) models were used to analyze differences between groups over time.

Results: We included 68 LTR (29 females) with a median [IQR] age of 61.8 [44.8-66.5] years at a median time after transplantation of 4.6 [2.0-7.4] and 4.8 [2.0-7.7] years for the IR and LCP tacrolimus group, respectively. Over 2 years, the objective tremor severity increased by 1.2 (0.1 to 2.3; p=0.023) in the IR group versus virtually no increase of 0.2 (-1.7 to 2.0; p=1.0) for the LCP group. The rate of change of change over time was not statistically different between the groups (p=0.3; **Figure 1**). The subjective tremor severity declined by 4.9 (-5.3 to 15.2; p=1.0) in the IR group and by 6.3 (-3.5 to 16.0; p=1.0) in the LCP group. The rate of change over time was not statistically different between the groups (p=1.0; **Figure 1**). Objective and subjective tremor scores per groups and the corresponding pairwise comparison analyses at each timepoint are shown in **Table 1**.

Conclusions: Switching from IR tac to LCP tacrolimus had no significant effect on objective nor subjective tremor severity in our study in 75 lung transplant recipients.

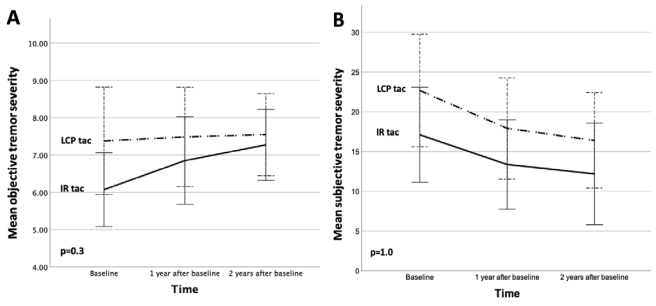

Figure 1 | Mean objective (**A**) and subjective (**B**) tremor severity over time compared between immediate-release (IR) tacrolimus and extended-release (LCP) tacrolimus in 68 lung transplant recipients. The p-value represents the significance of difference between the groups over time as assessed with a repeated measures generalized estimating equation model. Tremor was objectively measured with the Fahn-Tolosa-Marin Tremor Rating Scale Part B, and subjectively with a visual analogue scale.

Table 1 | Mean objective and subjective tremor severity score and differences between groups that use either immediate-release or extended-release tacrolimus in 68 lung transplant recipients.

	IR tacrolimus (n=35)	LCP tacrolimus (n=33)		
	Mean (95% CI) score	Mean (95% CI) score	Mean (95% CI) difference between groups	P-value
Objective tremor score				
Baseline	6.1 (5.2-7.1)	7.4 (6.1-8.9)	1.3 (-1.2 to 3.8)	1.0
1 year after baseline	6.9 (5.8-8.0)	7.5 (6.3-8.9)	0.6 (-2.1 to 3.1)	1.0
2 years after baseline	7.2 (6.4-8.2)	7.5 (6.6-8.7)	0.3 (-1.8 to 2.3)	1.0
Subjective tremor score				
Baseline	17.1 (12.3-23.9)	22.7 (16.9-30.5)	5.6 (-7.6 to 18.7)	1.0
1 year after baseline	13.4 (9.0-19.9)	17.9 (12.8-25.0)	4.5 (-7.5 to 16.5)	1.0
2 years after baseline	12.2 (7.4-20.0)	16.4 (11.6-23.2)	4.2 (-8.2 to 16.6)	1.0

Abbreviations: IR: immediate-release; LCP: extended-release; CI: confidence interval. The p-value indicates the Bonferroni-adjusted significance of the pairwise comparison between groups.

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PP_489 THE EFFECT OF SOCIOECONOMIC DEPRIVATION ON OUTCOMES AFTER KIDNEY TRANSPLANTATION: AN OBSERVATIONAL COHORT STUDY

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Background: Socioeconomic deprivation affects health outcomes, including these after kidney transplantation. Retrospective US and UK cohort studies showed higher post-transplant mortality and graft rejection in deprived patients. In this study, we examined the effect of socioeconomic deprivation on graft failure, mortality and rejection after kidney transplantation in Belgium, which has a universal healthcare system.

Methods: In this single-center cohort study, socioeconomic deprivation was quantified according to the Belgian Index of Multiple Deprivation (BIMD) among 1891 kidney transplant recipients. Post-transplant graft failure, mortality, and rejection were analyzed using univariable and multivariable Cox, and competing risks Fine and Gray models.

Results: The 10-year risks of graft failure were 16.0% (13.5%–18.7%) for the least deprived, 18.9% (14.9%–23.4%) for the moderately deprived, and 20.1% (15.3%–25.4%) for the most deprived group, and did not differ significantly (p= 0.335) (**Figure 1**). The 10-year mortality risks of 26.2% (23.0%–29.5%), 25.9% (21.2%–30.9%), and 32.5% (26.3%–38.9%) respectively, were likewise not significantly different (p= 0.304). Rejection risks differed significantly (p= 0.030), with 5-year risks of 46% (33.3%–57.9%), 42.7% (33.3%–51.7%), and 60.5% (38.9%–76.5%), respectively. Univariable and multivariable Cox and Fine and Gray models, including BIMD as a continuous variable (0-100), confirmed this association (HR 1.10, 95% CI 1.03–1.18; p= 0.004) (**Table 1**).

Conclusions: In Belgium, socioeconomic deprivation, measured by the BIMD, associates with rejection but not with graft failure or mortality after kidney transplantation. This suggests that, in contrast to the Anglo-Saxon experience, healthcare systems with universal access can partly alleviate adverse post-transplant outcomes due to socioeconomic deprivation. Future studies should evaluate whether socioeconomic deprivation is not hindering the access to transplantation.

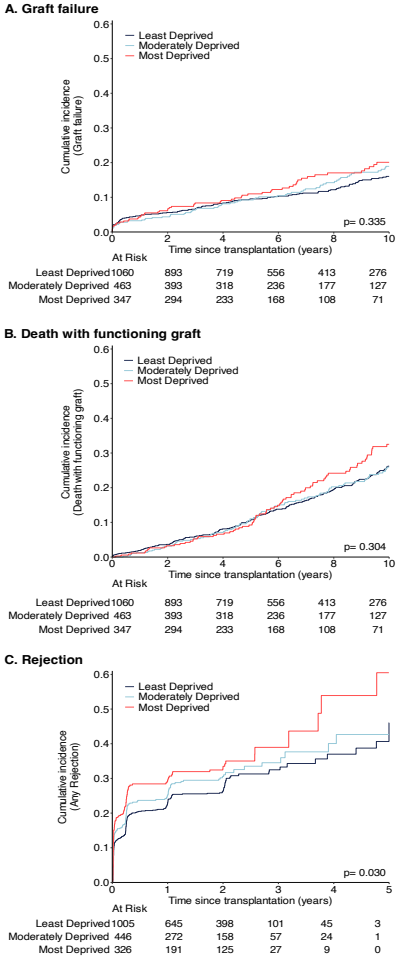

Figure 1. The cumulative incidence of (A) graft failure, (B) death with functioning graft, and (C) rejection by socioeconomic deprivation (least, moderately, most deprived), according to the Aalen-Johansen (graft failure and death) and the Kaplan-Meier (rejection) estimator.

Table 1: Cox Fine and Gray results. The table presents (subdistribution) hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the BIMD scores and the outcomes: graft failure and mortality (N=1870), and overall rejection (N=1777).

	Cox model				Fine and Gray			
BIMD for, per 10 increases	Univariable HR (95%CI)	p-value	Multivariable[a] HR (95%CI)	p-value	Univariable sHR (95%CI)	p-value	Multivariable[a] sHR (95%CI)	p-value
Graft failure	1.07 (0.97–1.17)	0.199	1.05 (0.95–1.16)	0.318	1.06 (0.96–1.16)	0.230	1.04 (0.95–1.15)	0.371
Mortality	1.07 (0.98–1.16)	0.117	1.07 (0.99–1.16)	0.074	1.06 (0.98–1.15)	0.165	1.07 (1.00–1.16)	0.059
Any rejection	1.10 (1.03–1.18)	0.004	1.09 (1.02–1.16)	0.013				

[a] Corrected for donor/recipient age, donor/recipient sex, repeat transplantation, pre-transplant HLA-DSA, and donor type (brain death; circulatory death; living).

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Transplant immunology & immunosuppression

PP_490 SAFETY AND EFFICACY OF WEIGHT-BASED MMF (CELLCEPT) DOSING IN KIDNEY TRANSPLANT RECIPIENTS: A QUALITY IMPROVEMENT STUDY

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Background: Mycophenolate mofetil (MMF) reduces the risk of acute rejection (AR) in kidney transplant recipients (KTRs) and improves post-transplant graft survival. MMF is usually prescribed in fixed doses (2 gm/day). Due to its side effects, MMF doses often require reduction. Weight-based MMF dosing (10-16 mg/kg/day) was correlated with therapeutic level in Asian KTRs. We are aiming to evaluate the safety and efficacy of weight-based MMF dosing at 15 mg/kg/day, adopted by our program in September 2021.

Methods: This is a single center retrospective quality improvement study evaluating the safety and efficacy of weight-based MMF dosing at 15 mg/kg/day, compared with non-weight-based doses (≤ 2 gm/day), to reduce the risk of MMF-associated side effects including leukopenia (WBC ≤ 3.5), BK- and/or CMV-viremia, while monitoring the risk of AR associated with reduced MMF doses. All KTRs followed in our kidney transplant clinic at Queen's University between September 1, 2021, and August 31, 2023, were included.

Results: 230 KTRs [Age 56.9±14.4 years, Female (36.1%), Caucasian (87.8%)] were included. By August 31, 2023, 112 (48.7%) patients were on MMF. 18 patients were on weight-based doses (15.9 (14.9-18.1) mg/kg/day). 17 patients were on fixed doses (20.7 (17.2-26.2) mg/kg/day). 68.8% of MMF patients were on reduced doses (14.4 (10.4-14.4) mg/kg/day) due to adverse effects, most notably leukopenia (25%) and BK-viremia (18%). At the end of the study, leukopenia, BK- and CMV-viremia were active in 4 (1.7%), 7 (3%) and 1 (0.4%) of all patients, respectively and none of them were on weight-based MMF doses. Median eGFR of MMF patients was higher than non-MMF patients (58 vs. 53 ml/min per 1.73 sm; P 0.37), and it was better among patients on weight-based MMF doses compared with fixed (68.5 vs. 51; P 0.035) and reduced doses (58; P 0.26).

Conclusions: Snapshot data showed a low rate of leukopenia, BK- and CMV-viremia/infection, likely due to effective MMF dose reduction. Further analysis will be done through our next retrospective cohort study to evaluate the outcomes of weight-based dosing.

PP_492 A MACHINE LEARNING MODEL IDENTIFIES IMMUNOLOGICAL PROFILES FOR SURVIVAL PREDICTION AFTER HEART TRANSPLANTATION

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Background: Despite improvements in survival rates an adequate profile associated with development of death remains a difficult task. Artificial intelligence shows promising results when used to predict graft function, morbidities, and mortality post-transplantation. We aimed to assess a semi-supervised machine learning model that allows identifying key immunological patterns and developing a predictive survival model in a cohort of heart recipients.

Methods: An exploratory data analysis was performed using unsupervised algorithms to facilitate the identification of immune patterns, and based on these patterns, a random forest classification model was constructed. Distinct immunological biomarkers evaluated prospectively were used at inclusion in transplant waiting list, at 7 and at 30 days post transplantation from a cohort of 265 heart transplant recipients at a single center.

Results: The combination of machine learning models has allowed us to identify two groups of patients (Clusters 0 and 1) with statistically significant differences in their survival curves. Being cluster 1 with the lowest median survival (p value: 0.012). The immune patterns associated with cluster 1 disclosed lower levels of IgG one week post transplant ($p < 0.001$), low levels of complement C3 ($p: 0.001$, $p < 0.001$ and $p < 0.001$) and CD4 percentage ($p < 0.001$, $p<0.001$ and $p<0.001$) at all indicated follow-up visits. The binary random forest classifier model developed from the identified clusters performed well. Its associated metrics showed a precision of 1 and 0.88, respectively, with an F1 score of 0.93. Furthermore, the features importance analysis of the model identified the percentage of CD4 T-cells as the most important parameter for discrimination between groups as a predictor of death during follow-up.

Conclusions: The potential role of immunological profiles combinining acquire and innate immunity as a prediction tool of death is highlighted in this study. The scaling of this bioinformatic analysis approach used could greatly help to differenciate, characterize and classify patients with different survival after transplantation as well as improve the ability to derive new knowledge over the traditional models of prediction of death in solid organ transplantation.

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PP_493 PRETRANSPLANT VIRTUAL EPITOPE-BASED CROSSMATCH IS ASSOCIATED WITH WORSE OUTCOMES AFTER KIDNEY TRANSPLANTATION

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Background: The epitope-based crossmatch (EpXM) is a promising tool for enhancing donor-recipient immunologic compatibility. However, its association with post-transplant outcomes remains uncertain, limiting its current use as a definitive decision-making tool in organ allocation. This study aimed to evaluate the long-term outcomes of a positive pre-transplant virtual epitope-based cross-match in patients with preformed donor-specific antibodies (DSA).

Methods: This was a retrospective single-center cohort study including deceased donor kidney transplants (KT) performed between January 2013 and December 2018. Patients included had preformed DSA detected by Luminex Single Antigen assay with >1,500 mean fluorescence intensity (MFI) and a negative complement-dependent cytotoxicity crossmatch (n=63). Epitopes were analyzed using the EpViX© digital platform, considering unacceptable HLA mismatches with >5,000 MFI. Patients were divided into two groups: EpXM positive (n=38) and negative (n=25). Follow-up was for a median of 9.0 ? 1.8 years.

Results: The cohort was predominantly female (63.8%), non-Caucasian (89.9%), with a mean age of 43.2 ± 13.7 years. 46% were retransplants, and 96.8% received standard criteria donor KT. Acute rejection (AR) occurred in 25%, graft loss in 30%, and 27% of patients died during follow-up. Positive EpXM was associated with higher AR rates (39.5% vs. 4.0%, p=0.002) and graft loss (39.5% vs. 16.0%, p=0.047), with no significant difference in patient survival. In multivariate analysis, positive EpXM was independently associated with AR (HR 10.0, 95% CI 1.31–76.6, p=0.03) but not with graft loss (HR 0.75, 95% CI 0.89–8.54, p=0.080).

Conclusions: Pretransplant EpXM was strongly associated with an increased risk of AR, underscoring its potential as a valuable tool for immunologic risk stratification in KT.

PP_494 CHRONICITY INDEX, BUT NOT ACTIVITY INDEX, IN PROTOCOL BIOPSIES IS ASSOCIATED WITH LATE RENAL GRAFT FAILURE

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Introduction: Chronicity index, but not activity index, has been associated with graft failure in patients with active antibody-mediated rejection. We aimed to evaluate the relevance of these indices in a large cohort of protocol biopsies performed at our center.

Patients and Methods: We analyzed protocol biopsies performed at 3 and 12 months post-transplantation between 2012 and 2022. Kidney allografts included in the study had stable renal function at the time of biopsy, defined as serum creatinine <2 mg/dL and a urinary protein-to-creatinine ratio <1 g/g. Histological assessment was performed according to the Banff criteria, with the activity index calculated as the sum of g-score, ptc-score, i-score, t-score, and (C4d-score ×2), while the chronicity index was defined as (cg-score ×2) + ci-score + ct-score + cv-score. HLA antibody detection at the time of biopsy was performed using Immucor technology

Results: We analyzed 379 biopsies (3 months) and 279 biopsies (12 months), with 234 paired cases. Clinical and histological data are summarized in the table. Associations between histological findings and death-censored graft loss were adjusted for serum creatinine, proteinuria, and presence of donor-specific antibodies (DSA). In the 3-month biopsies (39 events): Chronicity index was significantly associated with graft loss (HR: 1.27, 95% CI: 1.05-1.55, p=0.016), whereas activity index was not (HR: 0.99, 95% CI: 0.82-1.20, p=0.939). In the 12-month biopsies (28 events): Chronicity index remained a significant predictor (HR: 1.21, 95% CI: 1.01-1.47, p=0.049), while activity index showed no association (HR: 0.96, 95% CI: 0.77-1.29, p=0.696).

Conclusions: In protocol biopsies performed within the first two years post-transplant, chronicity index—but not activity index—was significantly associated with death-censored graft loss. These findings highlight the prognostic value of chronic histological changes in long-term allograft outcomes.

	3-month biopsy (n=379)	12-month biopsy (n=279)	p-value
Timing of biopsy (months)	4.5±1.5	15.9±4.3	n.a.
Serum creatinine (mg/dL)	1.42±0.41	1.34±0.37	0.0088
Proteinuria (g/g)	0.29±0.30	0.34±0.45	0.0454
cPRA (%)	15±31	15±31	0.9023
DSA (no / yes)	365/23	262/17	0.8720
g-score	0.18±0.50	0.33±0.70	0.0014
i-score	0.27±0.56	0.19±0.46	0.0364
t-score	0.31±0.62	0.32±0.58	0.7837
v-score	0.04±0.22	0.01±0.12	0.1058
ptc-score	0.21±0.52	0.26±0.59	0.2770
MVI (g+ptc)	0.39±0.90	0.59±1.15	0.0128
TI (i+t)	0.58±1.05	0.51±0.93	0.3561
ah-score	0.39±0.65	0.52±0.76	0.0124
cg-score	0.03±0.20	0.04±0.21	0.5201
ci-score	0.70±0.70	0.92±0.79	0.0002
ct-score	0.82±0.57	1.12±0.67	0.0000
cv-score	0.65±0.80	0.70±0.87	0.4312
mm-score	0.02±0.18	0.06±0.35	0.0607
i-IFTA	1.28±1.23	1.43±1.17	0.1249
C4d	0.04±0.18	0.04±0.30	0.9941
Diagnostic			
Minimal changes	148	78	
ABMR / MVI / probable ABMR	10	21	
Borderline	46	26	
TCMR	11	7	
IFTA	148	124	
Infection	6	8	
Recurrence	10	15	0.0000
Activity index (g+i+t+v+ptc+C4d*2)	1.10±1.83	1.23±1.87	0.4144
Chronicity index (cg*2+ci+ct+cv)	2.22±1.66	2.84±1.90	0.0000
Timing of follow up	86±37	77±33	n.a.

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e-POSTERS

Access to transplantation

EP_001 IMPACT OF AGE DIFFERENCE BETWEEN DONOR AND RECIPIENT IN RENAL TRANSPLANTATION

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Background: With the growing shortage of organ donors combined with the increasing demand for organs, more expanded criteria donors are being used. The age of donors and recipients is increasing, and recipients are very concerned about the age of the donor when they are matched. However, utilizing older donors among recipients is a way to similarly increase the donor pool for kidney transplants, Thus, we investigated the impact of donor-recipient age difference on graft outcomes after renal transplantation in our center.

Methods: Between April 1978 and June 2023, we assessed 854 renal transplantation patients. Based on recipient-donor age difference histogram, we stratified these patients into 5 groups: Group 1(15< Δage<50, n=175), Group 2(5< Δage<15, n=165) , Group 3(-5 <Δage<5, n=223), Group 4(-20< Δage<-5, n=156), and group 5 (-50< Δage<-20, n=135). Hazard ratios were analyzed to ascertain graft outcomes.

Results: There were no significant differences in clinical outcomes between 5 groups except eGFR at 12months after renal transplantation. Graft survival rate at 10 years after kidney transplantation was significantly different among the 5 subgroups (P = .015); the graft survival rate at 10 years was 94.8% in group 1; 91.8% in group 2, 93.5% in group 3, 92.5% in group 4; and 82.4% in group 5, respectively. In Cox proportional hazard models,, the recipient donor age difference <- 20 group showed a higher risk for graft failure than other group (HR 2.072, 95% CI 1.313-3.269).

Conclusions: Using older donors does not seem to have an impact on long-term survival, except when donors are used who are more than 20 years older than the recipient. This consolidates the concept that the use of elderly donors does not affect survival, allowing the pool of donors to be expanded.

EP_002 THE IMPACT OF THE EARTHQUAKE IN TÜRKIYE ON ORGAN DONATION AND TRANSPLANTATION

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Background: Organ shortage is a global issue. A disaster like an earthquake, not only increases the number of people in need of organs but also negatively affects the treatment processes of patients who have already undergone transplants. The aim of this study is to examine the impact of the earthquake that occurred on February 6, 2023, in Türkiye on organ donation and transplantation.

Methods: The study was conducted using open-access statistical data of 2022-2023 years available on the official website of the Tissue, Organ Transplantation, and Dialysis Services of the Ministry of Health in Türkiye.

Results: In this study, it was found that, the earthquake did not affect the number of organ transplants, organ donations, brain death diagnoses, and family consent in Türkiye, but it decreased the number of organ donations, brain death diagnoses, and living donors and increased the number of family consent in the provinces affected by the earthquake in total.

Conclusions: Strategies should be developed and implemented to support organ donation in earthquake disasters, and in particular to detect brain death.

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EP_003 STANDARDISATION OF ORGAN UTILISATION MEETINGS: PROMOTING LEARNING AND COLLABORATION ACROSS THE UK

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Background: The numbers of patients requiring transplantation continues to rise within the UK. In parallel, patients continue to die on the waiting list. The need to address this coupled with increasing donor complexity and variation in utilisation practices, led to the development of the Organ Utilisation Group (OUG) established by the Secretary of State for Health and Social Care in England. The OUG report drafted 12 recommendations (six themes) aiming to maximise the potential for organ transplantation. Theme 2 covers an operational infrastructure and within this recommendation 3 states that "Decline meetings in transplant units must be established as a mandatory requirement along with a nationally agreed profile and template".

Methods: In the UK, we have a national lead for organ utilisation for each organ and local utilisation leads across each transplant unit for all organs. A working group between the cardiothoracic and liver organ utilisation teams were developed. Recommendations were presented at the National Organ Utilisation Meeting, and feedback received. The consensus document was distributed to all local Clinical leads for organ utilisation for unit ratification ahead of NHSBT sign off.

Discussion: The overarching consensus was that a common proforma would encourage collaborative work and promotes education on organ offering system. It provides a forum for supportive and constructive discussion in a blame free culture. Fifteen recommendations were set out including frequency and attendance, key metrics, documentation and audit. It was felt important to name these meetings Organ Utilization Meetings to reflect the hard work of all units to ensure the best use of organs.

Conclusions: The development of a Nationally standardised utilisation meeting template will reduce variation across units and allow for more robust audit of outcomes and learning across the UK.

EP_004 COMMONWEALTH TRIBUTE TO LIFE - SHARED LEARNING

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Background: Thanks to the Commonwealth Tribute to Life project and memorandum of understanding between Commonwealth countries there are new opportunities for shared learning. During a sabbatical this project provided a first-hand opportunity to learn about the deceased donation program in India. The purpose was to engage in shared learning with Mohan Foundation in Chennai and Jaipur and gain understanding of consent for deceased donation in India. In the UK, the number of deceased donations and transplants from the Asian population is disproportionate whilst India is one of the highest countries world-wide for the number of transplants carried out annually.

Methods: The author observed and engaged with the work of Mohan Foundation for a period of 18 months. The aim was to gain understanding of deceased donation practice in India. Identify commonalities and differences between UK and India pertaining to approach and consent. Identify barriers to donation relevant to both countries.

Results: Over a period of 18 months, Midlands Specialist Nurse Organ Donation visited the Mohan Foundation in Chennai and Jaipur and engaged in a variety of shared learning activities including coordinator training course, ambassador engagements, public awareness campaigns and celebrations of deceased donors. The SNOD also spent time networking and learning about the many Indian cultures and religions, the variance in public versus private healthcare and the disparity between individual states and deceased donation programs.

Conclusions: This learning experience identified many areas where UK and India can learn from each other by ongoing sharing of best practice thanks to MOU under the Tribute to Life project. The project provides the ability for global engagement with healthcare professionals and improve the health of commonwealth citizens by developing deceased organ donation programs and delivering transplant for all who needs it.

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EP_005 SEMAGLUTIDE ENABLED WAITLISTING AND RENAL TRANSPLANTATION OF OTHERWISE INELIGIBLE OBESE CANDIDATES

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Background: Obesity is an increasing health concern among kidney transplant candidates. While transplantation should be encouraged to treat advanced chronic kidney disease (CKD), obesity often hinders access to transplant due to the higher rate of post-operative complications. Pre- transplant bariatric surgery provides significant weight loss but is not free of risk. 'Glucagon Like Peptide-1'analogues (GLP-1Ras) demonstrated efficacy for obesity treatment in the general population but data in renal transplant candidates are poor. This study aims to determine whether treatment with semaglutide enabled waitlisting and transplantation of otherwise ineligible obese renal transplant candidates.

Methods: Between 01/01/2021 and 30/10/2023, patients recused from renal transplantation due to obesity received pre-transplant subcutaneous semaglutide up to 1 mg/week.

Results: Of the 23 patients included, initial mean body weight, BMI and waist circumference were 106 Kg, 35.6 and 119 cm respectively. After a median of 13 months on semaglutide, these parameters decreased by 11 kg (p=0.001), 3.8 points (p=0.001) and 9.6 cm (p=0.001) respectively. 56.5% of patients initially rejected for transplant were listed within a median of 8 months, and 61.5% of them were transplanted within a median of 4 months. No major side effects were reported.

Conclusions: Treatment with semaglutide enabled waitlisting and transplantation of otherwise ineligible obese renal transplant candidates and should be included in the stepwise management of obesity in renal transplant candidates.

EP_006 OVERCOMING OBSTACLES: MANAGING HEREDITARY TYROSINEMIA TYPE 1 IN INDIAN SUBCONTINENT

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Background: Tyrosinemia type 1 (HT1) is an entity secondary to FAH gene variations. Owing to lack of universal health care, the treatment of choice i.e. NTBC's availability is still limited in the Indian subcontinent. Due to limited literature from this part of the world, we aimed to analyze the outcomes of Indian children with HT1 including need of liver transplantation (LT).

Methods: Eighteen children with confirmed HT1 (from 2013 to 2024) were evaluated for their treatment outcomes. Diagnosis was established either with elevated with urine succinylacetone (n=11) and/or on exome sequencing (n=7).

Results: Median age of symptom onset was 6 months (IQR 3.5-18 months) with a median diagnostic delay of 4.5 months (IQR 2-23 months). All had established cirrhosis at baseline with synthetic dysfunction in 88.9% and HCC in 27.8%. On follow up, new hepatic nodule formation observed in 9 cases: HCC (22.2%), regenerative nodule (22.2%) and dysplastic nodule (5.6%). Only seven children could be initiated on NTBC treatment. In the NTBC group (n=7), 3 children underwent LT, 3 (including 1 with HCC along with NTBC non compliance) died and there was only 1 surviving child with native liver. Among 11 children not receiving NTBC, 4 underwent LT (2 with HCC and 2 with decompensation) while 7 died (figure 1). Of the 7 children undergoing LT, at a median follow up of 38 months, the graft and patient survival was 100 % and 100 % without HCC recurrence.

Conclusions: The study highlights the difficulties faced by clinicians in managing HT-1 cases in the developing world with limited logistics. Due to delayed diagnosis secondary to lack of newborn screening, majority of the children present with advanced liver disease with very high proportion of them developing HCC either at diagnosis or during follow up. In such cases, even initiation of NTBC may not be of adequate benefit.

Keywords Hereditary Tyrosinemia type 1; liver transplantation; NTBC (2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione)

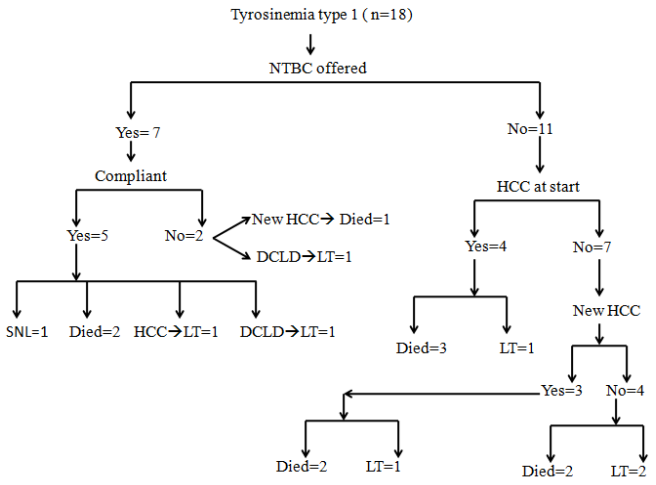

Figure 1: Outcomes of the Pediatric HT1 cases (n=18)

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EP_007 PSYCHOLOGICAL HEALTH AND SELF-CARE IN KIDNEY TRANSPLANT CANDIDATES

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Background: This study describes the psychological health and self-care behaviors of kidney transplant candidates enrolled in a pilot study evaluating a newly developed digital support program, including analysis of correlations with demographics and each other.

Methods: Baseline data from 28 patients was analyzed. Psychological health was measured using the Depression Anxiety Stress Scale (DASS). Self-care was assessed using the Self-Care of Chronic Illness Inventory, including dimensions maintenance, monitoring, management, and self-efficacy. Correlations were analyzed using Spearman's rho.

Results: Mean age was 56 years (SD 16), 55% were male and 61% were married or cohabiting. 28% lived with underage children, and 28% lived alone. A majority were on dialysis (68%, median duration 1–2 years), and 18% had undergone previous kidney transplantation. DASS scores showed that 50%, 29%, and 18% reported at least mild depression, anxiety, or stress, respectively, while 29%, 22%, and 15% had moderate or higher levels. Self-care scores ranged from 16 to 100 across dimensions, with median scores of 75 for maintenance, 84 for monitoring, 76 for management, and 77 for self-efficacy. Higher scores in each dimension indicate better self-care. Younger age and living with underage children were associated with higher anxiety ($rs = -0.65$, $p < 0.001$; $rs = 0.57$, $p < 0.006$) and stress ($rs = -0.42$, $p < 0.027$; $rs = 0.44$, $p < 0.042$). Anxiety was linked to reduced self-care maintenance ($rs = -0.42$, $p = 0.026$) and depression with lower self-efficacy ($rs = -0.40$, $p = 0.038$).

Conclusions: This study highlights the interplay between demographics, psychological well-being, and self-care in kidney transplant candidates. Many participants experienced psychological distress, with younger adults and those living with underage children being particularly vulnerable to higher anxiety and stress. Anxiety and depression were associated with reduced self-care maintenance and self-efficacy. The results underscore the need for targeted support to address psychological distress and enhance self-care behaviors for kidney transplant candidates. Future research should explore the benefits of integrating digital support programs in transplant care to nurture a more sustainable transplantation journey.

EP_008 ECMO IN PATIENTS WITH END-STAGE CARDIAC DISEASE

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Background: Extracorporeal membrane oxygenation (ECMO) is the standard of care for patients with refractory heart failure worldwide. We describe our initial experience of implementing an ECMO program in the Kovel-ECMO hospital district (1182) ELSO.

Methods: Since the launch of the ECMO program, between January 2023 and November 2024, 25 patients underwent ECMO, reflected according to our protocol, we retrospectively collected preoperative information, treatment course and clinical outcomes. All patients were divided into 2 groups: the first group (bridge to recovery – BTR) were patients who were connected to VA ECMO with acute heart failure in a state of cryogenic shock (11 patients) and the second group (bridge-to-transplant – BTT) were patients with chronic heart failure.

Results: Patients of the first group were on VA ECMO for 5 to 7 days. At the connection stage, the productivity was 3.7 l/min, at the disconnection stage, the productivity was 2.7 l/min. In the first group, 2 (20%) patients were connected in another medical institution, the time of connecting the patient to VA ECMO was up to 150 minutes. This is a perspective for the development of the ECMO program not only in the Volyn region, but also in Ukraine. Mortality in the first group was 3 (27%) patients, and survival was 8 (72%) patients. The cause of death was the progression of heart failure. In the second group, patients were on ECMO for an average of more than 20 days while waiting for a donor heart. Productivity started with 3.5 l/min at the connection stage, at the disconnection stage the productivity was 2.2 l/min. 2 (14%) patients of the second group underwent orthotopic heart transplantation. The survival rate of patients of the second group was 8 (57%) patients, 6 (43%) were disconnected and transferred from status I to status V of emergency distribution of donor organs, awaiting heart transplantation, 6 (43%) patients died.

Conclusions: The above results that we report are at least no worse than those obtained by many other ELSO member centers.

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EP_009 POOR EARLY OUTCOME OF LIVER TRANSPLANTATION WITH DONOR-RECIPIENT HEIGHT DIFFERENCE>30CM: UNOS STUDY

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Background: To evaluate the outcome of deceased donor liver transplantation focusing on the body size difference between the donor and recipient.

Methods: Among United Network for Organ Sharing (UNOS) database, non-pediatric primary deceased donor liver transplantations performed since 2000 were included in the study. Body size differences were calculated based on the height difference between the donor and recipient. Graft failure and death during the first month after transplantation were analyzed using logistic regression analysis. Two models were designed for this analysis. The model 1 included donor-recipient height difference and sex separately while model 2 combined these two variables for the analysis

Results: A total of 111557 patients were included in the study. The cutoff for donor-to-recipient height difference was selected as 30cm which was the 99th percentile. There were 38348 female recipients (34.4%) included. There were 1119 patients (1.0%) with donor-recipient height difference ≥30cm. Female recipient with a donor-recipient height difference ≥30cm were 912. (0.8%). In the multivariable analysis for 1-month graft failure, female with donor-recipient height difference ≥30cm showed significantly increased risk. (OR=1.457, CI=1.084-1.958, P=0.013). For 1-month overall survival, female with donor-recipient height difference ≥30cm showed significantly increased risk. (OR=1.481, CI=1.052-2.086, P=0.025).

Conclusion: Female recipient with a donor-recipient height difference ≥30cm has a higher risk of 1-month graft failure and 1-month death compared to those who are not.

EP_010 ATTITUDE TO RISK IN TRANSPLANTATION AND INCREASING SOLID ORGAN USE BY MODIFYING RISK TOLERANCE

Anna Brotherton[1], **Rebecca McDonald**[2], **George Gkoutos**[2], **Amalia Di Girolamo**[2], **Adnan Sharif**[3]

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Background: Findings from the Organ Utilisation Group were published in February 2023, with an Implementation Group established by the Department of Health and Social Care to action its recommendations in the UK. Many complex interplaying aspects contribute to the decision to accept or decline organs including clinical (e.g., donor- or recipient-related) factors and/or structural (e.g., staffing, capacity and/or infrastructure) restraints. However, an underappreciated factor is the behavioural component of decision making under risk (or specifically ambiguity). Variation in decision making between and within transplant units are influenced by human factors and lead to inequity of access for patients waiting for life saving or life enhancing transplants. The human factor of how individuals make decisions (both transplant professionals and patients) has not been studied in transplantation but has in the field of behavioural economics.

Project aims: The aim of this project is to; 1) understand decision making when considering organ offers for transplantation, 2) explore the importance and inter-play of risk elicitation, ambiguity elicitation, uncertainty elicitation etc. for transplant professionals and patients when considering organ offers, and 3) study possible interventions to try and improve organ utilisation. Ultimately, our ambition is to maximise organ utilisation and improve equity of access to transplantation opportunities.

Methods: Attitude to Risk in Transplantation and Increasing Solid organ use by modifying risk Tolerance (ARTIST) will be divided into five work packages as outlined in the Figure below. This two-year project is scheduled to start in 2025.

Discussion: ARTIST is the first study to empirically study the decision making process for organ offers and aims to translate expertise from the field of behavioural economics to clinical transplantation. The aim is to improve organ utilisation by increasing our understanding of the human component in decision making under risk and/or uncertainty with organ offers. ARTIST is a collaboration with several organisations and aims to support national organ utilisation efforts. For further information, or if you wish to collaborate, please contact Adnan.Sharif@uhb.nhs.uk.

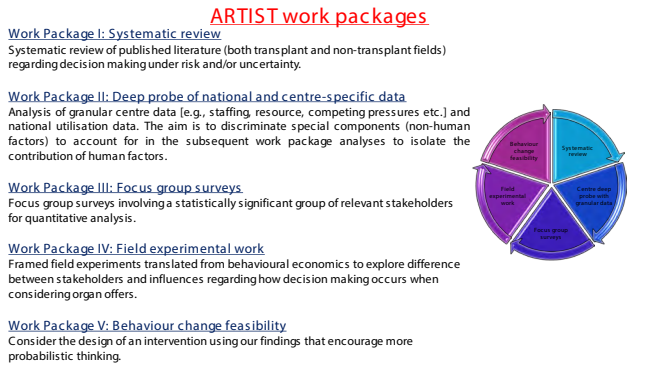

Figure. Work Packages for the ARTIST project

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EP_011 SCHOOL OF MEDICINE STUDENTS TRANSPLANT ATTITUDE AND BOUNDARIES: DATA FROM SCAMPIA UNIVERSITY AREA

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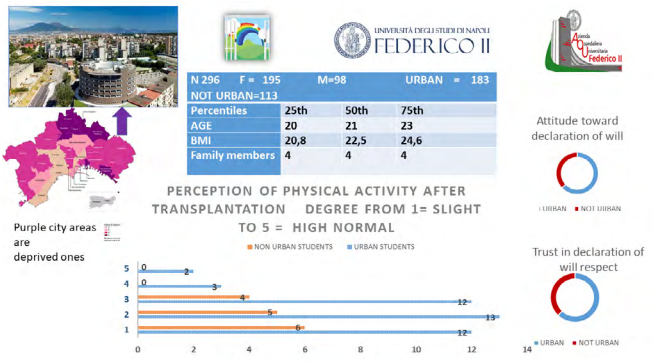
Background: Campania outcomes regarding Transplant Pathways are below the estimated potential. Moreover, the most efficient models cannot be easily replicated due also to social and economic boundaries. Literature suggests that one of the barriers to pre-emptive kidney transplantation is the lack of knowledge about treatment opportunities. A significant influencing factor is employment status: lower socioeconomic conditions are associated with a reduced likelihood of being prescribed for transplantation or being placed on the waiting list. Evidence assessed in a scoping review collected data from selected patient's populations, but few data are coming from youth population

Methods: The Scampia area is a peripheral region with sociodemographic deficiencies compared to neighboring areas. Regional Kidney waiting list does not have patients from there. The new "Federico II," University campus represents an opportunity to investigate and reduce disparities in access to care. In recent months, the Regional Public health unit "Sportello Amico" has carried out training activities for students enrolled in the Faculties of Medicine, Surgery, and Health Professions, as well as community-based training, conducting a survey among patients attending open days and the student population regarding their perception to transplant of and barriers to accessing care

Results: From the 296 questionnaires, involving students who represent a population with an estimated low metabolic risk, a good perception of transplantation programs, including living donor options evaluated by general linear model, emerged more than perceptions retrieved among patients. Certainty of cerebral death and attitude toward physical activity is higher in urban areas resident but living donation knowledge is slight lower. Self-Perception of high weight showed a worse impact in attitude toward declaration of will and trusting the respect of it ($p<0,05$), better outcomes are from Urban students. Prevalent uncertainties are centered on age limits, health determinants, and donor selection.

Conclusions: Preliminary data encourage to work on population data focusing on person related indicators.



EP_012 DUAL KIDNEY TRANSPLANTATION FROM AN EXTREMELY OLD AGE DECEASED DONOR

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Background: The demand for kidney transplants is rising, leading many countries to expand donor criteria. Dual kidney transplantation (DKT) helps reduce the waiting list and prevents viable organs from being discarded. And its positive outcomes are confirmed through numerous studies for both patient and graft survival.

Methods: Kidney transplant was performed from an 84-year-old deceased male donor. Despite old age and history of hypertension, maintained good kidney function, including stable urine output and no proteinuria. The kidney sizes were small (right kidney 10.3 cm, and left 9 cm). The recipient was a 43-year-old female. As no other institutions participated the allocation due to the donor's age, our center had the opportunity to perform a DKT.

Results: During procurement, the right kidney's ureter was damaged near the hilum. We opted for DKT on the same side with separate anastomosis into the right iliac fossa. The right kidney (RK) was positioned postero-superiorly and the left kidney (LK) antero-inferiorly. The recipient's external iliac artery had a diameter of 10 mm, with no calcifications, and the external iliac vein had a diameter of 15 mm. The internal iliac vein was ligated for mobilization. Both kidneys had a single artery and vein. We completed vessel anastomosis routinely. Due to the ureter injury on the RK, a pyelo-ureterostomy was performed, and the LK underwent cysto-neoureterostomy. Double-J stents were placed in both kidneys. The cold ischemia time was 6 hours, and the operation time was 325 minutes. The recipient was discharged on postoperative day 22 due to a delay in Foley catheter removal caused by high urine output.

Conclusions: In this case, a successful DKT was carried out from an 84-year-old deceased donor to a 43-year-old female recipient, despite the donor's age and ureter injury. DKT is a valuable approach for utilizing organs that may otherwise be discarded, addressing the growing need for kidney transplants, especially from elderly donors.

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EP_013 EVOLVING TRENDS IN ORGAN DONATION AND TRANSPLANTATION ACTIVITY ACROSS MUSLIM MAJORITY COUNTRIES

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Background: Transplantation is the treatment of choice for end-stage organ failure, but it is unclear how many Muslim countries have this option. The aim of this study was to examine trends in organ donation and transplantation across the global Muslim world between 2013-2023.

Methods: Data was analysed for 50 global Muslim countries (defined as countries where >50% of the population comprised of Muslims). Organ donation/transplantation rates between 2013 and 2023 were obtained from the Global Observatory for Donation and Transplantation and International Registry on Organ Donation and Transplantation. Data is reported with descriptive statistics only.

Results: The global Muslim population rose from 1.53 billion to 1.88 billion between 2013 and 2023. Organ donation and transplant activity data was reported for 21/50 countries. Deceased donation occurred in 10/21 and 13/21 countries in 2013 and 2023 respectively. Total actual deceased donors were 1,173 in 2013 and 1,681 in 2023, representing a 43.3% increase (almost exclusively donation after brain death). However, this led to a marginal 7.4% increase in deceased donor kidney transplant rates from 1,940 in 2013 to 2,084 in 2023. Living donor kidney transplants were 8,841 in 2013 (representing 82.0% of total kidney transplant activity, n=10,781) and 10,356 in 2023 (representing 83.2% of total kidney transplant activity, n=12,440). Liver transplant activity in 2013 was 2,543 (65.6% from living donors) and in 2023 was 3,913 (68.9% from living donors). Heart and lung transplant rates in 2013 and 2023 were 243 and 329 respectively (reported in 7 and 6 countries only). Small bowel transplantation rates in 2013 and 2023 were 14 and 13 respectively.

Conclusions: Most Muslim-majority countries fail to report any donation/transplant activity (presumed to be non-existent). The majority that reports data have non-existent or minimal donation/transplantation activity. For the few countries with established programs, transplantation activity is mostly driven by living donor activity. Development of organ donation and transplantation services in Muslim-majority countries is essential to ensure equity of access to transplantation for people living with end-stage organ failure.

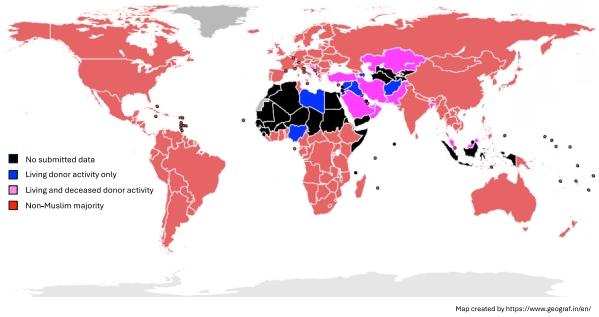

Figure. World map of Muslim countries and transplant activity based upon 2023 data

Country	Total LD activity 2023	Total utilised DD 2023	Country	Total LD activity 2023	Total utilised DD 2023
Afghanistan	459	0	Libyan Arab Jamahiriya	45	0
Albania	26	0	Malaysia	199	43
Algeria			Maldives		
Azerbaijan	41	0	Mali		
Bahrain			Mauritania		
Bangladesh	317	1	Morocco		
Bosnia and Herzegovina	10	4	Niger		
Brunei Darussalam			Nigeria	253	0
Burkina Faso			Oman	25	2
Chad			Pakistan	1846	2
Comoros			Palestine		
Djibouti			Qatar	51	18
Egypt			Saudi Arabia	1662	138
Eritrea			Senegal		
Gambia			Sierra Leone		
Guinea			Somalia		
Indonesia			Sudan		
Iran (Islamic Republic of)	1267	1000	Syrian Arab Republic	348	0
Iraq	1063	0	Tajikistan		
Jordan	224	0	Tunisia	46	16
Kazakhstan	717	7	Türkiye	4739	190
Kosovo			Turkmenistan		
Kuwait	80	33	United Arab Emirates	133	85
Kyrgyzstan			Uzbekistan		
Lebanon			Yemen		

Table 1: Living and deceased donor activity across Muslim majority countries in 2023

No submitted data

EP_014 HEART TRANSPLANTATION IN URGENT RECIPIENTS BRIDGED WITH ECMO: IS THEIR OUTCOME SO BAD?

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Background: advanced patients (PT) with decompensated heart failure (HF) may get worse, requiring fast intervention to reverse hypoperfusion and organ's damage. Veno-arterial extracorporeal membrane oxygenation (ECMO) as bridge to transplantation (HT) reduces waiting list time in urgent recipients, but controversial data is reported about their post-HT outcome.

Methods: we retrospectively evaluated post HT outcome of PT bridged with ECMO and that of other PT transplanted at our center between 2008 and 2021. Among 476 PT, we compared survival of 46 (9,2%) transplanted in priority status –status 1- to that of 46 transplanted in status 2A, (hospitalized for worsening heart failure, requiring i.v. infusions, or for LVAD complications) and 46 ambulatory PT in status 2B (admitted for donor availability), randomly matched.

Results: age and anthropometric characteristic were similar in the 3 groups. In the ECMO group time on waiting list was significantly shorter and in-hospital stay was longer. Univariate analysis with logistic regression showed that higher in-hospital mortality was associated with natriretic peptides at admission, with bilirubin, hemoglobin, and blood urea nitrogen and need for intra aortic balloon pump, renal replacement therapy and prolonged mechanical ventilation post HT. At 1 year and at the last follow-up there were no significant differences between groups in renal and graft function, acute cellular or humoral rejection, coronary graft vasculopathy and cytomegalovirus (CMV) related infections. Kaplan-Meier survival curves and log-rank test showed no significant difference in both 1-year and long-term mortality in the 3 groups.

Conclusions: in our experience HT recipients on ECMO have worse survival shortly after HT, probably due to severe pre- and post-operative clinical conditions and longer ischemia time; afterwards the rate of death and post HT complications are similar to those of the control groups. We think that we can't deny this option to these PT but larger studies or scores are necessary to identify strong predictors of bad outcome in recipients on ECMO support that could advise against HT.

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EP_015 IMPACT OF LAPAROSCOPIC LIVER SURGERY FOR HCC ON LIVER TRANSPLANT ACCESS: RETROSPECTIVE ANALYSIS

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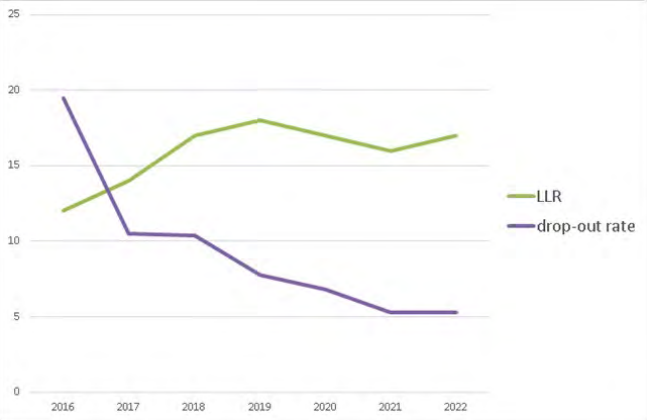
Background: Hepatocellular carcinoma (HCC) is the most common primary liver cancer, and both liver resection (LR) and liver transplantation (LT) are considered potentially curative options. We aimed to explore the impacting role of minimally invasive approach on entry and drop-out flows waiting list of a single regional center for LT in southern Italy with a very low deceased donation rate.

Methods: We retrospectively analyzed our experience performed during a 7-year period between January 2016 and February 2023 in patients treated for end-stage-liver-disease (ESLD) and/or with surgically unresectable early and intermediate stage HCC. Linear correlation was used to evaluate dependence between the number of laparoscopic LR (LLR) treatments for HCC on the following flows of enrollments on the waiting list during the study period:-Enrollments present at the beginning of the year.-Enrollments that took place during the year, the Intention-To-Treat (ITT, present at the beginning of the year+admissions during the year).-Registrations present at the end of the year, and waiting for transplants for transplanted patients.

Results: There were 282 HCC patients treated with a first-line approach of LLR (*n* = 116) or open LRs (*n* = 166), with an incremental number of LLR per months. Considering the number of LLR and the rate of drop-out of ITT population and the number of enrolled patients per year, we observed a strong inverse linear correlation (rho=-0.82,p=0.023).

Conclusions: Minimally invasive surgical therapies for HCC has a specific impact on drop-out percentage of overall ITT population, and waiting time for transplants for transplanted HCC patients.



EP_016 LIVER DISCARD RATE DUE TO CONSERVATIVE ESTIMATIONS OF STEATOSIS: AN INFERENCE-BASED APPROACH

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Background: On-site conservative estimations of steatosis could result in the unnecessary discard of donor livers. This study applied the body mass index (BMI) as an independent statistical indicator to determine the extent of this problem. We aim at quantitively evaluating if decisions based non-biopsy donor liver assessments are more conservative (inclined to reject marginal fatty livers) than biopsy-based evaluations.

Methods: The study processed intra-database comparisons using 177,081 datasets from Organ Procurement and Transplantation Network (OPTN) spanning 2004 to 2022 September in the United States. Post-matching BMI was applied as an independent indicator of statistical risk of HS.

Results: 7,420, 4,990, 5,994, and 7,523 pair of donors with/without biopsy records were matched in 2004-2010, 2011-2014, 2015-2018, and 2019-2022 September, respectively. *Consistent with our hypothesis*, absent biopsies, evaluations before and during organ procurement were observed to be more conservative, leading to the discard of 16.4% (2004-2010), 20.4% (2011-2014), 10.6% (2015-2018), and 10.3% (2019-2022 September) of potential donor livers.

Conclusions: The study concludes that there was a significant (10.3%–20.4%) disparity caused by on-site non-biopsy assessments of HS, leading to the unnecessary discard of potential donor livers. The findings emphasize the need to develop more accurate intraoperative techniques for assessing HS to optimize donor liver procurement.

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EP_017 A CASE OF ECLS BRIDGE TO TRANSPLANT WITH UNEXPECTED OUTCOME

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Background: we present a complex case of post-myocardial infarction cardiogenic shock complicated by mechanical complications and to describe the management strategy using extracorporeal life support (ECLS), with subsequent organ donation outcome.

Methods: the patient, with a history of angina pectoris and ischemic heart disease, was admitted to our hospital presenting with STEMI. A coronary angiogram revealed severely diseased vessels with total thrombotic occlusion of the right main coronary artery. Following revascularization, the patient developed cardiogenic shock within two hours in the ICU. Echocardiography showed right ventricular insufficiency and a ventricular septal defect (VSD). ECLS was initiated due to refractory shock.

Results: the patient was stabilized and remained conscious but required sympathomimetic support due to persistent anuria from admission. She was registered as status 1A urgent for heart transplantation. After three days on ECMO, her condition deteriorated, leading to respiratory arrest and signs of coma. An urgent CT scan revealed extensive neurological insult, resulting in brain death. Consent for organ harvesting was obtained from relatives, and the liver was deemed suitable for donation.

Conclusions: this case illustrates the complexities of managing cardiogenic shock in STEMI patients with significant comorbidities. The use of ECLS was critical in stabilizing the patient initially; however, subsequent neurological deterioration led to brain death and organ donation. This underscores the importance of timely intervention and multidisciplinary approaches in critical care settings for optimal patient outcomes. The successful liver transplantation further highlights the potential for organ donation in such critical scenarios.

EP_018 ATTITUDES AND PERCEPTION OF EXERCISE AND PHYSICAL ACTIVITY IN WAITLISTED KIDNEY TRANSPLANT PATIENTS

Sadia Tasleem[1], **Kamlesh Patel**[2], **James Hodson**[1], **Farah Mazhar**[3], **Laura Bedford**[4], **Felicity Williams**[5], **Simon Jones**[6], **Matthew Armstrong**[7], **Adnan Sharif**[8], **Dilan Debare**[9]
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Background: Increasing age and frailty of kidney transplant candidates has led to emerging drive to optimise patients before transplantation through increased physical activity. Lack of exercise has been linked with poor outcomes at all stages of the transplant pathway. The aim of this study was to evaluate the attitudes and perception to exercise in such patients and assess how these practises vary by demographics.

Methods: A single-centre, prospective, survey-based study was conducted between February and September 2023. Consecutive adult patients on the deceased donor kidney transplant waiting list attending a routine outpatient visit were recruited and completed survey. Patient demographic data were extracted from the case notes.

Results: A total of 103 patients (65% male; 56% Caucasian; mean age 47.8 years) completed the survey. Of these, 42% were on haemodialysis and 24% on peritoneal dialysis. Most patients agreed/strongly agreed that exercise was important whilst awaiting transplant (86%); that it would be reasonable to expect them to exercise regularly (85%); and that they would be willing to do so to optimise their health (97%). However, only 56% of patients currently exercised on a regular basis (average exercise 2 sessions of 20 mins/week; 85% walking). Young age (<40 years) and Black/Asian ethnicity reported significantly less exercise activity than their older and Caucasian counterparts; despite having similarly high rates of expectations and willingness. Fatigue (64% agree/strongly agree), time spent on haemodialysis (50%) and fluid restriction (50%) were the most common factors limiting patient's ability to exercise.

Conclusions: Whilst most kidney transplant candidates report understanding the benefits of exercise and being willing to do so, patients are less likely to put this into practice. The reported exercise frequency varies by age and ethnicity, and these differences should be accounted for in designing patient-centred prehabilitation interventions for kidney transplant candidates.

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EP_020 IMPACT OF RECIPIENT AGE IN REPEAT KIDNEY TRANSPLANTATION: A NATIONAL COMAPARATIVE ANALYSIS

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Background: While kidney transplantation (KT) offers survival benefits compared to dialysis, older recipients experience reduced patient and graft survival. However, the age-related immune system changes may decrease the risk of rejection. We hypothesized that immunological challenges associated with re-transplantation might be mitigated in elderly recipients due to immunosenescence.

Methods: In the Korean Organ Transplantation Registry (KOTRY) database, a total of 11,681 KTs were performed between April 2014 and December 2023. Of these, 794 patients who underwent more than one KT were include in the study. The patients were divided into two groups based on the recipient's age at the time of KT: young (<65 years, n=751) and elderly (≥65 years, n=43). Allograft outcomes and complications were compared between the two groups.

Results: The median follow-up period was 60.2 months (IQR 33.5-89.0). The two groups had similar immunologic risk, leading to no differences in desensitization or induction regimens. Death-censored graft survival showed no significant difference between the two groups (log-rank p=0.208). Specifically, the most common cause of graft loss in young recipients was rejection (10/32 cases), whereas no cases of graft loss due to rejection were observed in elderly recipients. Early-period biopsy-proven rejection rates were similar between the groups (14.9% vs. 11.6%, p=0.663). Infection-related hospitalization (3.9% vs. 9.3%, p=0.097) and mortality (2.4% vs. 9.3%, p=0.027) were higher among elderly recipients. While infection and malignancy were the leading cause of death in young recipients, infection and cardiovascular disease were predominant in elderly recipients.

Conclusions: Although elderly recipients are at higher risk of infection-related and cardiovascular complications, repeat KT in this population remains a viable option when managed cautiously to minimize over-immunosuppression, given their comparable rejection rates.

EP_021 A NATIONWIDE INSIGHT: CGA FOR OLDER KIDNEY PATIENTS ACROSS THE UK

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Background: End-stage kidney disease is more common in patients aged over 60. Demand for renal replacement therapy (including dialysis and transplantation) as well as supportive care in this cohort is increasing. Concerns regarding decision-making and poorer outcomes in this cohort have been raised. Evidence suggests these relate to frailty, multimorbidity and cognitive impairment, all seen frequently in older age. Comprehensive Geriatric Assessment (CGA) is a multidisciplinary methodology proven to optimise outcomes relating to this triad. A CGA model tailored to the need of older kidney patients could be transformative. This national UK survey aims to describe: 1. Attitudes/beliefs of UK renal physicians towards CGA for older potential kidney transplant recipients and those being considered for dialysis or supportive care. 2. Provision of CGA services for older potential kidney transplant recipients and older patients who are being considered for dialysis or supportive care in the UK. 3.Barriers and enablers to provision of CGA services in the UK

Methods: A 28-question electronic survey was developed. Renal physicians at the UK's 72 renal units were invited to participate electronically using a protected link (24/04/24-31/08/24).

Results: Response rate was 100%. Many respondents reported cognitive impairment was rarely assessed in the unit where they work (28/53) and was inadequately addressed by current services in patients being managed with dialysis (34/53). Although only 6 centres offered CGA services, respondents advocated CGA for older patients being considered for kidney transplant (47/55), patients being managed with dialysis (52/54) and patients receiving supportive care (51/54). Lack of funding to support CGA and optimisation services (45/51), lack of available staff to deliver CGA (44/51), and time constraints (36/51) were reported barriers to implementing CGA.

Conclusions: UK renal physicians support CGA for older kidney patients but have identified key barriers to establishing and sustaining these services. Research developing and implementing CGA for this population is essential to optimise outcomes and influence policy at a national level.

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EP_022 IDENTIFYING REQUIREMENTS FOR NEW KIDNEY TRANSPLANT PROGRAMMES IN LOW AND MIDDLE-INCOME COUNTRIES

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[1]Transplant Links, [2]Transplant Links; Transplant Links; Ceo Transplant Links, [3]University Hospitals Birmingham; Professor of Nephrology; Nephrology, [4]Dept of Nephrology Uhb; Renal Medicine; Nephrology

Background: Chronic kidney disease (CKD) affects over 9% of the global population. For patients who progress to kidney failure transplantation offers better outcomes than dialysis, but access is limited in low- and middle-income countries (LMICs). To help address this Transplant Links has worked for 18 years to develop sustainable kidney transplantation programmes in LMICs. Here we report the key requirements for successfully establishing a new transplant centre.

Methods: Using the Theory of Change Model, we mapped the pre-conditions (outcomes) required to develop a new transplant centre, utilising activities that included on-line education, remote support, and in-person assistance. A 6-stage development framework was used to track progress towards sustainable transplantation.

Results: On-line education has reached over 100 countries, with 9 receiving intensive support, including transplant visits. Two centres have achieved Phase 6 (independence), requiring external support only for complex/paediatric cases. The phases required are shown in the table. Key factors required for success include local team commitment, overseas fellowship investment, and sustained ministerial support. Barriers to progress include insufficient political support, funding limitations, and inadequate long-term planning.

Conclusions: Developing kidney transplantation centres in LMICs is achievable with local team commitment and sustained political and financial support.

Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6
Establish the legal/ethical/ funding and political framework Develop an initial prospective outline strategic plan Establish a memorandum of understanding	Identify key team members, steering group Define capability development needs	Preparation of first pairs for transplant	Early transplants Continued capability development	Phase 5a: Programme and capability development Phase 5b: Minimal TLC support needed (e.g. surgical only) whilst developing other capabilities	Independent Support only for difficult and paediatric cases Continued development of capability and succession planning - sustainability and resilience Deceased donor programme development
Through all phases maintain Political support/training fellowships/observerships/mentorship/educational symposia					

EP_023 EVALUATING THE IMPACT OF ORGAN ALLOCATION POLICIES ON BLACK PATIENTS: A SINGLE-CENTER ANALYSIS

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Background: Estimated glomerular filtration rate (eGFR) is a key criterion for assessing kidney function and determining eligibility for transplantation in patients with end-stage renal disease (ESRD). Until June 27, 2022, eGFR calculations included race-based adjustments, potentially overestimating kidney function in Black patients, delaying their referral for transplant evaluation and waitlist enrollment. To address this disparity, as of January 5, 2023, OPTN Policy 3.7D mandated transplant programs to modify wait times for candidates affected by these race-based eGFR adjustments. This study evaluates the policy's impact on equity in kidney transplantation.

Methods: Transplant candidates at UF Health Transplant Center were reviewed per OPTN Policy 3.7D to identify those qualifying for wait time modification. The study included Black candidates aged ≥18 years who identified as such at the time of review. Descriptive statistics were used to summarize demographic and clinical data, analyzed using SPSS version 29.

Results: Of 162 adult Black candidates reviewed in late 2023, 46 (28.4%) received wait time modification, 99 (61.1%) were ineligible due to insufficient records, and 17 (10.5%) did not provide requested labs. Among eligible patients, mean age at listing was 52 (SD 15), mean eGFR was 15 (SD 4), and 60.9% were female. Time gained ranged from 79 to 1839 days (mean 629, SD 518). Eleven eligible patients underwent transplantation, gaining an average of 592.6 days (SD 431), a 266% increase in wait time accrual, compared to an average of 782.18 days (SD 889), a 217% increase in non-transplanted patients.

Conclusions: Preliminary data suggest OPTN Policy 3.7D has improved access to kidney transplantation for Black patients, with eligible candidates gaining additional years of wait time accrual. Transplanted patients experienced greater proportional gains, highlighting the policy's potential to address systemic disparities. Further multi-center studies are needed to assess broader impacts.

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EP_024 ANGIOPOEITIN AND ANGIOPOITEIN LIKES IN KIDNEY TRANSPLANT PATIENTS WITH PTDM

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Background: Post transplant diabetes mellitus (PTDM) has direct impact on patients' immune system. Angiopoietin and angiopoietin like are intrinsic mediators induced by immune cells.

Objectives: We aimed to determine the relationship between circulating angiopoietin-1 and 2 (ANG-1, 2) and angiopoietin like (ANGPTL 3-8) in kidney transplant patients who develop PTDM in comparison to those who do not develop diabetes (control).

Methods: All patients enrolled in this study from Diabetes Education Department of Dasman Diabetes Institute and outpatient clinics of the Hamad Al Essa Organ Transplant Centre of Kuwait. The study included kidney transplant recipients:155 PTDM and 154 control, age- and sex-matched. We determined plasma ANG 1 ,2 and ANGPTL 3-8 by enzyme-linked immunosorbent assay (ELISA). We determined the correlation between plasma ANG 1 and 2 and ANGPTL3-8 levels in the 2 groups.

Results: In our cohorts, most of patients (56%) were Kuwaiti and the two groups were comparable regarding their original kidney disease, dialysis type, donor type and the type of both induction and maintenance immunosuppression ($P > 0.05$). Also, pre-transplant co-morbidities were comparable in both groups ($P > 0.05$). We found significantly higher plasma ANG-1, ANGPTNL 6, 7, 8 levels in PTDM group compared to control group ($P < 0.001$) but plasma ANG 2, and ANGPTNL 3, 4 were comparable in the two groups ($p>0.05$).

Conclusion: Plasma ANG 1, ANGPTNL6, 7, 8 levels may correlate with disease severity, chronicity in transplant patients who develop PTDM, and serve as a potential biomarker of the disease severity.

Key Word: Angiopoietin; Angiopoietin Like, Kidney Transplantation, PTDM, ELISA

EP_025 ADDRESSING DIGITAL EXCLUSION FROM PHYSICAL ACTIVITY DIGITAL HEALTH INTERVENTIONS: THE EX-TAB STUDY

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Background: The Kidney BEAM trial demonstrated that a physical activity digital health intervention is an effective intervention to improve mental health-related quality of life in people with chronic kidney disease including kidney transplant. A limitation was that people without digital literacy skills or access to digital devices were excluded from the trial. This sub-study evaluated the feasibility of providing a WIFI-enabled Kidney Beam device plus training compared to usual care.

Methods: A single-site randomised controlled sub-study of 40 participants without access to a WIFI-enabled digital device, or people with a low score on a digital health literacy screening tool, to the Kidney Beam Ex-TAB intervention or to usual care. Of the 40 participants, 11 were kidney transplant recipients. The intervention group were provided with a WIFI-enabled iPad with the Kidney Beam application pre-downloaded. Participants were provided with training to use the iPad and how to access the 12-week Kidney Beam programme (twice-weekly exercise and education sessions). The usual care group were provided with sign-up instructions to the Kidney Beam application only. Participants were assessed at baseline and at 12 weeks. Primary feasibility outcomes included screening, recruitment, retention, adherence, safety and experience and acceptability of the intervention. Secondary outcomes were the same as in the main study. Semi-structured qualitative interview took place.

Results:

	Ex-Tab		Usual care	
Measure	Baseline	12 weeks	Baseline	12 weeks
Kidney Beam median time		135 (13.5-244.5) mins		0 (0,0) mins
KDQoL-SF.13 MCS	49.20 [11.9]	51.25 [8.03]	50.46 [11.24]	50.51 [12.38]
KDQoL-SF.13 PCS	32.43 [10.07]	37.99 [11.49]	37.28 [10.75]	33.18 [11.93]
Mean STS60 repetitions	13.67 [5.38]	16.87 [5.38]	17.53 [7.78]	13.06 [11.38]
PHQ4 median	3.00 [0.00-7.00] units	0.00 [0.00-3.00] units	3.00 [0.00-6.00] units	1.00 [o.oo-7.00] units

Conclusions: This mixed-methods feasibility RCT revealed that providing devices, plus training, for people with low levels of digital literacy was feasible and acceptable to people living with kidney disease. This intervention would be acceptable pre and post kidney transplant. All pre-set feasibility criteria were met. Results provide insight into future trial design and a multi-center RCT is planned.

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EP_027 EXCESS MORTALITY COMPROMISES KIDNEY TRANSPLANTATION OUTCOMES IN TYPE II DIABETIC DISEASE

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Background: The incidence of DM-II related kidney failure is rapidly increasing. This study aims to estimate the impact of type-II diabetes (DM-II) on kidney transplant outcomes and graft utility.

Methods: A nation-wide registry-based study that evaluates outcomes for all primary kidney transplantations performed in DM-II (761 deceased and 364 living donor procedures) and non-diabetic patients between 2000 and 2022 in the Netherlands.

Results: DM-II patients were 6 (deceased donor procedures) resp. 11.5 (living donor procedures) years older than the non-diabetic controls. Short-term (≤90 days) transplant outcomes for living donor procedures were similar for DM-II and non-diabetic controls. Deceased donor transplants in DM-II patients associated with a doubling of 90-days mortality to 4.7% (HR: 2.19 (95% CI: 1.49-3.23), p< 0.0001); and a 20% increase in the incidence of delayed graft function (p<0.0002). Evaluation of long-term graft survival, with death as competing risk indicated an equal (deceased (sub-distribution Hazard Rate (sHR) 0.95 [0.74-1.23]); respectively compromised (sHR 1.91 [1.37-2.65]; p<0.001) survival for grafts from deceased or living donors. DM-II profoundly impacted recipient survival (HR for recipients of a deceased donor graft: 1.58 (95% CI: 1.42-1.77), p<0.001), with cardiovascular and infection as dominant causes of death. The compromised recipient survival profoundly impacted the utility of kidney transplantations (median functional years for DM-II vs non diabetic recipients: 7.0 vs 12.4 (deceased) and 8.7 vs 17.2 (living) (p<0.001).

Conclusions: The efficacy of kidney transplantations in DM-II patients is severely compromised by reduced recipient survival. While this deficit may partially relate to the older age-at-transplantation, the cause of death distribution suggests a role for immunosuppressive regimens in the excess mortality observed. A shift in focus from optimized transplant- to optimized patient survival is warranted for DM-II patients. The increasing burden of DM-II on the donor pool, and the low graft utility for grafts transplanted in DM-II patients call for development of DM-II specific allocation strategies.

EP_028 PYSCHOSOCIAL VARIABLES INFLUENCE ACCESS TO AND OUTCOMES AFTER PAEDIATRIC KIDNEY TRANSPLANTATION

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Background: Kidney transplantation is the gold standard management for children with end-stage kidney disease. A cross-sectional survey of 12 UK paediatric nephrology centres on their transplantation plans for all children registered with ESKD revealed that 19% of children had psychosocial factors listed as a barrier to transplantation. However, it is unclear what these factors are.

Methods: A prospective, multi-centre (12 UK paediatric nephrology centres) mixed-methods study with QUAL-QUANT and QUANT-QUAL phases, with the aim to investigate these psychosocial factors, has been designed, implemented and now completed recruitment. We approached all families whose child with ESKD was being prepared for kidney-only transplantation, including children whose previous allografts had failed. Age-appropriate and validated questionnaire packs for children and their carers were distributed at pre-transplant baseline. These questionnaire packs collected psychosocial data including quality of life (QoL), mental health, family dynamics and relationship with healthcare. Follow-up questionnaires were distributed again either 1-year later or at 3-, 6- and 12-months post-transplant. Baseline medical data were collected prospectively from medical notes.

Results: 125 families were recruited to the study. 66 families have responded to their questionnaires to date, giving a 53% response rate. Where ethnicity has been reported, the majority of families were White (76.6%), followed by Asian (11.7%), Mixed-race (7.8%) and Black (3.9%). The majority of families had two carers living in the same household (74.0%), followed by single carer (19.5%), two carers living in separate households (5.2%) and other configurations (1.3%). Most carers reported their highest level of education as a college or university degree (52.4%), followed by secondary education (14.3%), post-graduate education (11.9%) and primary education (2.4%).

Conclusions: These preliminary findings reveal the demographics of families most likely to engage in longitudinal research examining psychosocial factors influencing access to kidney transplantation. Further analysis is required to examine the changes in psychosocial factors over time and their associations with kidney transplantation access and outcomes.

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EP_029 KIDNEY TRANSPLANT OUTCOMES ACCORDING TO MATCHING OF KDPI AND EPTS SCORES

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Background: Efficient allocation of donor kidneys to appropriate candidates is mandated in Korea with a very long waiting time for deceased donor kidney transplantation (DDKT). This study evaluates the prognostic implications of organ matching using the Korean Kidney Donor Profile Index (K-KDPI) and Korean Estimated Post-Transplant Survival (K-EPTS) scoring systems.

Methods: This study analyzed 7,443 DDKT recipients from 2008 to 2022 using national databases, including the Korean Network for Organ Sharing and the National Health Insurance Data Sharing Service. Patients were classified into four groups: Class 1 (low K-KDPI [<70] to low K-EPTS [<20]), Class 2 (low K-KDPI to high K-EPTS [≥20]), Class 3 (high K-KDPI [≥70] to low K-EPTS), and Class 4 (high K-KDPI to high K-EPTS). Both patient and graft survival rates were compared among four groups.

Results: Compared to class 1, other classes demonstrated a higher risk for graft failure (hazard ratio [HR] = 1.71, P <0.01 for class 2; HR = 1.61, P <0.01 for class 3; and HR = 2.76, P <0.01 for class 4). For patient survival, class 2 (HR = 2.68, P <0.01) and 4 (HR = 4.05, P = 0.01) exhibited an increased risk compared to class I, whereas class 3 (HR = 1.09, P = 0.76) did not show significant differences. Additionally, we developed a predictive model for survival differences between DDKT and dialysis based on K-KDPI and K-EPTS scores, which could provide potential survival benefits of DDKT to each patient.

Conclusions: Considering the superior outcomes in Class 1, it is advisable to implement a longevity matching strategy that prioritizes the allocation of donor organs with low K-KDPI to recipients with low K-EPTS. Furthermore, given the lack of significant differences in patient survival between Class 3 and Class 1 and considering severe organ shortage in Korea, it would be appropriate to allocate high K-KDPI donor organs without restriction to the low K-EPTS group, rather than exclusively prioritizing high K-EPTS group.

	Graft survival rate			Patient survival rate		
	Adjusted HR	95% CI	*P-value*	Adjusted HR	95% CI	*P-value*
Class 1 (low K-KDPI to low K-EPTS)	Reference			Reference		
Class 2 (low K-KDPI to high K-EPTS)	1.71	1.36 – 2.15	*<0.01*	2.68	1.81 – 3.97	*<0.01*
Class 3 (high K-KDPI to low K-EPTS)	1.61	1.23 – 2.11	*<0.01*	1.09	0.61 – 1.95	*0.760*
Class 4 (high K-KDPI to high K-EPTS)	2.76	2.22 – 3.43	*<0.01*	4.05	2.76 – 5.96	*0.01*

EP_030 LONG TERM RESULTS OF KIDNEY BIOPSY GUIDED EVALUATION FOR SIMULTANEOUS LIVER KIDNEY TRANSPLANTATION

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Background: After the introduction of MELD score in liver allocation, the number of simultaneous liver- kidney transplantations (SLKT) significantly increased, contributing to the shortage of allografts for patients (pts) waitlisted for kidney transplantation. We analyzed the data in our high-volume transplant center with a stable number of SLKT and reviewed the long term outcomes of our biopsy-guided kidney allocation policy for pts with renal dysfunction undergoing liver transplantation (LT).

Methods: We analyzed LT and SLKT performed from April 2007 to April 2018. Significant renal impairment at time of enlisting was defined as serum creatinine ≥ 2 mg/dL, RRT or proteinuria 1 ≥1 g/g. The composite kidney outcome after 5 years for pts with renal impairment who only underwent LT was defined as CKD stages G4 or G5, RRT, or renal death.

Results: In total 1056 LT and 19 SLKT were identified. 129 pts met the criteria for renal impairment. There were 95 male pts (73, 6%). 13 pts had ESKD receiving RRT prior to referral for LT and were automatically enlisted for SLKT. In evaluation of other pts with renal dysfunction 22 renal biopsies (Bx) were performed. There were no major complications. The most frequent Bx finding was IgA nephropathy (63.6%), followed by ATN (18.2%) and diabetic nephropathy (9.1%). Other 94 pts were diagnosed with acute kidney injury/hepatorenal syndrome (AKI/HRS). The cut-off for SLKT enlistment was more than 40% IFTA; or more than 30% of globally sclerosed glomeruli. Based on Bx results additional 6 pts were enlisted for SLKT. None of the pts with presumed AKI/HRS who received only LT and survived for more than one-year post-LT required RRT at one-year post-LT. At 5 years after LT, only 9% of pts with renal impairment who did not receive a kidney allograft reached the composite kidney outcome.

Conclusions: Kidney Bx is an useful tool to avoid kidney graft wasting during enlistment for SLKT. Our findings suggest that percutaneous kidney Bx in pts with advanced liver disease is a safe procedure in experienced centers. Follow-up at 5 years revealed a low incidence of composite adverse kidney outcome, confirming the safety of our allocation approach.

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EP_031 THE BURDEN OF CORONARY ARTERY DISEASE IN LUNG TRANSPLANT CANDIDATES

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Background: Evaluation of lung transplant candidates with and without coronary artery disease (CAD) in order to optimize the selection criteria for pre-listing coronary angiography (CAG) and understand the impact of CAD on lung allograft function after transplant.

Methods: This was a monocentric retrospective study including all consecutive patients who received a CAG before listing (at our centre CAG is currently performed in individuals who have risk factors, i.e. smoking and/or severe dyslipidemia, and/or age > 50) and underwent lung transplantation at our institution between January 2015 and April 2023. We collected data on demographics, pre-transplant CAG and posttransplant graft function. Population was divided into three groups based on CAG results: CAD- (no CAD); CAD+ (moderate CAD); CAD++(obstructive CLAD).

Results: 102 patients were considered, 61 males, median age 58,4 years. See Fig1 for groups based on CAD; in these groups age (p value =0.003) and family history of CAD (p value = 0.015) were significantly different, especially between the CAD++ and the CAD- group. Over 80% ofCAD patients were older than 60 years. By constructing the ROC curve to calculate the sensitivity and specificity of the test, an optimal ratio was found at the age of 62.5 years (Fig.2). Following transplantation, no statistically significant differences were found between the three populations in terms of spirometry and walking tests, both immediately and 6 months after the transplant procedure.

Conclusions: Age represents a valid criterion for selecting patients that have to undergo pre-transplant CAG. However, in the future, consideration could be given to raising the minimum age for the examination. The study also highlights that CAD, whether moderate or obstructive, does not appear to impact short-term post-transplant mortality or the patients' functional recovery. Further studies will be necessary to understand the impact of CAD on transplant candidates and the appropriate age for performing pre-transplant CAG.

Fig. 1

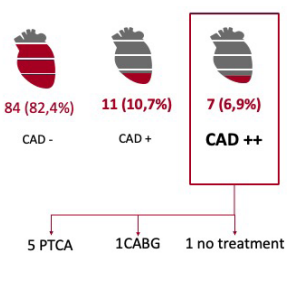
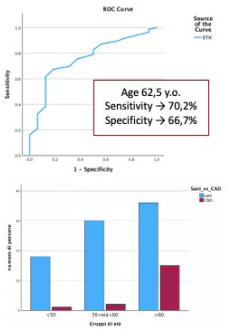


Fig. 2



EP_032 PREHABILITATION AND REHABILITATION PROGRAM IN LIVER TRANSPLANTATION: PRELIMINARY RESULTS

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Background: Sarcopenia and frailty are prevalent conditions amongst liver transplantation (LT) candidates consistently associated with increased morbidity and mortality. Prehabilitation and rehabilitation programs may optimise patient status before LT and enhance their recovery.

Methods: LT candidates on the waiting list (WL) at Puerta de Hierro Hospital (August 23 – October 24) were evaluated using bioelectrical impedance analysis and handgrip at listing, before LT, at discharge, and 3 months after LT, receiving nutritional and physical exercise interventions during follow-up. Sarcopenia was defined as a handgrip strength <27 kg in men and <16 kg in women, and/or a value <0.6 on a nomogram composed of gender, BMI, and phase angle (PA). Frailty and pre-frailty were defined as a Liver Frailty Index (LFI) >4.5 and 3.2-4.5, respectively. Wilcoxon and McNemar tests were used to analyze anthropometric changes, sarcopenia, and frailty status.

Results: Out of the 27 patients included, 37.5% exhibited frailty and 45.8% sarcopenia at WL inclusion, with no significant anthropometric changes during WL stay. Mean age at enlistment was 59.6 (SD 7.07) years, 33.3% were female and 3 (12.5%) had a BMI < 20.0 kg/m^2. Median MELD score was 15 (IQR 11-18). For the 16 patients who underwent LT, the median time in WL, ICU and hospitalization were 46 (IQR 26-19), 6 (IQR 4-12) and 26 (IQR 19-53) days, respectively. At discharge, a significant worsening of muscle mass, PA, and handgrip was observed (p0.005, p0.037, and p0.003, respectively) compared to baseline, increasing the rate of sarcopenia up to 85.7%. Importantly, neither sarcopenia nor frailty correlated with ICU stay, graft complications, or infections. Compared to hospital discharge, a loss of fat mass (p0.011) and body fat % (p0.003) were observed 3 months post-LT, along with an improvement in handgrip strength and muscle mass, albeit non-statistically significant. Furthermore, no patient was classified as frail (60% pre-frail) compared to 71.5% at discharge.

Conclusions: Sarcopenia and frailty exacerbate significantly in the following weeks after LT. Rehabilitation programs could improve body composition and mitigate frailty. Earlier and more prolonged interventions, along with larger sample sizes, are needed to evaluate the impact of prehabilitation in the LT setting.

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EP_033 EVOLVING TRENDS IN LIVER TRANSPLANTATION: INSIGHTS FROM ROMANIA'S PIONEERING CENTER

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Background: Over the past two decades, liver transplantation (LT) at Fundeni Clinical Institute has experienced significant evolution, mirroring global shifts in indications, patient profiles, and surgical innovations. Aim: To examine the evolution of patient listing, transplantation practices, and outcomes from 2000 to 2024, highlighting key trends in Romania's largest transplant program.

Methods: A retrospective analysis of LT data from 2000 to 2024 was conducted, dividing the period into three intervals: 2000–2009, 2010–2019, and 2020–2024. Cox regression was used to identify independent risk factors for wait list (WL) mortality and post-LT survival.

Results: Over time, WL patients presented with increasing age and disease severity (labMELD). While HBV- and HCV-related etiologies declined, HBV/HDV coinfection, alcohol-related liver disease, and metabolic-associated liver diseases became more prominent. The inclusion of HCC patients on the WL rose significantly ($p<0.0001$), with a marked increase in those exceeding Milan criteria. A total of 1,251 LTs were performed during the study period. Viral etiologies predominated in HCC cases, while alcohol-related liver disease was the leading cause among patients with decompensated cirrhosis. Pre-LT locoregional therapies were used in 42% of HCC patients on the WL. Median WL survival improved from 26.6 months (2000–2009) to 36.6 months during 2010–2019, while median survival for 2020–2024 has not been reached. Independent risk factors for WL mortality included higher MELD scores at listing, presence of HCC, hepatorenal syndrome, and episodes of hepatic encephalopathy. Post-LT survival for HCC patients was 84.4%, 61.2%, and 53.3% at 1, 5, and 10 years, respectively. Risk factors for HCC recurrence included the Duvoux score, exceeding Milan criteria, and BCLC class B.

Conclusion: The evolution of LT at our Center reflects significant progress in liver disease management and transplantation in Romania. These findings underscore the importance of refining MELD-based models and developing targeted strategies to optimize outcomes for a growing and increasingly complex patient population.

EP_034 UNDERSTANDING CARBON AND EQUITY HOTSPOTS IN THE LIVING KIDNEY DONOR ASSESSMENT PATHWAY

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Background: Living Kidney Donor (LKD) transplantation can increase the availability of kidneys for transplantation, reducing dialysis demand with benefit for both patients and the environment. However, the pathway for recruiting, screening and preparing a potential living donor is variable between services, sometimes lengthy, and can entail multiple journeys for investigation. This project aimed to identify drivers for variation between transplant services and opportunities to enhance environmental sustainability and equity.

Methods: Three UK living donor kidney transplant services provided insight into pathway variations in different contexts (urban/rural and transplant/non-transplant centre). The LKD assessment pathway for each service was mapped from initial donor contact to the pre-operative appointment. Lived experience interviews provided insight into donor experience. For carbon analysis, each activity, event, and product along the pathway was appraised. A hybrid approach was then used to estimate the carbon footprint of the assessment pathway for each service, using primary data and emission factors derived from published studies.

Results: The average carbon footprint of a LKD assessment pathway is estimated to be 114.2 kg CO_2 equivalent (kgCO2e). Donor travel is the largest contributor (62%), followed by blood and swab tests (17%), diagnostics (10%), staff travel (7%), overhead energy consumption (3%), urine tests (1%), and transporting blood samples (0.001%). Carbon footprints varied across the three services, from 92.3 kgCO2e to 139.0 kgCO2e per donor, with the number and location of appointments driving the differences.

Conclusions: Condensing investigations into fewer in-person visits and performing standard blood tests at a local hospital or GP surgery reduces the carbon footprint of the LKD assessment pathway. However, any carbon reduction model needs to accommodate the individual needs of potential donors and maintain equity of access to LKD transplantation, recognizing the significant carbon saving of LKD transplantation in comparison to continuation of dialysis treatment.

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EP_035 TRANSPLANT ASSESSMENT AND RELATIVE OPPORTUNITY TOOL (TAROT) READINGS - 2 YEAR OUTCOMES

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Background: Equality and equity of access to transplantation are principles central to organ allocation schemes. Following a significant growth in the proportion of highly sensitised renal wait-listed patients, we established a proactive approach to wait-list management. TAROT is a framework against which all renal wait-listed recipients are assessed and is delivered by the H&I lab with support from the complex immunology MDT (figure 1). It incorporates a stepwise delisting strategy that maximises an individual's opportunity for transplantation whilst balancing immunological risk that is acceptable to their clinical circumstances. Rate of progression through TAROT is based on active wait time and sensitisation status.

Methods: In this retrospective observational study, renal transplants performed 01/01/2021 - 31/12/2022 were categorised according to TAROT, and clinical parameters were assessed with a median follow up of 874 (range 515-1217) days.

Results: 223 deceased donor transplants were performed. Twenty-three (10.3%) occurred through TAROT. TAROT enabled transplants were more sensitised, with higher calculated reaction frequency, cRF (median cRF 91% TAROT vs 0% Standard, p<0.0001), and matchability points (median MP 8 TAROT vs 4 standard, p=0.0008). Despite a predicted increased wait time for TAROT patients (based on cRF and MP), they did not wait longer than standard patients (median wait time 1311 days TAROT vs 1036 days standard, p=0.0668). Twelve grafts were lost during follow up (n=2 TAROT, n=10 standard). There was no statistically significant difference in death-censored graft survival (p=0.5220, log rank). Ninety-seven living donor transplants were performed. Eleven (11.3%) were facilitated by TAROT. Three grafts were lost during the follow up (n=1 TAROT, n=2 standard). There was no statistically significant difference in death-censored graft survival (p=0.3031, log rank).

Conclusions: Early data demonstrates that TAROT has been successful in facilitating timely access to transplants in highly sensitised patients, with no detriment to outcome.

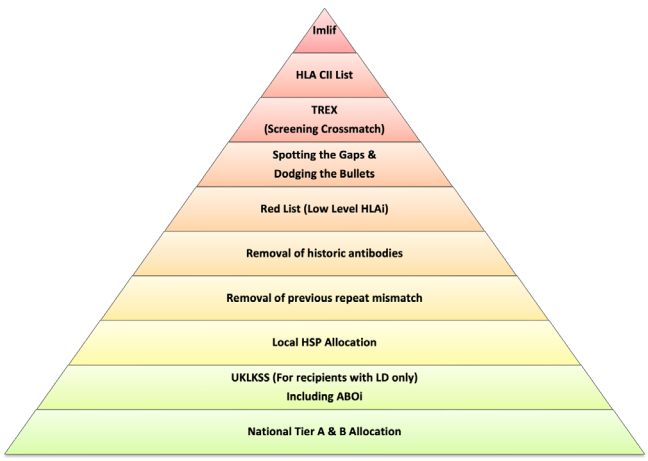

Figure 1. TAROT Framework

EP_036 EVALUATING THE READABILITY OF CHATGPT-GENERATED KIDNEY TRANSPLANT FAQS VS CONVENTIONAL RESOURCES: IS CHATGPT WORTH IT?

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Background: Patient education materials should target a 6th grade reading level to ensure accessibility. As large language models (LLMs) like ChatGPT are increasingly used by patients to educate themselves on medical topics, it is essential to evaluate their effectiveness.Kidney transplantation (KT) is a complex procedure that requires patients to have a clear understanding to ensure successful outcomes. This study aimed to evaluate the readability of ChatGPT-generated FAQs on KT topics compared to conventionally available resources.

Methods: Two ChatGPT models, ChatGPT-4o and ChatGPT-o1, were used to generate responses to 12 FAQs on KT. The responses were compared with FAQs from conventional online sources, including the National Kidney Foundation and NHS Organ Donation websites. Readability was objectively assessed using the Flesch Reading Ease Test (FRET), Flesch-Kincaid Grade Level Test (FKGLT), and the Simple Measure of Gobbledygook (SMOG). Statistical analyses was performed using a one-way ANOVA with Tukey post-hoc analysis to identify significant differences.

Results: Conventional resources showed superior readability, with higher mean FRET scores compared to ChatGPT-4o (p = 0.0285) and ChatGPT-o1 (p = 0.0003). Notably, both ChatGPT models outperformed conventional resources in addressing questions whose responses were based on interpretation of facts but underperformed in questions requiring careful explanation of personalised management plan.However, none of the 3 groups achieved to reach the suggested readability scores. FRET, FKGLT and SMOG numbers for all groups can be found in the table provided. Additionally, despite ChatGPT-4o performing better than ChatGPT-1o in across the majority of the questions, there was no statistical difference between the performance of the two models.

Conclusions: ChatGPT-generated materials show promise as a supplementary convenient tool for patient education in KT, offering readability levels comparable to conventional resources for certain, fact-based queries. Further research is required to improve AI-generated material and to evaluate their effectiveness across diverse languages and patient populations.

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EP_037 EQUITY IN KIDNEY TRANSPLANT ALLOCATION FOR ANTILLEAN PATIENTS WITHIN EUROTRANSPLANT

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Background: The Antilles are a group of islands in the Caribbean that are still part of the Kingdom of the Netherlands. The population of these islands is ethnically diverse, shaped by the historical transatlantic slave trade and migration. Since 1998, patients with kidney failure residing on these islands can enter the waiting list of Eurotransplant. However, the Eurotransplant donor database consists mainly of donors of Caucasian descent, which may result in a smaller donor pool for patients from the ethnically diverse Antilles. We compared the prevalence of broad HLA antigens between patients residing on the Antilles, patients residing in the Netherlands and Eurotransplant kidney donors.

Methods: A cross-sectional analysis of the Amsterdam kidney transplant waiting list as of 14-03-2024 was conducted. Patients residing on the Antilles or in the Netherlands were compared with deceased donors screened between January 2021 and January 2024. The primary outcome was the prevalence of broad HLA antigens and the percentage of overlap between patient groups and donors. Descriptive statistics, a Mann-Whitney U test and a Brown-Forsyth test were used to analyse the data.

Results: A total of 186 patients on the waiting list and 295 donors were included to assess HLA prevalence. The overlap of broad HLA antigen prevalence with the donors was 75.8% for Antillean patients as compared to 87.7% for Dutch patients (figure 1). The groups were not significantly different. However, the variance of the ratio's between groups was found to be significantly different (p= 0.04).

Conclusions: Patients residing in the Antilles on the Eurotransplant waiting list appear to have a lower compatibility with donors, in terms of broad HLA antigens, compared to patients residing in the Netherlands. This suggests a different distribution of (more rare) broad HLA antigens among the Antillean population. Such a disparity may lead to a reduced donor frequency and potentially longer waiting times for Antillean patients. To explore this further, we will investigate differences in donor frequency and waiting times between patients living in the Antilles and those living in the Netherlands.

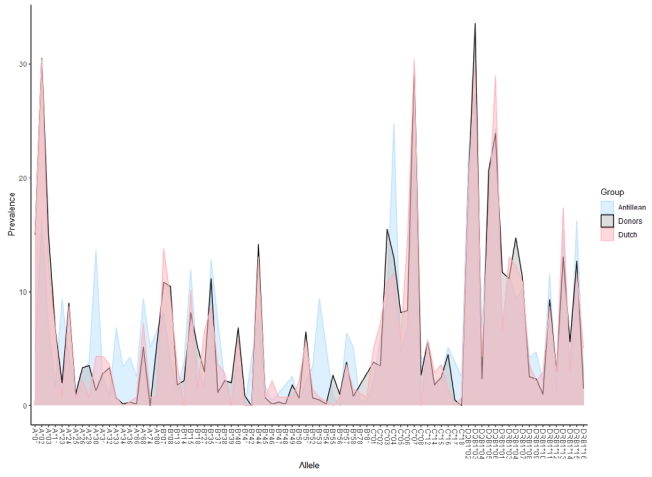

Figure 1: Prevalence of broad HLA alleles in the groups.

EP_038 ETHICAL, LEGAL AND ADMINISTRATIVE ASPECTS OF ORGAN ALLOCATION TO FOREIGN PATIENTS AT ISMETT

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Background: ISMETT is fully dedicated to organ transplant and advanced therapies for end-stage abdominal and thoracic diseases, and is an international partnership between the Regional Government of Sicily and UPMC, a global leader in medicine and research headquartered in the USA. Its International Patient Service Department has a 20-year long experience in managing the organization of foreign patients' medical care, before, during and after the patient's stay in Italy. All the above, including the excellent clinical outcomes, has made it a reference Center for the whole Mediterranean area and beyond, with requests for transplant from all over the world. National and international rules apply that are pivotal when a foreign patient is involved.

Methods: International agreements and collaboration with national and international Institutions have been established. Also, foreign patients are divided into different administrative categories, including self-paying, EU, humanitarian, illegal migrants, and other types. This division affects both administrative aspects and clinical management.

Results: All aspects are faced, from the financial standpoint (clinical costs must be covered, as foreign patients might not be entitled to healthcare in Italy free-of-charge), to the ethical standpoint (patients who do not live permanently in Italy might incur into organ loss months/years after surgery if proper post-op management is not guaranteed in the Country where patient lives). A dedicated Department has permitted foreign patients' access to medical care to while obeying the national laws and the international regulations.

Conclusions: Different approaches are needed based on patients' administrative category, Country of residence, social status, etc, so as to make sure that cadaveric organs are not waisted and public funds are not misused, while granting the best medical care and proper access to healthcare.

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EP_039 NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Normothermic machine perfusion (NMP) is employed for multiple indications, including increasing the margin of acceptable organ quality. Centers using NMP may assess the viability of hard to place livers and allocate them to patients with lower MELD scores, typical of the hepatocellular carcinoma (HCC) population. The impact of NMP on waitlist times and short-term outcomes remains understudied in HCC patients.

Methods: This retrospective, single-center study included patients who received a liver transplant (LT) using NMP from program initiation in July 2022-March 2024 (n=150). Waitlist time was defined as days from listing to transplant, with outliers excluded. Demographic features and medical history were extracted from the electronic medical record.

Results: MELD scores at listing and removal were lower in the 45 patients with HCC than other NMP patients, and 34 HCC patients had MELD exception points. Common etiologies for HCC were metabolic associated steatohepatitis (n=20), hepatitis C virus (n=12), alcohol-associated liver disease (n=9), and hepatitis B virus (n=9). NMP in HCC cases was primarily used for donation after circulatory death or viability assessment, with significantly higher mean donor risk index (DRI) scores compared to non-HCC cases. ICU length of stay, readmission in 30 days, peak AST/ALT in 7 days, biliary complications, and retransplantation rates were comparable. Reoperation rates were lower in HCC NMP patients. Waitlist days for all HCC patients decreased from 2021-2023 and from 2022-2023, but not from 2021-2022. The number of HCC transplants across years did not significantly differ.

Conclusions: HCC patients receiving LT with NMP received higher risk organs yet had comparable short-term outcomes and lower reoperation rates. Waitlist times for HCC patients have decreased since initiating our NMP program, possibly due in part to an expanded pool of rescued marginal organs matched with less critically ill patients with HCC.

		HCC		Non-HCC		P-value
		N	Frequency or Mean (SD)	N	Frequency or Mean (SD)	
Demographic features and medical history	Age	45	61.3 (10.9)	105	50.5 (11.8)	0.00*
	Diabetes mellitus	45	20	105	25	0.02*
	Hypertension	45	24	105	33	0.02*
	MELD at listing	45	12.9 (6.1)	105	24.9 (8.8)	0.00*
	MELD at removal	41	15.2 (7.2)	99	27.8 (9.3)	0.00*
NMP Indications and organ quality	DCD and/or viability assessment	45	40	105	70	0.01*
	Case complexity (i.e. multivisceral transplant, retransplantation)	43	3	91	21	0.02*
	DRI	27	1.72 (0.29)	64	1.54 (0.35)	0.02*
Outcomes	ICU LOS	41	8.3 (19.7)	97	11.5 (19.9)	0.39
	Readmission in 30d	26	8	56	14	0.58
	Peak AST first 7d	34	1944.4 (2105.9)	76	1785.4 (2624.4)	0.76
	Peak ALT first 7d	34	805.5 (703.0)	76	756.5 (818.6)	0.76
	Re-transplant	45	0	105	4	0.18
	Reoperation	38	6	94	31	0.05*
	Biliary complications diagnosed by ERCP	45	4	105	11	0.77

*$p \leq 0.05$ was considered statistically significant. Asterisks (*) denote significant p-values.

Table 1: Patient Demographics, NMP Indications, and Outcomes in HCC and non-HCC Cases

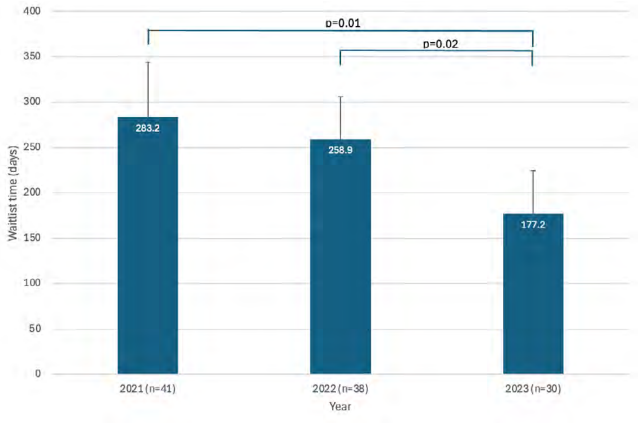

Figure 1: Trends in waitlist times from 2021-2023

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EP_040 SERUM REVOLUTION: TRANSFORMING PATIENT EMPOWERMENT IN RENAL TRANSPLANTS IN ARGENTINA

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Background: The serum bank is essential for deceased donor kidney transplantation in Argentina, where vast geographical distances complicate logistics and coordination. Despite patients on haemodialysis attending dialysis centers three times weekly, there is inconsistent availability and updating of sera in the serum bank. Legislation mandates dialysis centers to collect and ship samples for updates, yet this process remains inefficient. Recognizing that patients are most impacted by these shortcomings, we propose a paradigm shift that empowers them to monitor and request updates to their serum status.

Methods: An online platform will be developed to allow individuals on the kidney transplant waiting list to check their serum status in the serum bank and receive timely notifications. This platform will offer secure, personalized access and provide educational resources on the importance of serum in transplant compatibility. Collaboration between web developers and healthcare experts will ensure a user-friendly interface, with integration into existing health systems for data synchronization, security, and privacy compliance.

Results: Preliminary observations suggest that empowering patients to verify and update their serum status may streamline the transplant process, reduce waiting times, and foster shared responsibility among patients, dialysis centers, and medical teams. However, ensuring consistent data accuracy, overcoming technological hurdles, and protecting patient privacy remain significant challenges.

Conclusion: Creating a patient-centered platform to verify and update serum in the serum bank represents a significant step toward a more efficient and equitable kidney transplant system in Argentina. This approach could improve transplant outcomes and reduce delays by encouraging proactive involvement from all stakeholders. The next steps include pilot testing and phased implementation, with ongoing evaluations to refine and enhance the system's impact.

EP_041 RAISING AWARENESS ABOUT ORGAN DONATION AND TRANSPLANTATION AMONG HEALTHCARE PROFESSIONALS

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Background: Organ donation can be a life-saving opportunity for patients with severe organ failure. In Vietnam, the rate of organ donation of the deceased Vietnam population is execptionally low. This necessitates enhancing awareness regarding organ donation among healthcare professionals, which can motivate the general population.

Methods: In the 108 Military Central Hospital, we have implemented a number of solutions to help improve awareness about organ donation and transplantation among healthcare professionals such as: Conducting research about awareness of objects (basic information, sources of information, factor influencing the decision to donate organs,...), sending medical staff to extra classes about ODT, especially the class about approaching the family of potiential deceased donors, organizing consultations and propangoda on ODT, establishing independent recepient groups and donor groups to exchange information about ODT and establish a network of medical staff in the hospital to promptly detect brain-dead patients as potential organ donors.

Results: The number of brain-dead individuals identified as viable organ donors (50 cases) in the first half of 2024 has increased dramatically following the implementation of the aforemetioned methods (to match the entire number of patients identified tin the preceding five years). The sucessful organ donation rate reached 10%.

Conclusions: It is necessary to raise the knowledge of organ donation among healthcare professionals. Solutions related to establishing a network and training members related to thr topic of detecting potential brain-dead organ donors as well as mobilizing patients' families should be given special priority in hospital policy.

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EP_042 IMPACT OF CULTURAL BARRIERS, RESOURCE LIMITATIONS IN THE IMPLEMENTATION OF LIVING KIDNEY TRANSPLANTATION PROGRAM

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Background: Pre emptive living kidney transplantation is recognized the preferred treatment for those with End Stage Kidney Disease (ESKD) with improved survival, quality of life. In Italy, although kidney transplant rates have been increasing, there are multilevel barriers and disparities in access to a living transplant program. Blood type and crossmatch incompatibility slow down the goal of a pre emptive kidney transplantation. In Italy, National Kidney paired donation (KPD) program is well structured offering incompatible donor/recipient pairs the opportunity to match for compatible transplants. Despite its increasing popularity, very few pre emptive transplants have resulted from KPD.

Methods: We analyzed the pairs evaluated for living kidney transplantation in one year in our center by assessing the causes of ineligibility. All couples were offered desensitization in case of incompatibility or adherence to kidney paired donation.

Results: We evaluated 85 pairs for transplantation and performed 19 living kidney transplants, of which 11 were pre emptive. 5 couples joined the kidney paired donation program, but only two patients were kidney transplants but after a dialysis course. Few patients have accepted desensitization therapies.

Conclusions: KPD programs and AB0 incompatible transplantation have offered innovative solutions to overcome immunological incompatibilities. Unfortunately, participation in KPD is not universally accepted and there are many areas in Italy where KPD is not proposed. To perform pre-emptive living transplants, early nephrological referral to the transplant center is crucial; even today, patients are referred late. A better understanding of barriers may allow for systemic solutions which will increase the goal of pre-emptive living kidney transplantation.

EP_043 RANSOMWARE CRISIS TO RECOVERY: THE IMPACT OF INFORMATION TECHNOLOGY OUTAGE ON LIVER TRANSPLANT SERVICES

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Background: On June 3, 2024, a ransomware attack on the pathology provider for NHS Trusts in South-East London severely disrupted healthcare, including liver transplant (LT) services at King's College Hospital. Essential pathology, blood transfusions, and diagnostics were delayed, impacting transplant patient care. This review examines the impact on LT services and lessons learned.

Methods: King's adult LT waiting list, including active and suspended patients, was obtained from NHS Blood and Transplant. Declined offers due to the inability to perform transplants were recorded.

Results: During the 23 weeks outage period (until 10th November 2024), the average transplants per month decreased from 14 per month prior to outage to 9 per month during the outage. Due to strategies implemented, transplant numbers increased from 15 in the first 11.5 weeks of the outage to 34 in the next 11.5 weeks. The waiting list, active, and suspended patients grew by 9.8% (204 to 224), 12.5% (176 to 198), and 13.0% (23 to 26) respectively. 221 liver offers were declined due to the outage, including 21% named DBD through the National Liver Offering Scheme (NLOS), 21% fast-track DBD, 24% zonal DCDs, and 34% fast-track non-zonal DCDs. Of the 46 named DBD offers, 22 (48%) were single offers, and rest were multiple offers to five named patients. Eight patients were transferred to two "mutual aid" centres of which 3 were transplanted, 1 delisted, 2 died, and 2 handed-back. Key strategies during the outage included: 1. Prioritising emergency/urgent LTs; 2. Risk-stratifying high-risk cases; 3. Collaborating with "mutual aid" centres; 4. Limiting to one daytime LT every 24 hours; 5. Using machine perfusion for daytime transplants; 6. Ensuring effective communication with NHSBT, pathology, centres, and families.

Conclusions: The ransomware outage caused a backlog, limiting transplant activity due to logistical challenges in blood cross-matching. 79% of offers did not derive from the NLOS and a significant proportion of NLOS offers were solitary, exposing the unpredictability of the NLOS and reliance on alternative organ sources. It highlighted vulnerabilities in healthcare IT, underscoring the need for robust cybersecurity, data backups, contingency planning, mutual-aid agreements, and a national shared IT system for patient transfers.

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EP_044 ENDOVASCULAR STENTING OF THE EXTERNAL ILIAC ARTERY IS NOT A CONTRAINDICATION FOR KIDNEY TRANSPLANTATION

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Background: With increasingly ageing population, both end-stage renal disease and peripheral artery disease become more prevalent. Due to the benefits of minimally invasive surgery, peripheral artery disease is increasingly treated with endovascular procedures. Endovascular stenting of the external iliac artery (EIA) is often considered a contraindication for kidney transplantation, as clamping of the artery will lead to possible damage to the stent. In this study, we describe our first experiences of kidney transplantation with a graft placed on an endovascular stent.

Methods: We performed one kidney transplantation with a graft placed on a self-expandable metal stent and one kidney transplantation with a graft placed on a covered stent as part of an endovascular repair of the aortic bifurcation, using endovascular balloon occlusion for occlusion of the proximal side of the EIA in both cases.

Results: One recipient received a graft of a donation after circulatory death donor. The recipient experienced a short period of delayed graft function, but has a good kidney function at one year after transplantation, with an eGFR of 52 mL/min. The other recipient received a graft from a living donor. He experienced an episode of rejection after transplantation, but has an excellent kidney function at six months after transplantation, with an eGFR of 75 mL/min. Both recipients experienced no complains of ischemia of the ipsilateral limb.

Conclusions: This study shows our preliminary experience with implantation of a kidney graft on an endovascular stent in the external iliac artery. This demonstrates that implantation of a kidney graft on an endovascular stent can be safe and feasible, and is not necessarily a contraindication for kidney transplantation.

Figure 1: Kidney graft directly implanted on endovascualr stent in left exernal iliac artery

EP_045 ADVANCING EQUITY IN ORGAN DONATION & TRANSPLANTATION; PUBLIC-PRIVATE PARTNERSHIPS IN UNDERSERVED NORTH-EAST INDIA

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[1]Mohan Foundation; Managing Trustee, [2]Mohan Foundation, [3]Mohan Foundation; Nil

Background: MOHAN Foundation, an NGO focused on organ donation and transplantation for over 27 years, initiated a project in Manipur, a region with significant socioeconomic challenges and limited kidney transplant services. With only one government hospital offering these services, patients had to travel long distances for transplants. Partnering with local government bodies and healthcare organizations, the Foundation aimed to improve infrastructure, raise awareness, and enhance professional training in Manipur, starting with corneal and kidney transplant services. Supported by the SBI Foundation, this initiative showcased the potential of public-private partnerships in advancing healthcare equity.

Methods: The Jawaharlal Nehru Institute of Medical Sciences (JNIMS) in Imphal was upgraded to support kidney and corneal transplants. A surgeon received training at Coventry University Hospital and Cambridge, UK, to develop local expertise. The Foundation raised awareness, conducted training workshops for ICU staff and nurses, and engaged the community. The SBI Foundation's financial support ensured sustainability. Initiatives launched in 2017 experienced a 24-month hiatus due to the COVID pandemic.

Results: The collaboration achieved significant milestones, with the first living kidney transplant conducted on June 18, 2022, followed by 37 living donor kidney transplants. The first deceased organ donation occurred on August 2, 2023, with two more on October 11, 2023, and February 12, 2024. A corneal bank established on November 29, 2023, facilitated the first corneal transplantation on January 18, 2024, and the first deceased corneal retrieval on February 12, 2024. The initiative's success has led other government hospitals to seek similar partnerships.

Conclusions: The intervention in Manipur highlights the transformative impact of public-private partnerships in healthcare. Through awareness campaigns, training, advocacy, and the initiation of kidney and corneal transplants, the initiative addressed access and equity in underserved regions. Its success serves as a blueprint for similar efforts in other areas facing organ donation challenges.

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EP_046 RISK FACTORS ASSOCIATED WITH BROADENING SENSITISATION ON THE WAIT LIST IN THE CONTEXT OF MAINTAINED IMMUNOSUPPRESSION

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Background: For patients with failed allografts (GF) who are being considered for re-transplantation, de novo sensitisation whilst on the waitlist impedes chances of receiving another graft. This study aims to investigate the contribution of the immunological risk factors of the failed allograft to de novo sensitisation in the context of maintained immunosuppression.

Methods: From 672 allograft failures (GF) from a single centre, 169 patients who were reactivated on the waitlist were identified and analysed. The median follow up was 108 (59-150) months. As per centre protocol, all patients with allografts remaining in-situ are maintained on tacrolimus monotherapy. Monitoring for HLA antibodies follows national guideline recommendations. High sensitisation is defined as a cRF≥85%.

Results: Baseline patient and characteristics of the GF are shown in Table 1. At the time of GF, 83 (49.1%) were non-sensitised (NSP), 65(38.5%) sensitised (SP) and 21(12.4%) highly sensitised (HSP). The median time to activation following GF was 8(3-15) months, when 47(27.8%), 54(32.0%) and 68(40.2%) of patients were NSP, SP and HSP respectively. On adjusted analysis, HSP status at activation was associated with shorter allograft longevity (p=0.008), graft nephrectomy (p<0.001), but also total ABDR mismatch (p=0.046) and DSA at any time point whilst the graft was functioning (p=0.007). Time to activation and rejection at any time point was not associated with HSP status. Of 96 non-HSP patients, 32(33.3%) developed new HLAAb whilst on the waiting list, after a median follow up of 16(8-36) months, 10(10.4%) becoming highly sensitised. On adjusted analysis, risk factors for de novo HLA antibodies were any sensitisation at the time of activation (p<0.001), total ABDR mismatch (p=0.013), and rejection at any point whilst the graft was functioning (p=0.03).

Conclusions: Broadening of sensitisation whilst on the list is more likely in those who are sensitised at the time of activation or have immunological risk related to the failed allograft, even in the context of maintained immunosuppression.

		N=169 (%)
Age at GF (years)	Median	50 (39-59)
Gender	Male	100 (59.2)
Ethnicity	Black	39 (23.1)
	Caucasian	57 (33.7)
	South Asian	66 (39.1)
	Other	7 (4.1)
Graft Type	DD	85 (50.3)
	LD	62 (36.7)
	SPK	5 (3.0)
	ABOi/HLAi	17 (10.1)
Primary Allograft		146 (86.4)
Total ABDR Mismatch	Median	4 (3-4)
Sensitised at time of Transplant		105 (62.1)
DSA at any time pre-GF		74 (43.8)
Rejection at any time pre-GF		80 (47.3)
Transplant Longevity (years)	Median	4 (1-7)
Early GF (first 30 days)		25 (14.8)
Graft Nephrectomy		77 (45.6)
Time to Graft Nephrectomy	Years	3.2 (0-19) months
HLA Sensitisation Status at activation	Non-sensitised (NSP)	47 (27.8)
	Sensitised (SP)	54 (32.0)
	Highly Sensitised (HSP)	68 (40.2)
Median Time to Activation	Months	8 (3-15)

Table 1. Patient and Failed Allograft (GF) Characteristics

EP_047 UNUSUAL GRAFT LIVING DONOR LIVER TRANSPLANTATION FOR FUTURE DONOR POOL EXPENDITUREA

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Background: Since its first success in 1989, living donor liver transplantation (LDLT) has been accepted as a valuable treatment for patients with end-stage liver disease. LDLT is viewed as an important opportunity to expand the overall donor pool for liver transplantation (LT), shorten waiting times for a life-prolonging LT surgery, and reduce LT waitlist mortality. Potential opportunities for expanding living liver donor and recipient candidate criteria include using donors with more than minimal hepatic steatosis, evaluating older donors, performing LDLT in older recipients to facilitate timely transplantation, and providing candidates who would benefit from an LT, but may otherwise have limited access (ie, lower MELD scores), an avenue to receive a life-prolonging organ. The main concerns when using LDLT in adult patients are the appropriateness of the size of the graft that can be safely harvested from the donor, such as residual liver volume and vascular variation.

Methods: A survey was conducted on patients who were tested as donors at Seoul National University Hospital from July 2011 to May 2024. Dynamic CT and MRI were taken as imaging tests, volume was measured using Dr. Liver volumetry software, and fat fraction was measured using MRI.

Results: There were 2343 recipients and HBV recipients were 1286, or 54.9%, and ABOi patients were 602, or 25.7%. There were 3,225 donor candidates, 1,273 donors were eliminated and anceled due to recipient issue was 783. There were 34 donors who were eliminated because the GRWR was less than 0.8, 166 donors who were eliminated because the remaining liver volume was less than 30%, 8 donors who were eliminated because they were given lower priority compared to other donors due to vascular mutations, and 108 donors who were eliminated due to severe fatty liver. The number of patients who was thought to be a possible 2nd staged LT for a donor who was eliminated as a non-HBV recipient is estimated to be 87.

Conclusions: For small grafts, two-stage surgery after partial transplantation is possible, but HBV patients are excluded. HBV patients is decreasing and alcoholism and MASLD are increasing. So, it is thought that the donor pool can be increased by using various grafts or transplanting small grafts through two-stage surgery.

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EP_048 EMPOWERING CHANGE: THE IMPACT OF 'ORGAN DONATION AMBASSADOR' TRAINING PROGRAM

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Background: In developing countries, low public awareness significantly hinders organ donation rates. To address this, MOHAN Foundation launched the Angels of Change program in 2017, training volunteers to raise awareness, as agents of change. Initially in-person, the program transitioned to an online format during the COVID-19 pandemic, becoming the Organ Donation Ambassador Training. This presentation highlights the program's impact and delivery.

Methods: The Organ Donation Ambassador training is designed into three key sections: 1 **Gift of Life Course**: A four-hour, interactive online course covering: • Process and significance of deceased organ donation. • Legal and ethical aspects. • Religious perspectives on organ donation. • Voluntary whole-body donation. 2 **Interactive Meetings**: Participants engage with experts, including transplant professionals and donor families, through video conferencing. This provides valuable insights and an opportunity to address any doubts. 3 **Ambassador's Activities**: Volunteers are encouraged to actively promote organ donation through awareness initiatives. They are supported with a variety of communication materials, including flyers, the Foundation's films on organ donation, and dedicated resource persons to assist them.

Results: Over three years, 460 ambassadors were trained in 33 batches, reaching over 20,000 people through: • 139 awareness talks and information desks. • 16 online workshops. • 33 social media campaigns. • 16 online projects. • 23 participations in MOHAN Foundation events and surveys. • 4 created organ donation chatbots. • 22 held student competitions. • 2 podcasts. • 1 creative poster design. • 1 organ donation chapter in a book. • 35 rallies. Some activities, such as personal conversations or distributing donor cards, couldn't be quantified. Youth embraced the online modules, while senior ambassadors needed more interaction and support. A WhatsApp group helps with communication, resource sharing, and healthy competition.

Conclusions: The shift to online training allowed MOHAN Foundation to expand its reach across India, creating a strong network of committed volunteers. Their ongoing efforts continue to support the foundation's mission to raise awareness about organ donation.

EP_049 K-FIT- ESTABLISHING A NOVEL WEIGHT LOSS SERVICE FOR PEOPLE LIVING WITH END STAGE KIDNEY DISEASE AND OBESITY

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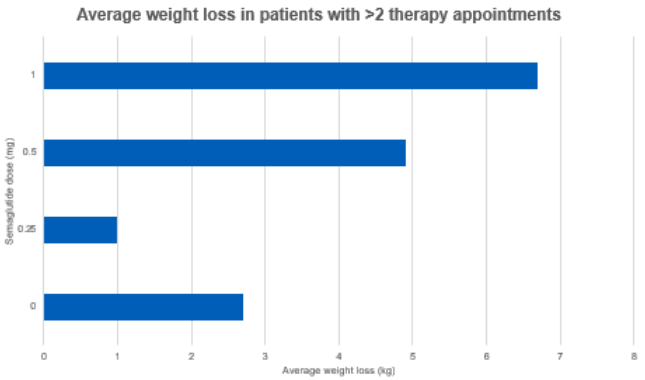
Background: Obesity is a significant barrier to kidney transplantation. Patients with a body mass index>35 and truncal obesity have increased peri-operative risks and higher risk of delayed graft function. 52% of patients on The Trust's transplant waiting list are ineligible due to obesity, with 60% from BAME backgrounds. UK medical weight loss programs are less effective for transplantation compared to bariatric surgery. Local data shows< 17% of eligible patients are successfully referred to bariatric services. This highlights the need for a structured, multimodal weight loss protocol for patients with obesity. Emerging evidence also supports using GLP-1 receptor agonists for managing obesity in renal patients.

Methods:K-Fit employs a MDT approach, integrating psychology, dietetics, physiotherapy, and pharmacology to manage obesity. Patients are assessed by a psychologist for suitability. Those accepted are seen by dietitian, physiotherapist, and pharmacist every 4 weeks for 6-12 months. Additional psychological educational sessions, based on Acceptance and Commitment Therapy(ACT) are also available. Semaglutide is prescribed to aid weight loss. Weekly MDT meetings assess all patients ensuring obesity is the only barrier to transplantation. Patients have specific weight or waist-to-height ratio targets for transplant list activation.

Results: To date 40 patients are enrolled on the programme. 3 patients have met targets and have been activated on the transplant list.

Conclusions:K-Fit demonstrates that a structured, MDT programme incorporating psychological support, dietary interventions, physiotherapy, and pharmacological treatments can significantly enhance access to kidney transplantation for obese patients. By directly linking weight management efforts to transplant eligibility, this programme offers a viable alternative to bariatric surgery, addressing a critical gap in the care pathway.



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EP_050 KIDNEY TRANSPLANTATION DEVELOPMENT IN YOGYAKARTA: A HISTORICAL AND CONTEMPORARY OVERVIEW

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Background: Kidney transplantation is a life-saving treatment for end-stage renal disease (ESRD), improving survival and quality of life compared to dialysis. In Indonesia, transplantation programs face challenges such as financial barriers, cultural resistance, and limited infrastructure. The program at RSUP Dr. Sardjito began in 1988 under Prof. Sja'Bani, who laid its foundation despite significant obstacles. A pivotal moment came in 2014 with the implementation of BPJS, Indonesia's universal health insurance, which expanded access by subsidizing costs and ensuring financial equity. However, systemic challenges like the COVID-19 pandemic tested program resilience and adaptability.

Methods: This study used a mixed-methods approach to evaluate kidney transplantation at RSUP Dr. Sardjito from 2017 to 2024. Historical accounts provided context on foundational milestones, while quantitative data assessed transplant rates, demographics, and clinical outcomes, including pre- and post-operative creatinine and hemoglobin levels. Special attention was given to BPJS's role in improving accessibility and innovations during the pandemic, such as virtual consultations and shortened hospital stays. Trends and milestones were visualized to demonstrate progress.

Results: Annual transplants grew from 2 in 2017 to 16 in 2024. Clinical outcomes improved significantly, with creatinine levels dropping from 4.3 to 1.33 mg/dL and hemoglobin levels rising from 9.3 to 11 g/dL. Non-related donors, contributing 35.8% of donations by 2022, expanded the donor pool, reflecting cultural shifts. During the pandemic, the program sustained operations, achieving a graft survival rate of 91.1%. BPJS ensured service continuity, democratized access, and supported long-term sustainability.

Conclusions: RSUP Dr. Sardjito's kidney transplantation program exemplifies resilience, innovation, and systemic collaboration. Future priorities include establishing a national donor registry, increasing public education to address cultural resistance, and investing in advanced technologies. These efforts are crucial to ensuring accessible, sustainable, and equitable transplantation for future generations in Indonesia and beyond.

EP_051 CAN AUDITS ENHANCE SUSTAINABILITY IN ORGAN DONATION AND TRANSPLANT PROGRAMS? A UAE QUALITY ASSURANCE APPROACH

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Background: Despite advances in organ donation and transplantation, several challenges hinder the sustainability of these programs, such as difficulties in managing potential donors and a lack of awareness about donation potential. Quality assurance mechanisms, particularly audits, provide effective solutions by reviewing processes, ensuring best practices, and optimizing resources. In the UAE, where the demand for transplants is increasing, audits play a critical role in enhancing the sustainability of organ donation programs. This study aims to show that audits can enhance the sustainability of organ donation programs by improving efficiency, increasing the use of deceased donor organs, and ensuring equitable access within the UAE healthcare system.

Methods: A systematic review of organ donation audits identified best practices and successful models. In 2024, on-site audits were conducted at six hospitals with high potential for organ donation, focusing on ICUs where patients meet criteria for donation after neurological death (DNC). Mortality data from these hospitals were compared with referrals to the UAE National Center for Regulating Donation and Transplantation (NCDT). Discrepancies were assessed, and data were analyzed to evaluate donation processes and identify areas for improvement.

Results: The audit team visited six hospitals, conducting 12 visits. Of 175 deaths evaluated, 144 were identified as potential donors and referred to the NCDT, with 110 donors utilized in 2024, 18 of whom came from these hospitals. The audit confirmed that DNC diagnoses were consistent with regulations, but gaps in donor identification and management were identified. These gaps led to improvements in training and protocols for healthcare professionals involved in organ donation.

Conclusions: Regular audits are essential for enhancing the sustainability of organ donation programs. They improve donor identification, optimize organ maintenance, and ensure equitable access. In the UAE, audits can address gaps in donor detection and consent processes, improving efficiency and helping meet the growing demand for organs. To maximize impact, standardizing audit protocols, overcoming resource constraints, and securing continued support from policymakers and healthcare systems is crucial.

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EP_052 TRANSFORMING LIVES: ENABLING ORGAN TRANSPLANTS FOR THE ECONOMICALLY UNDERPRIVILEGED USING CROWDFUNDING

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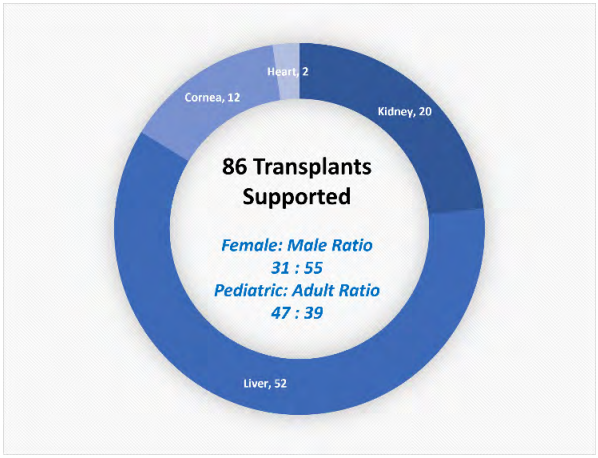
Background: The rise of crowdfunding has greatly facilitated organ transplants in India. Despite public hospitals offering free or subsidized transplants, only 15% of the 18,378 transplants in 2023 occurred in these facilities due to infrastructural and workforce limitations. Most transplants, especially liver and heart, are performed in the private sector, costing between $25,000 to $30,000, with kidney transplants ranging from $10,000 to $12,000. Without comprehensive health insurance, many Indians facing organ failure are unable to afford these life-saving procedures. Crowdfunding has made transplants accessible to economically disadvantaged individuals. MOHAN Foundation, an NGO, has effectively used this platform to raise funds, aiding 86 low-income patients since 2021 in receiving liver, kidney, heart, and corneal transplants.

Methods: In February 2021, MOHAN Foundation launched 'Anudaan – Making Transplants Affordable,' leveraging crowdfunding to partially fund transplants for economically disadvantaged patients. A committee evaluates applications, prioritizing children, submitted exclusively by partner hospitals that subsidize transplant costs. Additional funding is sourced from NGOs, trusts, and government schemes. Crowdfunding campaigns are organized through: • Musical concerts featuring renowned artists, coordinated with corporates, associations, and societies to raise funds from employees, members, and families. • Student-led initiatives in schools.

Results: Over four years, MOHAN Foundation raised over $193,000 through crowdfunding, assisting 86 patients across India, with many more awaiting support. The breakdown included a Pediatric: Adult ratio of 47:39 and a Female: Male ratio of 31:55. Over 20 partner hospitals nationwide collaborated in this effort.

Conclusions: Crowdfunding has proven highly effective, bringing together numerous donors on a single platform. MOHAN Foundation skillfully utilized this method to make transplants affordable for the underprivileged. Success hinges on expanding the donor base and showcasing patient impact. This initiative has enabled MOHAN Foundation to offer the Gift of Life, primarily to children, allowing them to lead healthy, contributive lives in society.



EP_054 ZERO TO ONE: THE CHALLENGES OF ESTABLISHING A NEW LIVER TRANSPLANT CENTER IN DUBAI, UAE

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Background: Organ Transplantation saves lives and changes the quality of life for patients with terminal organ failure. Solid organ transplant programs are growing in number and size but still very far from the global needs. The UAE health sector is rapidly advancing, and the Organ Donation and Transplantation programme in the UAE is one of the fastest growing programmes in the world. In line with the vision of the nation, leadership of UAE and the growing demand for a robust transplant programme, King's College London-UAE successfully established first ever accredited liver transplant center in Dubai.

Methods: The visionary leadership of King's London-Dubai identified the need for establishing an accredited liver transplant programme adhering to the regulations of the Dubai Health Authority. The association with King's College Hospital in London, a world leader in Liver Transplantation has helped to establish the programme with shared clinical pathways, multidisciplinary working and UK visiting faculty programme. The Dubai Hills hospital was inspected by an international committee set up by National Center for Organ Donation and Transplantation, Ministry of Health, UAE and after a thorough check of the credentials of the team members as well as the facilities and logistics, a license for liver transplant was granted in November 2023.

Results: The first ever liver transplant in Dubai from a deceased donor was carried out on the 29th of November 2023. The new transplant programme carried out 14 lifesaving liver transplants from the deceased donors with in the first year of license.

Conclusions: Establishing a new liver transplant programme in Dubai is a critical advancement in healthcare infrastructure for Dubai and the United Arab Emirates. The process is complex and extremely challenging with high regulatory approvals, significant investment in infrastructure, training and building a highly competent multidisciplinary team capable of providing comprehensive care from pre transplant assessment to post transplant long term care. The healthcare costs in the UAE are considerably high, and the financial elements related to insurance limits and coverage for liver transplant remain a significant hurdle for the progress of the programme.

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EP_055 EMPOWERING TRANSPLANT PROFESSIONALS: AN INNOVATIVE ONLINE TRAINING FROM A DEVELOPING COUNTRY

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Background: In 2009, the MOHAN Foundation, a Non-Government Organisation, launched structured training programs for medical and paramedical professionals to enhance organ donation rates in India and neighboring countries. Initially conducted in person, these courses transitioned online in 2017 to accommodate busy schedules of healthcare workers.

Methods: MOHAN Foundation offers various online courses via MOODLE, an open-source platform with interactive plugins. These courses feature text, PowerPoint, video modules, and integrated assessments. The courses offered include: • A one-year Post Graduate Diploma in Transplant Coordination and Grief Counselling, featuring blended learning. • A six-week Transplant Coordination Professional Certificate course. • Brainstem death - Identification, certification, donor optimization, and supported through free downloadable apps. • Family counselling and conversations on organ donation through simulations and case discussions. • Legal aspects of organ donation & transplantation and their applications in hospital setting. The duration of these courses ranges from 20 to 480 hours.

Results: This online educational effort has attracted 1,620 participants from India and globally from Nov 2020 to Feb 2024. The affordability (ranging from $25 to $250) and high-quality content have drawn candidates not only from India but from other diverse countries, including Vietnam, Qatar, Nepal, Spain, Pakistan, Botswana, Sri Lanka, Malaysia, Nigeria, Singapore, Bangladesh, Ghana, and Saudi Arabia. An impressive 99% of participants rated the training as good to excellent, with 95% finding the course content particularly engaging. Word-of-mouth recommendations significantly contributed to enrolments. While imparting soft interpersonal skills online remains to be a challenge, newer learning techniques such as gamifications of the content has been tested to enhance learning experiences.

Conclusions: The shift to online education by the MOHAN Foundation has significantly broadened the training reach for healthcare professionals, improving organ donation practices worldwide. The interactive learning experience is enhancing the capacity of healthcare professionals not just from India and South Asia, but globally.

EP_056 HALF A CENTURY OF RENAL TRANSPLANTATION ACTIVITY IN THE BUSIEST UNIT OF OUR COUNTRY - HOW FAR HAVE WE GONE

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Background: Kidney transplantation (KTx) is the gold standard therapy of renal failure affecting the quality and longevity of life. Our country has introduced KTx early in the 70's and the first one performed in our unit was in 1971. Since then, a lot has changed and in 1984 the transplant unit started running in the current legal status.

Methods: We performed a retrospective analysis of the transplant activity in our unit

Results: Since 1971, 3249 KTx procedures were performed through the end of 2024, 1558 from deceased donors and 1691 from living donors. 6 patients were treated with autotransplantation, 4 simultaneous pancreas and kidney and 2 combined liver and kidney transplants. 66.7% of patients were male. Since 2005, the incompatible programme of KTx started, initially ABOi and consequently HLAi. To overcome the incompatibility issues, the paired pool donation was added, with the first one performed intercontinentally in 2011. 4 pairs were transplanted and 12 live donors donated to the cadaveric waiting list for their incompatible potential recipient. 10 year survival rate of the iKTx was 91.9%, with graft survival 75.6% compared to the survival rate of comp KTx of 93.7% and graft survival 79.4%. The surgical challenge for the unit was the introduction of the laparoscopic donor nephrectomy in 2018. Since then, only 3 donors had an open procedure. The paediatric KTx are also part of the program initially sporadically but since 2019 as an organised program in collaboration with the paediatric hospital and the support of the anaesthetic department 34 kids were transplanted (23 live donor and 8 deceased) with a mean age of 13.6 years. Our unit is the 2nd in Europe that started using Imlifidase as part of desensitisation protocol in potential recipients with preformed antibodies to the donor and positive cross match. So far 4 patients were transplanted with only one experiencing acute rejection on the table and subsequent nephrectomy.

Conclusions: We are optimistic that new horizons will open in transplantation, as with the support of the government the deceased donation rate has increased from 4.4 donors per million population in 2019 to 10 in 2024. Improving the transplant candidate work-up, optimising maintenance on the waiting list, and providing outstanding post-transplant care will be vital to the continued success of KTx.

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EP_057 PUBLIC TRUST IN DECEASED ORGAN DONATION AND TRANSPLANTATION. DESIGN AND VALIDATION OF A CROSS-CULTURAL QUESTIONNAIRE

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Background: Despite the widely held belief that public trust plays a crucial role in shaping deceased organ donation rates, the empirical support for this assumption remains limited. To tackle this knowledge gap, we developed a conceptual model (Author et al, XXXX). The aim of the ODT scale is to test this model empirically, measuring public trust in deceased organ donation and transplantation systems and to understand to what extent trust influences the willingness to donate and family approval/refusal across societies. This information can provide a comprehensive understanding of trust dynamics in Organ Donation and Transplantation and offer valuable insights to inform interventions and policies aimed at enhancing organ donation rates.

Methods: The validation process followed the step-by-step procedure defined by Boateng et al. (2018). It was carried out in three phases: **Phase 1: Item Development**, **Phase 2: Content Validity**, and **Phase 3: Scale Evaluation**. During Phase 1, the research team conceptualized the dimensions of interest and developed the items to measure them. An expert panel was sought to evaluate these proposals using the Delphi methodology. In Phase 2, the scale was pre-tested by administering the questionnaire to participants as a pilot study. This stage also served to extract factors and establish sample sizes that ensured sufficient statistical power. Phase 3 involves conducting several tests to assess dimensionality, reliability, and validity. For the collection of responses, two panels will be considered: the general population, recruited through market research platforms (e.g., Netquest or IMOP in Spain or Prolific in the UK) of our proposed trust distribution network, given that all citizens constitute potential donors and/or recipients, or their relatives at any given time; and a professional panel, recruited through expert forums.

Results: The resulting questionnaire proposal after carrying out Phases 1 and 2 will be presented during the conference.

EP_058 BREAKING BARRIERS: THE FIRST NATIONAL PAIRED KIDNEY EXCHANGE PROGRAM IN SAUDIA ARABIA AND THE MIDDLE EAST

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Background: Kidney transplantation remains the optimal treatment for end-stage renal disease. However, the lack of suitable donors presents a significant barrier, especially for highly sensitized patients or those with blood group incompatibility. Paired kidney exchange (PKE) programs offer a solution by facilitating donor-recipient matching between incompatible pairs. This study reports the establishment and outcomes of the first national PKE program in Saudi Arabia, the first of its kind in the Middle East.

Methods: The national PKE program was initiated to address donor-recipient incompatibilities across transplant centers in Saudi Arabia. A centralized matching system identified compatible pairs through donor-recipient swaps between different transplant centers . Between August 2024 and December 2025, 10 paired kidney exchanges were performed at multiple centers. Inclusion criteria included highly sensitized patients and those with blood group incompatibilities. Comprehensive preoperative assessments and standardized immunosuppressive protocols were implemented across all centers.

Results: All 10 transplants were successfully performed with a 6-month patient and graft survival rate of 100%. The program enabled transplantation for patients who otherwise lacked compatible donors, including highly sensitized individuals and those with blood group incompatibility. No major postoperative complications or graft losses were reported.

Conclusion: The establishment of the national PKE program in Saudi Arabia demonstrates its feasibility and effectiveness in overcoming donor-recipient incompatibilities. This initiative sets a precedent for the Middle East and highlights the potential for regional collaboration in expanding access to kidney transplantation.

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EP_059 UNACCEPTABLE ANTIGENS UNDER THE SCOPE: REVIEWING ARGENTINA'S TRANSPLANT PRACTICES

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Background: Highly sensitized patients (Panel Reactive Antibody > 85%) pose a significant challenge in kidney transplantation due to the elevated risk of antibody-mediated rejection. In Argentina, the SINTRA system introduced an unacceptable antigens filter intended to reduce incompatible allocations, but this filter only automatically excludes HLA A, B, DR, and DQ antigens. Antibodies against other loci—such as HLA C, DP, and DRB3/4/5—may therefore go unaccounted for, potentially resulting in unnecessary physical crossmatches.

Methods: This retrospective cohort study analyzed the crossmatch outcomes of highly sensitized patients in the Autonomous City of Buenos Aires between August 17th, 2023, and August 17th, 2024. Flow cytometry crossmatches (FCXMs) were performed to detect donor-specific anti-HLA antibodies, with positivity identified by a shift in fluorescence intensity relative to a negative control. Data on sensitization levels, FCXM results, and the use of the SINTRA filter were collected to evaluate the filter's efficiency over one year.

Results: Among 505 FCXMs performed in highly sensitized patients, 41 (8.12%) tested positive, indicating persistent risk despite the SINTRA filter. Additionally, 25% of the organ procurement processes included at least one candidate who was excluded due to a positive crossmatch. These findings highlight the filter's shortcomings in accounting for important loci beyond HLA A, B, DR, and DQ.

Conclusions: Although the SINTRA unacceptable antigens filter aims to reduce antibody-mediated rejection, it may fail to capture relevant antibodies against loci not automatically excluded. Expanding HLA typing—potentially through Real Time PCR in cadaveric donors—and consistently updating patients' single antigen reports could reduce unnecessary physical crossmatches, streamline allocation procedures, and improve overall transplant outcomes for this challenging patient population.

EP_060 DISCREPANCIES IN THE VALUE AND THE IMPACT OF A LIVING DONOR KIDNEY TRANSPLANT PROGRAM FROM DIFFERENT SKATEHOLDERS

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Background: The implementation and consolidation of a living donor kidney transplant (LDKT) program requires following certain values to achieve the mission of a quality, excellence and integrative program. The vision has to be based on the values of all the members that make up this ecosystem. Our objective is an analysis of the value of a LDKT program according to the different stakeholders involved.

Methods: Prospective two-phase study of value curve and attribute map development. First phase: identification of key aspects that add value to LDKT (group of national and international experts). Second phase: a questionnaire. Stakeholders: LDKT committee (group A), expert professional in advanced chronic kidney disease (group B), expert physicians in transplantation (group C), and patients and donors (group D). The different value curves and positioning map have been created and compared with the different stakeholders. Study approved by the Ethics Committee.

Results: 122 opinions on the key aspects of the 6 experts (2023-2024): 17 from group A, 16 from B, 44 from C and 45 from D. Average age: 50.23 years, lower in groups B and C (p = 0.004); 62.1% women. Team experience and professionalism, Experience in complex cases, Speed of response, and Personalized programs that adapt to needs have been the values most voted by all groups. Team experience and professionalism is the only coincident that adds the most value among the 4 groups. Center-related aspects have been identified, Improvements in Information, which is not what adds the most value for national experts (C) and patient-donors (D); Speed of response is for everyone except for the LDKT committee (A). Personalized programs that adapt to needs are necessary for groups B/C, and Experience in complex cases is not the most for group B. None identified Volume of Activity, Safer Surgeries or Achieving Results (the latter only C) as aspects that provide the most value to a LDKT program.

Conclusions: Team experience and professionalism are the most valuable assets for a LDKT program and the only ones that are shared by the different members of the ecosystem interviewed among all the values perceived as fundamental. Given the differences between the different stakeholders, we need to know and work based on a value analysis to implement and sustain a LDKT program.

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EP_061 ECMO AS A BRIDGE TO HEART TRANSPLANTATION IN LATIN AMERICA`S LARGEST TRANSPLANT CENTER

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Background: Heart transplant is the gold-standard of the Heart Failure`s treatment. One of the treat lives is the extracorporeal life support (ECLS). To evaluate outcomes of ECMO use as a bridge to heart transplantation (HTx) in the largest heart transplant center in Brazil and Latin America, focusing on early postoperative outcomes (up to 5 days), 30-day mortality, and long-term survival (up to 10 years).

Methods: This retrospective cohort study included HTx recipients from 2013 to 2024 who were prioritized (Status 1) due to ECMO as a bridge to transplantation. Demographic data of donors and recipients, including blood type, body mass index (BMI), etiology of heart failure (HF), and Predicted Heart Mass Index (PHMI), were analyzed. Postoperative echocardiographic assessments of right ventricular function and left ventricular ejection fraction (LVEF) were conducted daily from postoperative day 1 to 5. Outcomes included 30-day and long-term survival (up to 10 years).

Results: Between 2013 and 2024, 543 consecutive HTx were performed, with 27 patients (4.98%) bridged using ECMO. **Donors:** 85.19% were male with a mean age of 32 years (SD = 8.39; 95% CI: 29.4–30.9). Blood type distribution was 81.48% O, 14.81% A, and 3.70% B, with a mean BMI of 27.17 kg/m² (SD = 3.1; 95% CI: 25.6–26.1). TBI was the leading cause of death (62.96%), while stroke accounted for 7.41%. **Recipients:** Median waitlist time was 33 days (IQR: 1–229), with 85.19% male and a mean age of 43.7 years (SD = 12.8; 95% CI: 38.6–48.7). Blood types were distributed as 59.26% O, 29.63% A, and 11.11% B. The mean BMI was 24.8 kg/m² (SD = 3.56; 95% CI: 23.4–26.2), and idiopathic HF was the most common etiology (55.56%). The mean PHMI was 1.13 (SD = 0.23; 95% CI: 1.04–1.23). Mean ischemic time (IT) was 208 minutes (SD = 51.4), with 25.93% exceeding 240 minutes. **Outcomes:** 30-day survival was 70.4% in the ECMO group versus 86.4% in non-ECMO recipients. After 10 years, survival rates were 48.2% for ECMO recipients and 66.6% for non-ECMO recipients (HR: 1.95; 95% CI: 1.08–3.5; p = 0.026).

Conclusion: While ECMO serves as a viable bridge to HTx, outcomes remain inferior compared to recipients who do not require ECMO support. Further studies are needed to optimize this approach.

EP_062 TRANSPLANTING THE NEGLECTED GUY: RISK FACTORS AND CHALLENGES IN PATIENTS LISTED FOR HYPERTROPHIC CARDIOMYOPATHY

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Background: Hypertrophic cardiomyopathy (HCM) is a less common indication for heart transplantation (HT); transplanting these patients (pts) is challenging because they are rarely candidates for a bridging strategy with LVAD and most allocation systems don't have a dedicated priority status; exceptions are frequently asked. We sought to identify risk factors for mortality on the waiting list (WL) according to patient's characteristics at time of listing and for post-HT outcomes.

Methods: We included all adult pts with HCM listed for HT in our Center (2000-23), and collected echo and hemodynamic data at listing. In Italy, HCM pts can undergo to a urgent HT only if inotrope/MCS dependent. The outcomes evaluated were 2-yrs survival from death on the WL or urgent HT including exceptions (censoring at the time of HT) and 2-yrs survival after HT.

Results: 75 pts (51±15 yrs, 39% females, 47% non dilated) were listed 9 months (IQR 3-26) after the first evaluation. 51% had PVR >2.5 WU; pts with non dilated LV had more frequently pulmonary vascular resistances (PVR) >2.5 and higher LVEF, with doses of diuretics similar to non dilated LV. Overall, PVRs did not change throughout the WL. 53 pts (49±12 yrs, 39% females) received HT after 7 (IQR:2-18) months; 21% were transplanted urgently, of whom 55% with exceptions, and 11 died, accounting for a 2-yrs WL survival of 39.7≤±10.2%. Clinical variables at listing predicting 2-yr WL outcomes were (univariate analysis): furosemide >150 mg/d (HR: 3.8), PVR >2.5 WU (HR:4.3), p<0.02 all, while dilated vs non dilated LV and LVEF were not associated with increased WL mortality; at multivariate analysis, high doses of diuretics were the only independent predictor of death/urgent HT (HR:2.5, p=0.02). Among parameters used for allocation, recipient weight ≤70 kg (HR:5.9) and non-A blood group (HR:6.9) predicted WL outcomes (p<0.01); of note, all pts O or B were died or HT urgently at 2 yrs. PVR>2.5 increased the risk of death 2-yrs after HT (HR:3.8,p=0.05)

Conclusions: The high risk of death of patients with HCM is independent from LV dimensions. While PVR increase both the risk of dying on the WL and in the early post-HT phase, our data suggest that patients requiring high doses of diuretics, especially if have low weight and non-A blood group, require a dedicated urgency category even if not on inotropes.

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EP_063 CAN WE PREDICT THE TRANSPLANT WE WISH WE HADN'T DONE?

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Background: With an ageing, comorbid general population, coupled with organ shortage, there has been a move in recent years to use organs that we would not have used a decade ago. In longevity schemes, older donors are matched with older recipients which may amplify risk. We sought to devise a risk score to predict outcomes in higher risk transplantation.

Methods: Data was collected on 1895 adult renal transplants conducted in our unit, from 2008-2024, of which 1305 from deceased donors. A poor outcome was defined compared with remaining on dialysis, using a composite of patient survival, graft survival and function at 1 year. Risk factors were analysed by developing multivariate logistic regression models in a training set with the two leading models evaluated in a validation set.

Results: Recipient age, donor age, CIT, and DGF >7 days were all associated with higher risks of poor outcome. Recipients over 65 with DGF > 7 days had 51% risk of poor outcome. The best performing predictive model included DGF status and achieved sensitivity 39% and specificity 73%; while the best model using only information known at the time of decision to transplant was more sensitive (51%) but less specific (53%).

Conclusions: Transplant outcome is difficult to predict using only factors known at the time of kidney offer, but transplanting kidneys likely to have prolonged delayed graft function into old recipients should be avoided.

EP_064 MACHINE LEARNING IS NOT ALWAYS BETTER THAN STANDARD STATISTICS IN PREDICTING GRAFT OUTCOMES AFTER KIDNEY TRANSPLANTATION

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Background: Over the last decade, the use of machine learning (ML) techniques in problem modeling and solving has increased significantly, including in kidney transplantation. Numerous studies have used ML to predict outcomes such as delayed graft function (DGF). This study compares various ML models with logistic regression (LR) in predicting DGF, focusing on donor characteristics.

Methods: We analyzed 831 deceased donor kidney transplants performed between 1989 and 2020 across three transplant centers. The dataset included 14 donor, 7 transplant, and 60 recipient features. Four problem types were defined based on variable combinations: donor-only (D), donor + transplant (DT), donor + recipient (DR), and donor + transplant + recipient (DTR). The dataset comprised 44.7% DGF-positive and 55.3% DGF-negative patients, split into 80% for training and 20% for validation/testing. Six ML models—Support Vector Machine (SVM), Decision Trees (DET), Random Forest (RF), Gradient Boost (GB), Extreme Gradient Boost (XGB), and Multilayer Perceptron (MLP)—were compared with LR. Hyperparameters were optimized using Random Search and 10-fold Cross Validation. Accuracy was the primary performance metric.

Results: The best-performing model for each problem type achieved accuracies of 55% (SVM), 58% (XGB), 58% (RF), and 64% (XGB) respectively for D, DT, DR, and DTR. LR results were 47%, 62%, 55% and 60%. Across most models, significant predictors included donor creatinine and age, cold and warm ischemia times (transplant variables), and recipient calcium levels.

Conclusions: While most ML models outperformed LR, the differences were not substantial.This may be attributed to the small dataset size, which likely contributed to the overall poor performance. We recommend using these complex models with high-quality datasets that include a sufficient number of variables and observations to fully leverage their potential. The key question for future research is determining the dataset size required for ML to become the primary analytic tool for predicting kidney transplant outcomes.

	Accuracy	
Models	Best ML model	Logistic Regression
Donor	SVM: 55%	47%
Donor + Transplant	XGB: 58%	62%
Donor + Recipient	RF: 58%	55%
Donor + Transplant + Recipient	XGB: 64%	60%

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EP_065 QUALITY OF LIFE: WHAT MATTERS TO PATIENTS ON THE WAITING LIST AND HOW DOES TRANSPLANT OUTCOME AFFECT THIS?

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Background: Patient Reported Outcome Measures (PROMS) are increasingly used to improve patient experience. In our unit, we had collected quality of life (QOL) metrics as an interim PROM from 2021 to 2024, to satisfy a government reporting requirement and we decided to review this data.

Methods: We used 2 validated questionnaires, EQ-5D-5L, and RDQoL. Data was at five different time points: on the waiting list, on day of admission, and at 3, 6, and 12 months post operatively. The RDQoL includes rating of the importance of each domain to the individual patient, which is used to weight the responses, but also allows study of which domains matter most to different groups of patients.

Results: 1519 total QOL questionnaires were completed by 602 patients who agreed to complete them. Demographics were mean age 53.6 years, 45% female, 14.7% ethnic minority. There was a trend of improvement in the change in EQ5D index and visual analogue score after transplant. There was also an improvement in RDQoL Average Weighted Index after transplant. The RDQoL domains that were most important to patients were family, relationships, travel and physical health. Work was a very important domain for those under the age of 60 but not in older patients. Interestingly, eGFR at 3 months did not seem to affect change in quality of life; but patients who had readmissions totalling >30 days within the first three months, had worse quality of life in these domains than they had on the waiting list.

Conclusions: QOL has been found to improve following transplant, however frequent and prolonged readmissions are associated with failure to improve quality of life.

EP_066 ACUTE MYOCARDITIS, THE HIDDEN DISEASE: RISK FACTORS AND DIAGNOSTIC WORKFLOWS.

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Background: The diagnosis of acute myocarditis (AM) relies on biopsy (EMB) or magnetic resonance (CMR); its onset can vary from a fulminant presentation (FP) needing MCS to milder cases, mimicking other syndromes. The aim of our study is to describe the process for AM diagnosis and to investigate predictors of mid-term outcomes after the acute phase.

Methods: We retrospectively screened patients (pts) hospitalized for suspected AM (2018-23), and we included both those in whom AM was confirmed and those receiving a subsequent diagnosis of AM, despite a different initial clinical suspicion. We collected data on demography, clinical variables, diagnostic tools and therapy . The outcomes were survival free from MACE at 3 years censoring after the first month and change in left ventricular ejection fraction (LVEF) from admission to discharge.

Results: Among 109 pts admitted for suspected AM, diagnosis was confirmed by EMB and/or CMR in 86 case; AM was also found in 39 cases admitted for acute coronary syndrome (ACS) and 4 for heart failure. Study cohort included thus 129 pts (41±16y, 34% women, 24% FP). The first tool was more frequently EMB for pts with FP and coronary angiography for those with suspected ACS . AM was confirmed by 54% of the 80 EMBs and by CMR in 43% of cases with EMB- . Survival at 3 years was 78.2±4.5%. At multivariate analysis, FP and LVEF <55% at discharge were the only independent predictors of MACE (HR: 10.5 and 3.2, p<0.05 all). Steroids were given more frequently in pts with lower LVEF (30±11 vs 52±12%) , FP (80% vs 10%) and autoimmune disorders (37% vs 10%), p<0.05 all, and led to a LVEF improvement only in those admitted with a LVEF>25% (p <0.01), while neither steroids at discharge nor HF therapy influenced long-term outcomes.

Conclusions: AM can require both EMB and CMR for diagnosis and can be erroneously confused with ACS. While confirming the prognostic role of FP even in the long term, our data highlights the importance of LVEF at discharge and suggest a potential role of steroids in pts with moderately or mildly reduced LVEF.

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EP_067 POSTOPERATIVE COMPLICATIONS AFTER KIDNEY TRANSPLANTATION CAN BE PREDICTED AND THEY BETTER FORECAST GRAFT FUNCTION

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Background: A key challenge in kidney transplantation is optimizing graft allocation to maximize graft survival, recipient survival, and dialysis-free survival time. Variables such as delayed graft failure (DGF) and serum creatinine are widely recognized as reliable prognostic factors, and most allocation algorithms use these values as surrogate markers, relying on donor, recipient, and transplant data. This study aimed to investigate whether other transplant-related outcomes, such as early post-transplant complications, could be predicted with similar accuracy to DGF and serum creatinine.

Methods: We analyzed 831 kidney transplants performed between 1989 and 2020 across three transplant centers using machine learning (ML) models. The dataset included 14 donor variables, 7 transplant variables, and 60 recipient variables. Four problem types were defined based on independent variable combinations: donor-only (D), donor + transplant (DT), donor + recipient (DR), and donor + transplant + recipient (DTR). Of the patients, 355 (42.7%) experienced at least one complication during the first three months post-transplant, while 476 (57.3%) did not. Complications included biopsy proven acute tubular necrosis, vascular and urological complications, lymphocele, urinary tract infection, renal arterial stenosis, or atheromatous disease. Six ML models were used: Support Vector Machine (SVM), Decision Trees (DET), Random Forest (RF), Gradient Boost (GB), Extreme Gradient Boost (XGB), and Multilayer Perceptron (MLP). Performance was evaluated using accuracy and AUC-ROC metrics.

Results: The best AUC-ROC scores were: • D: 80% (Decision Trees). • DT: 78% (Gradient Boost). • DR: 83% (Random Forest). • DTR: 80% (Random Forest and Gradient Boost)

Conclusions: Although the highest predictive performance was achieved using donor and recipient data, donor-only data effectively predicted post-transplant complications. This finding underscores its potential use in assessing donor quality and improving graft allocation decisions.

EP_068 MACHINE LEARNING TO PREDICT THE TRANSPLANT OUTCOME OF THE NEXT THREE MONTHS AFTER THE PROCEDURE

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Background: Optimizing graft allocation is a major challenge in kidney transplantation, aiming to maximize graft survival, recipient survival, and dialysis-free survival. While Donor Quality Indices (DQIs) are used globally, Chile lacks its own. This study explored whether a DQI could be developed using existing transplant data and predictive models for clinical outcomes.

Methods: We analyzed 831 kidney transplants (1989–2020) from three centers. The dataset included 14 donor, 7 transplant, and 60 recipient features. Predictions with Machine Learning (ML) targeted: • Delayed graft function (DGF), • Appearance of postoperative complications (APC) within the first three months, • Serum creatinine (SC) and Mean arterial pressure (MAP) levels at one and three months. Clustering models were used to identify transplant risk groups, and predictions were combined to develop a DQI reviewed by clinical staff for validation using a survey.

Results: **DGF and APC prediction:** Decision tree models achieved the best AUC-ROC scores, with 61% for DGF and 80% for APC. • **SC prediction:** High error rates were observed for SC at one month (72% Normalized RMSE) and three months (40% NRMSE). • **MAP prediction:** MAP levels showed low error rates (11% NRMSE at one month, 13% at three months). DGF and SC predictions aligned with clinical expectations but had lower performance metrics, while APC and MAP predictions were accurate but less interpretable. Clustering analysis identified four risk groups varying in DGF and the APC categorization. A DQI was constructed using a risk classification based on DGF and APC predictions, as preferred by potential users.

Conclusions: Despite data limitations, predictions for APC and MAP were accurate, whereas DGF predictions were less reliable but clinically interpretable. The proposed DQI balances performance and transparency, combining DGF and APC predictions to guide donor evaluation. Further refinement and higher-quality data are essential for improving DGF predictions and advancing DQI implementation to optimize transplant outcomes. ML models certainly can be improved as feeding clinical data allows that.

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EP_069 A FLAWED KIDNEY ALLOCATION SYSTEM CAN LEAD TO A CONSISTENTLY LOW DONATION RATE. THE CHILEAN CASE MODELED BY GAME THEORY

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Background: The kidney allograft supply and demand mismatch is well-documented globally. Chile, with its low organ donation rate, is no exception. To address this, an initiative was adopted in which one kidney is allocated to a patient on the waiting list of the procuring institution (commonly called a "house kidney" - HK), while the other kidney is given to the recipient with the best match on the national waiting list (the "pool kidney" - PK), according to the national allocation algorithm. Our aim is to analyze whether this policy has helped increase kidney donations in the public system.

Methods: We extracted data on the origin of all organ donors and the destination of all kidney transplants in Chile between 2010 and 2020 from public registries. For hospitals without a transplant program, we assigned their procured organs to the nearest transplant center for simplicity. We converted the data into per million population (pmp) rates and calculated a transplant-to-donor ratio for each transplant center, comparing them using descriptive statistics.

Results: Throughout the study period, the national organ donation rate did not increase significantly (slope $\beta = 0.26$; $p = 0.097$). However, the slight increase could be attributed to the introduction of new procurement hospitals into the system (slope $\beta = 1.4$; $p < 0.001$). The transplant-to-donor ratios remained stable across all 11 public transplant centers during the period. These centers were grouped into three categories based on their ratios: less than 1.0 (n = 4), between 1.0 and 2.0 (n = 5), and greater than 3 (n = 2), and they maintained their respective categories over time, as shown in Figure 1.

Conclusions: The HK - PK allocation system does not increase the national organ donation rate, but it encourages a "prisoner's dilemma" behavior. Specifically, the two centers with a transplant-to-donor ratio greater than 3 act as "free riders", exploiting the new centers entering the system, similar to a Ponzi scheme.

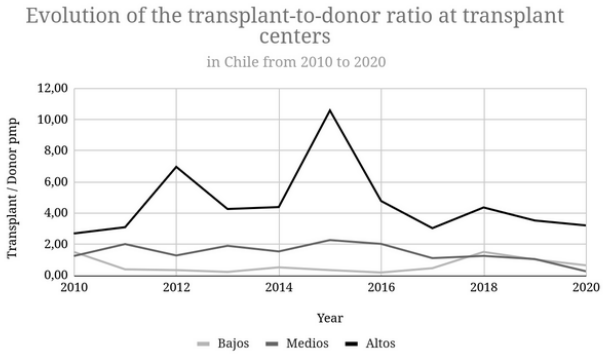

Figure 1: Evolution of the transplant-to-donor ratio at transplant centers in Chile between 2010 and 2020.

EP_070 SELF-ESTEEM AND SELF-PERCEPTION IN THE WORLD'S FIRST WHOLE EYE AND PARTIAL FACE TRANSPLANT RECIPIENT

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Background: Facial vascular composite allografts (fVCA) offer innovative solutions to severe facial injuries, aiming for functional restoration and social identity reclamation. Despite the evolution of face transplants over 18 years, patient-reported outcome measures (PROMs) for fVCA recipients are notably lacking. In a unique case of partial face and whole eye transplant, established surveys were utilized to gauge patient-reported outcomes (PROs).

Methods: A 46-year-old male, severely injured by high-voltage electricity, underwent a partial face and whole eye transplant. The patient consented to periodic surveys assessing psychological and social health, administered pre- and post-operation using four validated scales: Derriford Appearance Scale (DAS), Body Image Disturbance Scale (BIDS), Rosenberg Self-Esteem Scale (RSES), Social Desirability Scale (SDS). To maintain reproducibility and minimize confounding variables, surveys were administered by an independent third-party without providing clarifications to the patient's inquiries.

Results: The survey results show an overall increase in self-esteem and self-perception of image. RSES score increased from 10 (low self-esteem) pre-operatively, to 16 (moderate self-esteem) at 8 months post-operative. There was a decrease in scores across all subcategories of DAS from pre-op to 8 months post-op, as well as improvement in BIDS score. Finally, the SDS remained consistent from pre-op to 8 months post-operative with the subject in the "Average Scorers" category.

Conclusions: This case highlights the significant psychosocial improvements post-facial and eye transplant, assessed using established PROMs. The findings advocate for the development of VCA-specific PROMs and broader incorporation of PROMs in protocol evaluations to enhance patient-centered care, post-operative interventions, and overall quality of life for VCA recipients.

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EP_071 INTRA-AORTIC BALLOON PUMP AS A BRIDGE TO TRANSPLANTATION: A DECADE OF EXPERIENCE IN BRAZIL

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Background: The intra-aortic balloon pump (IABP) is a widely used form of mechanical circulatory support (MCS) for patients awaiting heart transplantation (HTX). Its affordability, simplicity, and ease of use make it essential, especially in Brazil, where it is crucial for heart allocation prioritization. Despite advancements in MCS technologies, the IABP remains a reliable tool for bridging patients to HTX. This study analyzes the characteristics, outcomes, and survival rates of HTX recipients supported with IABP over a decade in Brazil's largest transplant center.

Methods: A retrospective, cross-sectional study included 510 consecutive HTX performed from 2013 to 2024. Adult patients supported exclusively with IABP and classified as priority status (PS) 2 were analyzed. Hearts were preserved using Brettschneider HTK solution with cold static preservation. Recipient and donor demographics, waiting list duration, and outcomes were evaluated.

Results: Among the 510 HTX cases, 277 recipients (54.3%) were supported with IABP, with 60% male and a mean age of 47 years (SD = 13). Waiting times showed that 76% were transplanted within 30 days, 16% within 30–90 days, and 8% waited longer. Mortality for the IABP group was 40%, with early mortality (24%) linked to multiple organ failure (50%), infections (33%), and graft failure-related cardiogenic shock (17%). Late mortality (16%) was predominantly infection-related (75%). Notably, 53% of all HTX recipients during the study were IABP-supported, reflecting its widespread use in Brazil.

Conclusions: The IABP is an effective bridge-to-transplant strategy, even for extended durations or with subclavian/axillary access. It remains particularly valuable in Brazil, where advanced MCS options are cost prohibitive. Our findings underscore IABP's critical role in HTX programs, demonstrating favorable outcomes and suggesting its expanded use in resource-rich and resource-limited settings alike.

EP_072 INNOVATIVE AVIATION LOGISTICS MODEL: TRANSFORMING ORGAN RECOVERY IN BRAZIL`S NATIONAL TRANSPLANT SYSTEM

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Background: The Brazilian Transplant System faces logistical barriers that contribute to the loss of viable organs. Between 2017 and 2019, 1,529 organs were rejected due to logistical issues, with São Paulo alone accounting for 487 rejections, representing 12% of all organs made available in the state. Heart transplants, where efficient logistics is critical, experienced the discard of 466 hearts between January 2014 and September 2024, 266 of which were from other states. To address these issues, the TransplantAR Program was created, inspired by the Pledge Aviation model, to enhance organ transport logistics and reduce both organ discard rates and waiting-list mortality.

Methods: TransplantAR is a public-private partnership that optimizes organ recovery logistics by using donated flight hours from private aircraft owners. These hours are allocated to the public transplant system in São Paulo. From October 1, 2024, to January 15, 2025, the program facilitated 13 flights that transported 19 organs: 12 adult hearts, 1 pediatric heart, 4 lungs, and 2 livers. Seven airplanes (three jets and four turboprops) and six helicopters were utilized, with flight distances ranging from 77 km to 901 km, 50% of which exceeded 500 km. All organs were transported within the recommended ischemic time, yielding estimated cost savings of €70,000.

Results: The initial phase of TransplantAR benefitted 19 patients, achieved significant cost savings, and demonstrated the capability to support long-distance organ recoveries while adhering to ischemic time limits. Flights exceeding 500 km were particularly impactful, showcasing the program's logistical reach and efficiency.

Conclusions: The TransplantAR Program has proven transformative in addressing logistical challenges within Brazil's organ transplant system. Expected outcomes include reducing organ discard rates from 20% to 10%, increasing organ availability by up to 30%, and improving operational safety for transplant teams. By fostering transparency and alignment with ESG principles, offering a scalable, economically sustainable model that enhances organ utilization and reduces waiting-list mortality, particularly in resource-constrained settings.

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EP_073 "EQUITABLE DONOR ASSESSMENT MODEL (EDAM)" A QUANTITATIVE MODEL FOR ASSESSING DECEASED DONOR KIDNEY QUALITY

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Background: This study aims to develop an equitable framework for assessing deceased donor kidney quality by exclusively utilizing donor-derived factors, deliberately excluding donor ethnicity in alignment with recent United Network for Organ Sharing (UNOS) policy changes.

Methods: We conducted a retrospective cohort study using UNOS data from January 1, 2010, to January 1, 2018, with follow-up through June 2023. The analysis included 88,920 adult recipients of deceased-donor kidney transplants, excluding multi-organ transplants and incomplete cases. Donor characteristics analyzed encompassed age, BMI, cause of death, serum creatinine, diabetes, hypertension, CMV status, proteinuria, non-heart-beating status, blood group, cold ischemia time, HLA mismatches, and cPRA. A competing-risks regression model using the Fine–Gray subdistribution hazard approach was employed. Kaplan-Meier (KM) survival curves and cumulative incidence function (CIF) analyses were performed over a 10-year follow-up.

Results: Higher categories were significantly associated with increased graft failure risk (Category 2: HR=1.089, P=0.018; Category 5: HR=2.033, P<0.001). The model achieved a C-index of 0.614 (95% CI: 0.582–0.646), indicating a moderate level of discrimination. When stratified by donor ethnicity, the C-index was 0.661 (95% CI: 0.579–0.743) among Hispanic donors and 0.610 (95% CI: 0.548–0.673) among Black donors, suggesting similar or slightly better model performance in these subgroups. Age-based stratification (<65 vs. ≥65 years) showed C-index values of 0.610 (95% CI: 0.576–0.644) for younger donors and 0.605 (95% CI: 0.537–0.673) for older donors, indicating consistent discrimination across these age categories.

Conclusions: This novel risk stratification model, focusing solely on donor factors and excluding ethnicity, offers a robust and equitable tool for assessing deceased donor kidney quality. It enhances organ allocation precision and aligns with contemporary UNOS guidelines, potentially improving transplantation outcomes and promoting fairness in organ distribution.

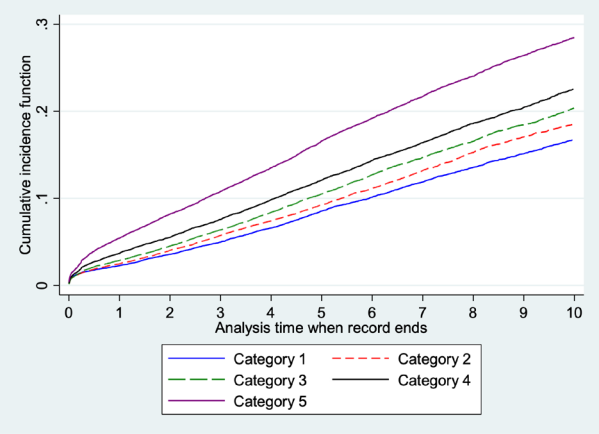

Figure 1: Cumulative incidence function across the five categories up to 10 years follow-up

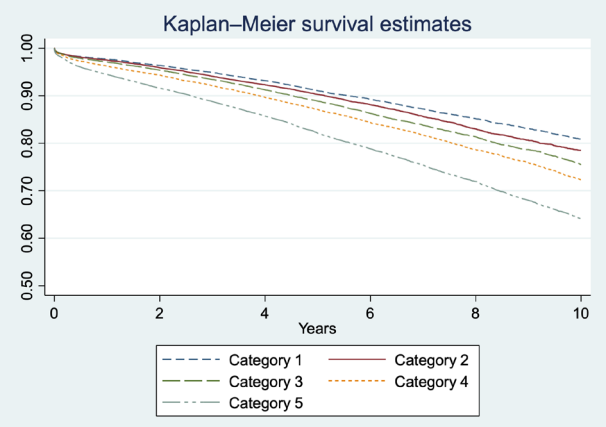

Figure 2: Kaplan meier estimates across the five categories up to 10 years follow-up

EP_074 LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE: WAITING LIST AND OUTCOMES OF AN ITALIAN NATION-WIDE COHORT

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Background: Acute Liver Failure(ALF) is a life-threatening condition which, in certain cases, can be treated only with liver transplantation. However, it is not clear today which patient or donor factors play a dominant role in the outcome of eventual liver transplantation. This study aims to report outcomes in Italy and to identify predictive factors.

Methods: Retropsective registry study on patients inscribed to the Italian National waiting list. All patient waitlisted in Italy for ALF between 2012 and 2022 were eligible for inclusion.

Results: In the study time-frame 284 were waitlisted for ALF in Italy and 282 had available data. 51.2% of patients were male and 59.3% were in the intensive care unit at the time of listing. Viral aetiology was predominant (44.2%), followed by drug-related (17.5%) and intoxication with amanita phalloydes toxin (7%). As many as 30% had "other" aetiology. Liver transplantation was undertaken in 85.8% (n.242) while 14.2% of patients died while awaiting a donor organ. Overall survival was 91.5% in the liver transplantation group and 77.7% in the intention to treat group. At multivariate analysis only young age and mushroom-related aetiology appeared to (positively) affect outcome.

Conclusions: Waitlist outcomes of ALF are acceptable and in the range of other, especially when LT is undertaken. Young patients and those who have mushroom-related liver disease may have the more favorable prognosis.

EP_075 VALIDATION OF THE KDPI SCORE IN A RENAL TRANSPLANT CENTER IN BRAZIL

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Background: The incongruous scenario of kidney transplant queues leads to the inaccessibility of this therapy to the portions of the population that had a worse prognosis. This reality motivated UNOS (United Network for Organ Sharing) to develop the concept of "marginal kidneys" through the creation of the Expanded Donor Criterion (ECD). The new organ allocation policy is based, among other things, on the KDPI (Kidney Donor Profile Index), a numerical score that scores variables related to the donor's history and measures the quality of the graft. The criteria analyzed by the KDPI are: age, height, weight and ethnicity, history of hypertension or diabetes, serum creatinine, hepatitis C serology, cause of death, and whether it was a donation after cardiac death.

Methods: The objective of the present study was to validate the use of the KDPI score in the Brazilian reality of kidney transplantation and its prognostic capacity in the overall survival of the patient and the graft. To this end, a retrospective analysis was carried out, whose final sample consisted of 249 patients who underwent kidney transplantation between 2010 and 2017 at a University Hospital in Curitiba. DCE organs were those that obtained KDPI calculated > 85%.

Results: 33 patients were considered DCE through the calculation of the KDPI. A significantly higher percentage of death was described in the DCE group during the analysis period 24% (p=0.005), while the group considered with standard graft had a death percentage of 2.7% (p=0.003).

Conclusions: The results lead us to believe that the KDPI can measure the quality of the graft in the Brazilian population. Because it is an instrument of low complexity, low cost and high reproducibility, it should be more used by transplant services across the country and worldwide aiming sustainability.

EP_077 THE CHANGES BEFORE AND AFTER THE REVISION OF THE LUNG TRANSPLANT URGENCY CRITERIA IN KOREA

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Background: Lung transplantation is a critical treatment for end-stage lung disease, but limited organ availability necessitates prioritization based on urgency. Under the pre-revision urgency criteria, patients classified as urgency status 0 (on mechanical ventilation or ECMO) often underwent transplantation in critical conditions. To address this, urgency criteria were revised in May 2023, introducing restrictions on wait times for urgency status 0 patients. We aim to identify the differences before and after the revision.

Methods: This study included patients who underwent lung transplantation at Seoul National University Hospital between January 2020 and December 2024. Data were collected from the medical records, with patients classified according to the urgency status before and after the revision.

Results: There was a significant difference in the changes in urgency status before and after the revision (p<0.000). Before the revision, 71% (n=41) of patients were classified as urgency status 0, and 28% (n=16) as status 1. The average waiting time for status 0 was 62±46days, and for status 1, 59±42 days, with a 3month survival rate of 86%. After the revision, 32% (n=18) were in status 0, and 68% (n=38) were in status 1. The average waiting time for status 0 was reduced to 10±7 days, while for status 1, it increased to 208±217 days, with a 3month survival rate of 95%.The revision of the criteria led to a decrease in the number of status 0 patients and an increase in status 1 patients, resulting in the 3month survival rate increased by 9%. The duration of mechanical ventilation before surgery was 38±34 days before the revision and 17±20 days after the revision, while the duration of ECMO before surgery was 34±26 days before the revision and 16±10 days after the revision. The waiting period by blood type was not significant.

Conclusions: Although survival rates have improved, they remain at a short-term level, highlighting the need for continued follow-up to evaluate long-term outcomes. The increase in waiting time is attributed to patients who were previously in status 1 under the old criteria but now receiving transplants according to the revised criteria. Long-term follow-up will be essential to determine whether the waiting time decreases over time.

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EP_078 A MULTICENTER RETROSPECTIVE COHORT STUDY OF INDIAN EXPERIENCE WITH KIDNEY PAIRED DONATION TRANSPLANTATION

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Background: Approximately one-third of healthy, willing living donors are rejected due ABO incompatibility (ABOi) or sensitization in living donor transplantation programs in a country like India, where deceased donation is in infancy. No large-scale data are available on swap transplants in developing countries.

Methods: We report a multicenter retrospective cohort study of 1839 kidney paired donation (KPD) transplants (2000-2024) from 65 centers and 213 liver swap transplants (2009-2024) from 8 centers in India. This study highlighted the landscape of swap transplants. Only near-related donors were allowed to participate in swap transplants, without altruistic, and deceased donors. Complete transplant work-up of donor-recipient pairs before non-anonymous manual allocation and simultaneous surgeries were common features.

Results: Of 1839 KPD analyzed, 86.67%(n=1594), 7.99%(n=147), 2.39%(n=44), 1.09%(n=20),1.31%(n=24), and 0.54%(n=10) transplants were generated from 2-way, 3-way, 4-way, 5-way, 6-way and 10-way KPD, respectively. Reasons for joining KPD in transplanted pairs were ABO incompatibility (n =1610, 87.54%), compatible pairs (n = 126, 6.96%), and sensitization (n=103, 5.6%). Non-simultaneous surgeries were performed in 77(4.18%) recipients with 0% donor renege. There was notable gender disparity, as more male were recipients (1504, 81.78%) and females were donors (n = 1469, 79.88%). Table 1 shows the way forward to overcome challenges to increase access to swap transplants

Conclusion: Our largest-to-date cohort study supports that swap transplants are medically simple, but logistically complex. Access to swap transplants is unequal, under-used, and increasing. If replicated, our experience could increase access to transplants and help combat the looming threat of commercial transplants.

EP_079 COGNITIVE IMPAIRMENT AND QUALITY OF LIFE IN ELDER PATIENT IN HEART TRANSPLANT PATH: A SYSTEMATIC REVIEW

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Background: Heart transplantation (HT) is a critical option for patients with end-stage heart failure, especially as life expectancy increases. Recent trends show a rising number of older transplant candidates, with studies indicating that patients over 70 can achieve acceptable outcomes when selected using specific criteria. Despite improved survival rates, the impact of frailty and cognitive decline on HT and can modify the quality of life (QoL) during all the transplant paths.

Methods: This systematic review, following PRISMA guidelines, evaluates studies from 2013 to June 2024 on assessment and impact on the morbidity and mortality of cognitive outcomes in HT recipients and consequences on QoL, focusing on older populations. Databases including PubMed, Scopus, and Embase were searched using a validated query, combining terms related to HT, HF, QoL, and cognitive impairment.

Results: The review examined nineteen studies on cognitive assessment in heart failure patients, focusing on their role in survival prediction, and QoL as a protection factor. Psychiatric and psychological factors including treatment adherence, mental health, substance abuse, cognitive impairment, and socioeconomic status, were key determinants of postoperative outcomes. Moreover, cognitive status prior to the transplant shows that cognitive outcomes after HT are not solely attributable to pre-existing impairment but are also directly influenced by the procedure itself. In fact, studies show that, two years after HT, patients who recover cognitive domains have better survival outcomes.

Conclusions: Despite evidence that diagnosing cognitive deficits in heart failure patients is highly predictive of outcomes, our review highlights the rarity of pre-transplant cognitive assessment. Studies emphasize the urgent need for multidimensional approach and further research to better understand the pathophysiological mechanisms of cognitive decline in heart failure, which differ from those related to neurodegenerative diseases.

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EP_080 PSYSOCIAL NEEDS IN TRANSPLANT PATIENT A NEW WAY TO HANDLE PROSPECTIVE

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Background: With the increasing number of patients in need of solid organ transplantation and the ethnographic, anthropological, and social changes in the patient population, it has become necessary to analyze the social needs of the patients during a pre-transplant screening. These needs may include the lack of a caregiver, unstable and unsuitable housing, missing identification documents, challenges with health bureaucracy, transportation and insufficient financial resources. Thus, in February 2024, thanks to the collaboration with the Sant'Orsola Foundation, the first welfare desk within a hospital dedicated to the psychosocial needs of transplant patients was inaugurated.

Methods: The retrospective research will concern the analysis of the requests collected during 2024 from the Welfare for Transplant patients (WELT). The current project envisions the establishment of a dedicated service within the hospital to support patients during their transplant journey. The social support desk is integrated into the transplant care pathways of the IRCCS-Azienda Ospedaliero-Universitaria in Bologna and will involve the S.S. Service of Clinical Hospital Psychology, the operative units of Internal Medicine for the Treatment of Serious Organ Failure, Hepatobiliary Surgery and Transplantation, the S.S.D. Heart Failure and Transplantation, the Lung Transplantation Program and the Complex Structure of Nephrology, Dialysis and Transplantation.

Results: This research is in the start-up phase. The enrollment will include the analysis of approximately 120 patients to define the social needs and the options for solving them.

Conclusions: The anticipated effects of the social support desk within the hospital include: a prompt and effective management of patients' social requirements by skilled professionals; improved accessibility and decreased duration of the transplant process; a more comprehensive psychological assessment; the implementation of services without burdening the patients; a beneficial influence on the physical and psychological well-being of patients before and after transplantation.

EP_081 STATUS OF FOREIGN BRAIN-DEATH ORGAN DONATION IN KOREA AND SUGGESTIONS FOR REVITALIZING DONATION

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Background: Brain death notifications among foreigners in Korea are increasing due to growing immigration, but organ donations remain low. Cultural and linguistic barriers, legal constraints on family verification, and limited communication of donation information are key obstacles. This study examines the current status of organ donation among foreign brain death cases and proposes policy recommendations for a multicultural society.

Methods: Using data from the Korean Organ Donation Agency(KODA) from 2020 to 2024, key indicators were analyzed, including the proportion of foreign cases among total brain death notifications and organ donations, family interview and consent rates, and reasons for donation failures. The data were evaluated to identify trends and challenges in organ donation among foreigners.

Results: From 2020 to 2024, 12,385 brain death notifications were reported, with 347 cases (2.8%) involving foreigners. The family interview rate for foreigners was 27%, 13.7% lower than the domestic rate of 40.7%. However, the consent rate for foreigners averaged 45%, 11.7% higher than the domestic rate of 33.3%. Among 2,205 total organ donations, 38 cases (1.7%) involved foreigners, with the majority from China (34%), followed by Thailand (24%), Vietnam (16%), the United States (11%), and Uzbekistan (5%). Before 2020, organ donations from foreigners involved 10 countries, including China. Since 2020, Uzbekistan, Kazakhstan, and Malaysia have been added, expanding the pool to 13 countries.

Conclusions: Despite higher consent rates among foreigners, organ donation remains limited due to cultural and procedural challenges. Successful donations have relied on embassy collaboration for family contact and documentation. To enhance foreign organ donation, measures such as embassy partnerships, remote interviews, written consent systems, and respectful repatriation of donors are essential.

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EP_082 ANALYSIS OF THE LIVER TRANSPLANTATION WAITING LIST IN ARMENIA

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Background: Living donor liver transplantation (LDLT) is a crucial treatment for patients with end-stage liver diseases. At Astghik Medical Center, we have a waiting list of 55 patients, comprising 55% males and 45% females, with a median age of 43 years (ranging from 18 to 60). To analyze the characteristics and challenges associated with the waiting list for liver transplantation at Astghik Medical Center and propose solutions to improve donor availability and patient outcomes.

Methods: A retrospective review of the waiting list for liver transplantation was conducted. Data on patient demographics, primary indications for transplantation, and reasons for the lack of suitable living donors were collected and analyzed.

Results: The primary indications for LDLT include HBV or HCV-associated cirrhosis (55%), autoimmune cirrhosis (34%), cryptogenic cirrhosis (6%), and other causes such as alcohol-associated cirrhosis and hepatocellular carcinoma (5%). Despite the importance of LDLT, 89% of patients lack suitable living donors due to incompatible blood groups (3%), unwilling potential donors (5%), financial constraints, and critical health conditions. The MELD score of patients ranges from 15 to 30. Child-Pugh classifications are as follows: 21.4% of patients are class A, 61.8% are class B, and 16.8% are class C.

Conclusions: Establishing a cadaveric donor liver transplantation program is imperative to address the gap in donor availability and improve outcomes for patients in urgent need of liver transplantation.

EP_083 WHAT DO YOU KNOW ABOUT RENAL TRANSPLANTATION IN SINGAPORE? A SURVEY-BASED QUESTIONNAIRE

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Background: Kidney transplantation is the preferred treatment for end-stage renal disease (ESRD). Public perceptions towards organ donation are influenced by cultural and socio-economic factors. This study aims to identify barriers, enhance willingness, and improve care for donors and stakeholders.

Methods: A web-based survey on organ donation knowledge, attitudes, and perceptions was distributed online and via social media. Data was collected using FormSG, a government survey platform, and analyzed using descriptive statistics and chi-square tests.

Results: Of 633 respondents, 91% were Singaporeans, 55.8% female, 20.7% with a medical background, 81.6% with university or higher education, and 59.5% reported household incomes above SGD 8000. 70% were aware of the Human Organ Transplant Act (HOTA), but only 35.8% correctly identified the organs included. While 66.7% were willing to donate kidneys, 53.2% stated they would not request one from relatives, with a significant proportion of willing donors holding this view ($p=0.021$). The main reason for donation was to alleviate suffering (66.0%), and 80.5% prioritized the donor-recipient relationship in their decision-making. Ethnicity was the top consideration (32.1%) for receiving an organ, surpassing factors like age, comorbidities, or cadaveric vs. living donors. Misconceptions were prevalent: 75.2% believed donor surgery involved open surgery (including 23.1% with medical backgrounds), though healthcare workers were more likely to answer correctly ($p<0.01$). Additionally, 89.5% overestimated post-operative recovery time, believing it extended beyond several weeks.

Conclusions: Survey findings highlight gaps in knowledge about kidney transplantation in Singapore, including among healthcare workers. Sociocultural and economic factors may influence barriers to donation despite Singapore's diverse and inclusive society. Further research is needed to address misconceptions, improve awareness, and develop interventions to enhance donor willingness and expand the donor pool.

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EP_084 TRUST IN THE HEALTHCARE SYSTEM MAKES A DIFFERENCE IN DONATION RATES IN POLAND

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Background: [...] a truly sustainable future—where the expectation of gifting and receiving organs is normalized and valued by all in societies—can only happen with trust.[...] Trust that one's most personal gift of a public good is valued." (1). „Trust as a component of social capital related to organ donation rates." (2)

Methods: Cross-sectional survey to explore the relationship between general trust, trust towards the healthcare system, religious practice, and self-declared intention to become an organ donor (OD) in the Polish population. Sample (n=1128) online and face-to-face survey in three Poland regions (West Pomerania -WP, HighPoland- HP, Subcarpathia – SC) with yearly organ transplantations per capita proportions.

Results: Regional consent for OD: (HP) b=-.08, SE 0.04 (SC) b=-.22 SE =0.039 . Trust toward healthcare system (HP) b= -0.10, SE=0.05 (SC) b= -0.14, SE=0.05. Influence healthcare system trust on consent to organ donation b=0.9 SE =0.02.

Conclusions: The regional organ donation rates predict the differences in the declared consent to become a donor with the level of trust towards the healthcare system.

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EP_085 BREAKING BARRIERS: THE FIRST NATIONAL PAIRED KIDNEY EXCHANGE PROGRAM IN SAUDI ARABIA AND THE MIDDLE EAST

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Background: Kidney transplantation remains the optimal treatment for end-stage renal disease. However, the lack of suitable donors presents a significant barrier, especially for highly sensitized patients or those with blood group incompatibility. Paired kidney exchange (PKE) programs offer a solution by facilitating donor-recipient matching between incompatible pairs. This study reports the establishment and outcomes of the first national PKE program in Saudi Arabia, the first of its kind in the Middle East.

Methods: The national PKE program was initiated to address donor-recipient incompatibilities across transplant centers in Saudi Arabia. A centralized matching system identified compatible pairs through donor-recipient swaps between different transplant centers. Between August 2024 and December 2025, 10 paired kidney exchanges were performed at multiple centers. Inclusion criteria included highly sensitized patients and those with blood group incompatibilities. Comprehensive preoperative assessments and standardized immunosuppressive protocols were implemented across all centers.

Results: All 10 transplants were successfully performed with a 6-month patient and graft survival rate of 100%. The program enabled transplantation for patients who otherwise lacked compatible donors, including highly sensitized individuals and those with blood group incompatibility. No major postoperative complications or graft losses were reported.

Conclusions: The establishment of the national PKE program in Saudi Arabia demonstrates its feasibility and effectiveness in overcoming donor-recipient incompatibilities. This initiative sets a precedent for the Middle East and highlights the potential for regional collaboration in expanding access to kidney transplantation.

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EP_086 EXPANDING THE DONOR POOL: OPERATIVE CONSIDERATIONS & OUTCOMES IN OBESE PATIENTS UNDERGOING LIVER DONOR NEPHRECTOMY

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Background: Shortage of organs suitable for transplant has led to the expansion of the Living Kidney Donor (LKD) pool to include obese (BMI ≥30kg/m^2) donors. Higher BMI is risk factor for progression of kidney disease, development of cardiovascular disease, and risk of surgical and anaesthetic complications. Risks remained unquantified in this group, which makes operative planning and determining donor appropriateness difficult. We aim to describe nephrectomy outcomes and determine if donor obesity is associated with peri-operative morbidity or operative difficulty.

Methods: 132 consecutive LKD donors at a UK regional renal transplant centre were stratified into groups according to BMI: Obese (BMI >30kg/m^2) vs Non-obese (BMI <30kg/m^2). Median follow up was 19 months (range 1 – 42 months). Demographics, pre-operative and post-donation biochemistry were collected. 5-year Kidney Failure Risk Equation was calculated. Anaesthetic and surgical time, mode of operation, intra- and post-operative complications, length of stay and re-admission data were collected. Group data were compared using binomial logistic regression.

Results: 19/132 (14.3%) of donors were 'obese' (range 30 – 33.7kg/m^2). There was no significant difference between groups in demographics or presence of respiratory/gastrointestinal/diabetic co-morbidities. Obese donors were more likely to be hypertensive at the time of donation (OR 9.2, 95%CI 1.8 – 45.8, p=0.007). No significant difference was found between groups in baseline nor follow-up renal function, operative times, or length of stay. Rates of intra- or early post-operative complications, re-admission and mortality were comparatively low in both groups.

Conclusions: Nephrectomy outcomes in obese donors is comparable to non-obese individuals, with no demonstrated detriment to peri-operative morbidity, operative or anaesthetic timings, or medium-long term renal function. Obese patients are at higher risk of hypertension, identifying a group for potential targeted interventions/monitoring. These findings may inform selection criteria and discussions with obese individuals considering donation and should encourage the selection of more obese donors.

EP_711 EFFECTIVENESS OF DESENSITIZATION-FACILITATED LDKT VERSUS DDKT RECIPIENTS AND WAITLISTED IN ELDERLY PATIENTS

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Background: Elderly patients with end-stage renal disease (ESRD) often face prolonged waiting times for deceased donor kidney transplantation (DDKT), leading to increased mortality risks. Desensitization-facilitated living donor kidney transplantation (dLDKT) can potentially expedite transplantation by overcoming donor–recipient incompatibility. This study evaluates whether early access to LDKT through desensitization improves patient survival compared to DDKT registry cohort (including recipients and waitlisted) in the elderly.

Methods: This retrospective study utilized data from Seoul National University Hospital from 2005 to 2020. Patients aged 60 and older without prior organ transplants were categorized into two groups: those undergoing dLDKT and those either on the DDKT waiting list or receiving DDKT. Propensity score matching (PSM) was performed to balance baseline characteristics, resulting in 43 patients in the dLDKT group and 258 in the DDKT registry cohort. Survival outcomes were compared using Kaplan–Meier (KM) analysis, Cox proportional hazards models, and time-dependent Cox regression. Secondary outcomes included graft survival and biopsy-proven acute rejection (BPAR)-free survival among transplant recipients.

Results: Post-matching baseline characteristics were comparable between groups, except for pre-transplant dialysis duration. KM survival analysis showed superior survival in the dLDKT group (p=0.0018). Cox regression revealed a higher mortality risk for the DDKT registry cohort (HR 3.30; 95% CI 1.34–8.14; p=0.009). Time-dependent Cox regression demonstrated significant mortality reduction post-transplant (dLDKT HR 0.39, p=0.061; DDKT HR 0.34, p=0.0003). Post-transplant outcomes showed no significant differences in patient survival (p=0.59), graft survival (p=0.51) or BPAR-free survival (p=0.17) between the two groups.

Conclusions: For ESRD patients starting dialysis at age of 60 and above, early transplantation via dLDKT significantly improves patient survival compared to prolonged waiting for DDKT, with comparable post-transplant outcomes. These findings support the proactive use of dLDKT in elderly ESRD patients with incompatible donors.

Baseline characteristics, after Propensity score matching

Variables	Desensitization-facilitated LDKT (n=43)	DDKT recipients and Waitlisted (n=258))	P-Value
Age, years[1]	64.1 ± 2.5	64.6 ± 3.8	0.243
Sex, male	20 (46.5%)	159 (61.6%)	0.089
BMI, kg/m2	23.5 ± 4.8	23.4 ± 3.5	0.912
HTN	34 (79.1%)	226 (87.6%)	0.204
DM	15 (34.9%)	121 (46.9%)	0.194
Cause of ESRD	-	-	-
- Diabetes	10 (25.0%)	86 (33.6%)	-
- Hypertension	1 (2.5%)	31 (12.1%)	-
- Glomerular disease	5 (12.5%)	32 (12.5%)	-
- Polycystic kidney disease	5 (12.5%)	34 (13.3%)	-
- Other disease	6 (15.0%)	10 (3.9%)	-
- Unknown	13 (32.5%)	63 (24.6%)	-
PRA score, %[2]	10.6 ± 21.6	15.1 ± 28.9	0.239
Dialysis duration, months[3]	9.7 ± 13.7	62.5 ± 31.0	0.000

[1] Age was measured at dialysis initiation.
[2] PRA score was the first recorded value after dialysis initiation, using the higher of class I and II.
[3] Dialysis duration was until transplantation, death, or last follow-up.

Table1.

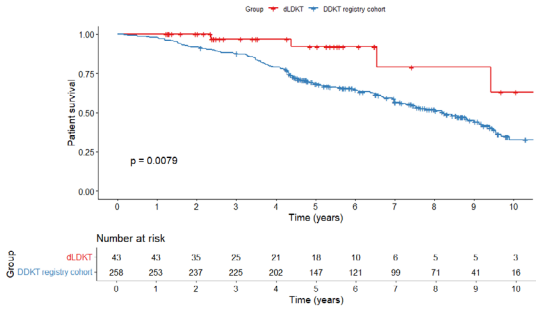

Figure1. KM analysis of patient survival, dLDKT versus DDKT registry cohort.

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EP_087 INTERNAL VALIDATION OF COAGULATION FACTOR V AS A PREDICTIVE TOOL FOR EARLY GRAFT DYSFUNCTION

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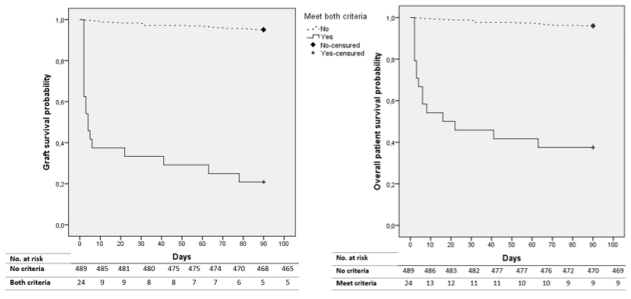
Background: Early graft dysfunction (EAD) is a significant complication after liver transplantation (LT), often leading to retransplantation or death. The lack of consensus on its definition causes heterogeneity across studies, complicating comparisons and decision-making in clinical practice. Coagulation Factor V (FV) and ALT are key biomarkers for assessing liver function, yet their role in predicting graft loss is not fully validated. This study aims to internally validate the use of FV and ALT in predicting graft loss within the first 90 postoperative days (POD).

Methods: We conducted a retrospective cohort study with 513 adult LT recipients from 2012 to 2023 at the Regional University Hospital of Malaga. Based on the results of our pilot study, FV and ALT levels were measured on 2POD, and patients were categorized based on FV <37.5 and ALT >1539. The association with 90-day graft loss was analysed, defining four risk groups. Survival analyses were conducted for graft and patient outcomes. A subanalysis was also performed for graft loss within the first 7 days.

Results: Graft loss occurred in 43 patients (8.4%) within 90 days. FV<37.5 and ALT>1539 on 2POD showed 99% specificity and 94% efficiency in predicting graft loss, associated with a 74-fold increase in risk. Predicted probabilities for each risk group were 68%, 36%, 11%, and 3.2%. In the 7-day subanalysis, sensitivity, specificity, and efficiency were 100%, 98%, and 98%, respectively, with an OR of 807.2. Predicted probabilities of graft loss were 95.2%, 26.3%, 17.1% and 0.4%. Figure 1 shows significant differences in graft and patient survival (Log-Rank test).

Conclusions: FV and ALT levels on 2POD are early markers for predicting graft loss, allowing risk stratification and guiding decisions on early retransplantation. FV<37.50 + ALT>1539 is also linked to overall patient survival in the first week and 90POD. These findings provide a foundation for future multicentric studies to further validate the clinical utility of these biomarkers in a broader population.

Figure 1. Kaplan-Meier Survival Curves for Graft and Overall Survival at 90 Days



Groups:

- **Does Not Meet Criteria (dotted line)**: This group includes patients with FV ≥ 37.5 and/or ALT ≤ 1539.
- **Meets Criteria (continuous line)**: This group includes patients with FV < 37.5 and ALT > 1539.

EP_088 FLOTRAC VERSUS HYPOTENSION PREDICTION INDEX GUIDED HEMODYNAMIC MANAGEMENT IN KIDNEY TRANSPLANT

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Background: Intraoperative hypotension (IOH) is inevitable during moderate to high-risk surgeries. In kidney transplantation, intraoperative hypotensive events can badly affect post-operative graft and patient outcomes. Traditionally, central venous pressure (CVP) monitoring has been regarded as a fundamental aspect of intraoperative haemodynamic management during kidney transplantation. Recently, the focus has changed by including newer haemodynamic tools (Flotrac, Hypotension prediction index, etc.) to reduce intraoperative hypotensive events and post-operative complications.

Methods: This study was done retrospectively to observe the effect of haemodynamic monitoring on intraoperative hypotension. Recipients with dilated cardiomyopathy, aged 18-60 years who underwent kidney transplantation from June 2022 to May 2024 were included. The primary objective was to record time-weighted average (TWA) of intraoperative hypotension. Secondary outcomes were to record average number of hypotensive events per patient and average duration of each hypotensive event.

Results: Twenty-eight patients having dilated cardiomyopathy were included. Primary outcome taken as a time-weighted average (TWA) of area under threshold (AUT) (MAP < 65mmHg) per patient was more in patients in Flotrac group in comparison to the HPI group (*P*=0.613). Secondary outcomes like the incidence of hypotensive events per patient and total time of hypotension were significantly higher in Flotrac group as compared to HPI group (*P*<0.0001).

Conclusions: HPI provides superior intraoperative haemodynamic management in kidney transplant recipients with dilated cardiomyopathy in terms of reduced duration, incidence and severity of intraoperative hypotension.

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Current challenges in transplantation procedures

EP_089 LIVER TRANSPLANTATION IN THE PHILIPPINES: LIGHT AT THE END OF THE TUNNEL

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Background: End-stage liver disease is arguably one of the leading burdensome diseases among developing countries such as the Philippines. While liver transplantation is considered the treatment of choice for decompensated cirrhosis, the establishment of a robust transplant program locally has been protracted as numerous obstacles continue to plague our transplant landscape. Issues on cost, options of having the transplant done overseas and low rates of deceased donation are some of the difficulties that hamper our program's progress and development. In this article, we aim to present our experience and discuss hurdles, describing the current status of liver transplantation in the country. Herein we report our initial 68 liver transplants covering 35 years.

Methods: A retrospective review was performed including all transplants done in four active transplant centers from August 1988 to December 2023.

Results: Recipients were mostly males (69%) with hepatitis B as the most common (32%) primary liver disease. Deceased donor liver transplant was more common (65%) with recipients having a median MELD score of 22. Among living donor liver transplants, 58% of the grafts were from the left lateral segment. Outcomes can be divided into two eras, with the first era (1988-2010) having a 1-year graft survival of only 25%. The second era (2011-present) was marked with surgical refinements and advancing knowledge, improving 1-year graft survival to 64% and 67% for adult and pediatric transplants, respectively.

Conclusions: Indeed, the establishment of a liver transplant program requires a team approach and most fundamentally, full training in liver transplantation and the management of its complications. Optimal patient selection remains essential in achieving excellent survival outcomes. Lastly, Filipinos with liver cirrhosis now have an opportunity for a significant improvement in their quality of life by undergoing transplantation in their native country.

EP_090 USE OF LIGASURE IN KIDNEY TRANSPLANTATION: AN INITIAL EXPERIENCE

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Background: Worldwide, kidney transplantation is done as a renal replacement therapy for end-stage kidney disease patients. Lymphocoele is a common complication following renal transplantation, with an incidence varying between 0.6% and 33.9%. The use of the electrothermal bipolar sealing device (LigaSure) has proven superior to other vessel sealing techniques in several reports. As such, LigaSure device is expected to provide an alternative method to the standard silk-tie method during kidney transplantation. This study aims to describe our experience on using Ligasure device in kidney transplantation at the National Kidney and Transplant Institute.

Methods: A prospective descriptive cross sectional research design among patients who underwent iliac vessel dissection using Ligasure device during kidney transplantation. Clinical outcomes were determined including operative time during iliac vessel dissection using LigaSure device, total and average JP drain output. Incidence of lymphocoele was observed by performing an allograft ultrasound on post operative day 14, 60 and 90.

Results: Ultrasonographically, none of the patients in this study developed a lymphocele. Average use of Ligasure device during iliac vessel dissection was 16.92 minutes. Average daily JP drain output was 123mL and average JP drain output prior to JP drain removal was 25.44mL.

Conclusions: We did not observe any incidence of lymphocoele among patients wherein Ligasure device was used during iliac vessel dissection. Routine use of Ligasure device can be done without the risk of lymphocoele formation and can serve as an alternative from the traditional silk-tie method during iliac vessel dissection.

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Current challenges in transplantation procedures

EP_091 HEPATIC ARTERY RECONSTRUCTION USING PTFE AS AN ILIO-HEPATIC CONDUIT IN LIVER TRANSPLANTATION

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Background: A sufficient and patent arterial flow is crucial in orthotopic liver transplantation to a greater extent among living than deceased donors as vessels are oftentimes shorter and smaller in caliber. Noteworthy complications such as thrombosis may bring about graft necrosis, liver abscess, ischemic cholangiopathy or graft failure, leading to increased mortality. In deceased donor transplantation, meticulous vessel preparation at the back-table and the availability of longer segments of artery with an aortic patch allow surgeons to maximize the artery at hand during implantation.

Methods: The usual method of arterial reconstruction is an end-to-end anastomosis between the donor and recipient hepatic artery. Various alternative options are available when the recipient hepatic artery is not suitable for anastomosis namely, more proximal arteries, interposition grafts, stored cadaveric vessels or rarely, prosthetic vessel conduits.

Results: We present a case of a 40-year-old male who underwent deceased donor liver transplantation wherein a hepatic arterial reconstruction was performed by fashioning a polytetrafluoroethylene (PTFE) graft between the recipient external iliac artery and donor celiac artery (ilio-hepatic conduit).

Conclusions: Patient remains asymptomatic with good graft function and patent hepatic artery after 1 year of follow-up.

EP_092 ASSESMENT OF ARTERIAL BLOOD FLOW IN A KIDNEY TRANSPLANT ON THE DEVELOPMENT OF VASCULAR COMPLICATIONS

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Background: In clinical practice, positive results of vascular reconstruction, as well as the severity of reperfusion injury to the graft, are often based on the subjective assessment of the surgeon and some objective signs, such as immediate diuresis, as well as turgor and color of the kidney graft. Intraoperative flowmetry (IF) is a non-invasive method that measures the “transit time”. The use of IF in clinical practice in kidney transplantation will reduce the incidence of intraoperative vascular complications, which directly affects long-term results.

Methods: From May 2022 to July 2023, 298 kidney transplants were performed. The study included 285 patients with end-stage chronic kidney disease, of whom 49 patients underwent intraoperative flowmetry (n = 49, 17.2% of the total number of subjects. Intra- or postoperative vascular complications were observed in 6 cases (12.2%), which were corrected intraoperatively. In 43 cases (87.8%) there were no complications.

Results: It was found that statistically significantly lower values of volumetric blood flow velocity in the renal artery after reperfusion (p=0.002) and after neoureterocystostomy (p=0.006) were observed in the group of patients with vascular complications intraoperatively. The PI (pulsatility index) after graft reperfusion, on the contrary, was statistically significantly higher in patients with identified complications (p=0.037). If the volumetric blood flow velocity after reperfusion is less than or equal to 120 ml/min, it is possible to predict the development of vascular complications intraoperatively or in the postoperative period (area under the ROC curve (AUC) = 0.872±0.78, p<0.001, sensitivity 83.3%, specificity 88.4%). If the volumetric blood flow rate after neoureterocystostomy is less than or equal to 230, it is permissible to predict the development of vascular complications (AUC = 0.723±0.118, p=0.060, sensitivity 83.3%, specificity 79.1%).

Conclusions: The volumetric blood flow rate in the renal artery, both after reperfusion and after neoureterocystostomy, are predictors of vascular complications.

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Current challenges in transplantation procedures

EP_093 NATIVE NEPHRECTOMY IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Background: Autosomal Dominant Polycystic Kidney Disease (ADPKD) often leads to end-stage renal disease (ESRD), requiring native nephrectomy (NN) as part of kidney transplantation (KT) management. This study evaluates 25 years of single-center experience with NN in ADPKD patients, focusing on the outcomes of acute versus planned procedures.

Methods: This retrospective study included ADPKD patients undergoing NN between 1999 and 2023. Data on surgery duration, blood loss, complications, and hospital stay were collected. Patients were categorized into acute and planned NN groups, further divided into unilateral and bilateral surgeries. Statistical analyses were conducted to compare outcomes between the groups.

Results: Of 152 ADPKD patients post-KT, 89 (58.6%) underwent NN, with 42 (37.8%) acute and 69 (62.2%) planned. Acute NN had significantly longer surgeries, more blood loss, and higher complication rates compared to planned NN. Complication rates for unilateral acute NN were 23.8%, compared to 2.9% for planned cases (p<0.001).

Conclusions: Acute NN in ADPKD patients is associated with higher risks and complications. Planned NN offers better outcomes, emphasizing the need for careful surgical planning to optimize patient care.

Characteristic		Acute N=42	Planned N=69	P value
Mean operation duration ± SD [min]	Unilateral Bilateral	106 ± 66 115 ± 80	76 ± 36 86 ± 57	0.009 0.044
Mean blood loss ± SD [mL]	Unilateral Bilateral	290 ± 170 308 ± 105	158 ± 57 225 ± 79	<0.001 <0.001
Mean hemoglobin before native nephrectomy ± SD [g/dL]	Unilateral Bilateral	12.2 ± 1.6 12.1 ± 1.2	13.1 ± 1.5 12.7 ± 1.6	0.004 0.027
Mean hemoglobin before native nephrectomy ± SD [g/dL]	Unilateral Bilateral	9.3 ± 1.9 8.9 ± 2.1	10.1 ± 1.3 10.2 ± 1.5	0.019 <0.001
Mean length of stay ± SD [days]	Unilateral Bilateral	8.3 ± 2.8 9.2 ± 3.6	6.7 ± 1.9 7.1 ± 2.1	0.002 0.001
ICU admission N (%)	Unilateral Bilateral	28 (93.3) 12 (100)	12 (29.3) 15 (53.6)	<0.001 <0.001
Vasopressors N (%)	Unilateral Bilateral	5 (16.7) 6 (50)	2 (4.9) 3 (10.7)	<0.001 <0.001
Perioperative complications* N (%)	Unilateral Bilateral	10 12	2 3	<0.001 <0.001

**Surgical reintervention (6, 5.4%), surgical site infection (5, 4.5%), transfusion (4, 3.6%), ileal perforation (4, 3.6%), wound dehiscence (3, 2.7%), pulmonary embolism (2, 1.8%), bleeding (2, 1.8%), stroke (1, 0.9%). No patient died.*

EP_094 LIVING DONOR LIVER TRANSPLANTATION WITH A PORTAL VEIN LESS THAN TWO MILIMETERS IN DIAMETER

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Background: In children, hemodynamic disturbances may occur due to portal vein (PV) hypoplasia. In cases like this, PV reconstruction is usually performed using vein graft. We present a successful anastomosis between the distal part of hypoplasic recipient PV including confluence and the donor PV without the use of a graft.

Methods: Our case with biliary atresia was 18 months old and weighed 8 kilos. Her model for pediatric end-stage liver disease score was 22.2. Vascular structures were evaluated with preoperative CT angiography (CTA) and no flow could be seen in PV. Living donor LT was performed from her father. To obtain sufficient front flow into the graft, the main collateral vessels of the portal system were ligated. The hypoplasic PV was dissected until the cofluence of superior mesenteric vein and splenic vein. Intraoperative measurement showed that the diameter of the distal part of the portal vein was less than 2 mm. The graft portal vein was anastomosed with a lateral incision 9 mm proximal part to confluence with 6-0 polydioxanone monofilaments. Intravenous heparin infusion was given for the first 1 week postoperatively and portal vein flow monitoring was performed with Doppler ultrasonography.

Results: Doppler ultrasonography on postoperative day was 2 revealed stenosis in the portal vein. This stenosis was were treated with a course of percutaneous transhepatic PV dilatation and stent placement.

Conclusions: In cases of diameter mismatch between the recipient and graft portal vein due to portal vein stenosis in biliary atresia, graft use may cause unexpected morbidity in the recipient or donor. Therefore, with careful dissections using microsurgical techniques in an experienced center, successful results can be achieved without the use of grafts with anastomoses to areas with suitable diameter for anastomosis such as superior mesenteric vein-splenic vein confluence.

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Current challenges in transplantation procedures

EP_095 SAFE AND EASY METHOD TO PREVENT BILE LEAKAGE IN LIVER TRANSPLANTATION: PLACING DOUBLE J CATHETER

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Background: The incidence of biliary complications after liver transplantation (LT) is 15-65%. Various suture techniques, internal and external stents have been used in the literature to prevent biliary leaks. We evaluated the preventive effect of double J stents (djs) placed in the biliary anastomosis on biliary leakage.

Methods: We used 3Fr X 12cm DJS in the biliary anastomosis of 26 patients. Biliary anastomosis was performed using a 2.5 magnifying surgical loupe, via end bile duct to side Roux-en-Y hepaticojejunostomy (n = 3), hepaticoduodenostomy (n=4), and duct-to-duct choledochocholedochostomy (n=19). We performed interrupted suture with 6-0 absorbable material. After complete posterior row, we inserted djs into the intrahepatic bile duct. After that we complete the anastomosis with interrupted sutures of the anterior wall. In biliary anastomoses with multiple ducts, djs were placed separately in each duct.

Results: We used 30 DJS in the biliary anastomosis of 26 patients. 24 of the patients were living donor LT. Three were auxiliary partial orthotopic LT and 1 was domino LT. Of the grafts, 6 were left lateral lobe, 8 were left lobe, 12 were right lobe, 1 was whole graft. Three graft had two bile ducts. Bile leakage from the anastomosis was observed only in 3 patients. In first patient with anastomotic leakage, DJS was endoscopically removed and an internal stent was placed. The other patients anastomosis was hepaticoduodenostomy and DJS moved to jejenum. We operated for biliary leakage, reinserted DJS and performed primary repair of the anastomotic line. Complete recovery was achieved in both of patients without the need for additional intervention and without the development of stenosis.

Conclusions: In biliary anastomoses, DJS can be safely used to prevent anastomotic leaks in both pediatric and adult patients, regardless of graft type and anastomosis technique.

EP_096 EVALUATING LIVER TRANSPLANTATION OUTCOMES IN BUDD-CHIARI SYNDROME: SINGLE CENTER STUDY

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Background: Budd-Chiari syndrome (BCS) is an uncommon condition, caused by obstruction to hepatic venous outflow and can progress to chronic liver failure. The final treatment for patients who do not respond to medical or interventional treatments is liver transplantation. We present the results of patients who underwent liver transplantation due to BCS at our center.

Methods: Between December 1988 and August 2024, 193 patients were diagnosed with Budd-Chiari Syndrome (BCS), and 17 liver transplants (LT) were performed on 13 of these individuals. Recorded data included the age and sex of the transplant recipients, CHILD-PUGH scores, Model for End-Stage Liver Disease (MELD) scores, histopathological findings, interventional treatments, graft types, hepatic vein anastomosis techniques, post-transplant complications, and mortality rates.

Results: Within the study period, 17 liver transplants (LTs) were performed on 13 patients diagnosed with Budd-Chiari Syndrome (BCS). Of these recipients, six were female. The mean age at transplantation was 27.2 years (range: 9–50 years). We had liver transplantation once for 10 patients, twice for 2 patients and three times in 1 patient with BCS diagnosis. Survival rates post-transplantation were 90% at 1 year, 80% at 5 years, and 30% at 10 years. Notably, only two patients succumbed postoperatively following their second LT.

Conclusions: LT can be conducted safely in patients diagnosed with BCS when chronic liver failure ensues and alternative therapeutic approaches are unsuccessful.

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Current challenges in transplantation procedures

EP_097 ENDOSVASCULAR STENTING IN HEPATIC VENOUS OUTFLOW OBSTRUCTION FOLLOWING LIVER TRANSPLANTATION

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Background: Hepatic venous outflow obstruction (HVOO) after liver transplantation is a graft-threatening condition. HVOO that does not improve after balloon angioplasty should be treated with a stent. Our study aimed to evaluate the effectiveness of stents in hepatic vein stenosis that develops after liver transplantation.

Methods: Between August 2011 and August 2024, 11 patients who had liver transplantation and had stenosis in the hepatic vein and had stent placement were included in the study retrospectively. Demographic data of the patients, number of stents, procedure success and complication rate were evaluated.

Results: 11 patients were enrolled in this study (63.6% females and 36.4% males; mean age: 31 years; range: 1–62 years). A total of 14 stents were placed, a sinle stent in eight patients and two stents in three patients. There were no major complications. Technical success was 100%.

Conclusions: Hepatic vein stenting is a safe and effective treatment method for patients who develop HVOO after liver transplantation.

EP_098 PERCUTANEOUS MANAGEMENT OF PORTAL VEIN STENOSIS AFTER LIVER TRANSPLANTATION

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Background: Portal vein stenosis is a relatively rare complication after liver transplantation but has severe consequences. Our aim is to evaluate the efficacy and long-term results of the endovascular treatment methods for portal vein stenosis.

Methods: From October 2011 to August 2024, we treated 26 patients (7 female, 19 male) with portal vein stenosis using endovascular methods. Doppler ultrasound was used for initial diagnosis, considering flow rate increase over stenosis, absence of flow, or reduced anastomotic segment size (>50%). Angiography served as the gold standard, with a pressure gradient above 5 mm-Hg indicating the need for treatment. Technical success criteria were defined as less than 50% stenosis remaining and/or a pressure gradient below 5 mmHg. Transhepatic approach was used for all patients. Balloon angioplasty was initially performed, and stents were reserved for patients in the early post-operative period or those unresponsive to balloon angioplasty.

Results: The technical success rate was 100%. Mean age was 27.1 years (SD 21.9, 4 months to 63 years). Mean time from transplantation to intervention was 271 days (0-3135). Angioplasty was successful for 7 patients (26.9%). Of 19 patients who underwent stent placement 12 (46.1%) were in the early post-operative period, in other 7 (26.9%) results of angioplasty were not satisfactory, and stents were placed. Within 3 month of transplantation, 3 patients were lost due to other complications. Among the patients with stents, 2 required reintervention, resulting in the reestablishment of good portal venous flow. During the mean follow-up of 24 months (15 days-9 years), 23 patients (88%) had portal flows within normal limits.

Conclusions: Endovascular approach is a safe and effective treatment option in the management of PVS in liver transplant patients both in adult and pediatric population in the early or late period.

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EP_099 A HOMEMADE INTERNAL PLASTIC STENT FOR TREATING BILIARY STRICTURES IN LIVER TRANSPLANT

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Background: Endoscopic and percutaneous treatment options for hepaticojejunostomy (HJS) strictures after liver transplantation (LT) are limited. The aim is to assess the efficacy of a novel method combining an internal-external biliary drainage catheter (İED) and a custom internal plastic stent, both inserted simultaneous through percutaneous access, for the treatment of biliary strictures in LT recipients with HJS.

Methods: Seventeen patients included in the study. First, a balloon dilatation, and an İED was placed for biliary anastomotic stenosis. In a follow-up procedure, an internal plastic stent was placed dually along with a drainage catheter from the same access. The plastic stent is produced from the standart biliary drainage catheter by cutting the distal end of the catheter to fit the required size. The proximal part of the catheter used like the pusher in double J stent systems. First, stent is placed over one of the wires across the anastomosis then İED is placed side by side with the internal stent. This method effectively doubles the diameter at the site of stenosis using an access point only one catheter wide. The patient is followed at least six weeks with this dual system. The drainage catheter and internal plastic stent were removed when follow-up cholangiography showed improved passage with no recurrence of symptoms or elevation of biochemical markers.

Results: Technical success was achieved in all 17 (100%) patients. Clinical success was achieved in 13 (77%) patients, and drainage catheters with internal plastic stents were removed after a mean period of 3.1 months. During the follow-up, the primary patency rates were 76%, 94% at 6 and 12 months, respectively. Four (%23) of the 17 patients developed recurrent symptoms after the removal of both internal plastic stent and drainage catheter.

Conclusions: Our novel technique is a safe and effective method for treating persistent anastomotic stenosis in LT patients with HJS.

EP_100 SPECIFIC CHALLENGES OF RENAL TRANSPLANTATION IN FRENCH GUIANA

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Background: French Guiana, a tropical and multicultural region, has a chronic kidney disease (CKD) prevalence twice that of mainland France. This creates unique challenges for renal transplantation, influenced by infectious, genetic, environmental, and sociocultural factors. These factors require adaptations in medical practices and organisational strategies to ensure optimal outcomes. This study aims to identify the clinical, epidemiological, and sociocultural specifics of kidney transplantation in French Guiana and propose context-specific strategies.

Methods: We analyzed local data on chronic kidney disease and associated pathologies, incorporating medical, infectious, and sociocultural factors influencing organ donation and transplantation.

Results: *Infectious Challenges:* High HIV and HTLV-1 prevalence complicates transplant management due to drug interactions and increased opportunistic infections. Endemic diseases, including Chagas, tuberculosis, leishmaniasis, and tropical mycoses (e.g., histoplasmosis), require strict prophylaxis to prevent reactivation post-transplant. *Genetic and Autoimmune Factors:* Sickle cell disease, prevalent in French Guiana, and other genetic or undetermined nephropathies are major causes of end-stage renal failure, requiring personalised treatments. Autoimmune diseases such as lupus complicate immunosuppressive management. *Sociocultural Barriers:* Spiritual beliefs, mistrust of the healthcare system, and reliance on traditional medicine hinder organ donation and complicate post-transplant care adherence. HIV-related stigma further limits access to care for eligible patients. *Environmental and Infrastructure Constraints:* The tropical climate increases the risk of environmental infections. Geographic isolation and limited infrastructure hinder post-transplant follow-up and specialised care access.

Conclusions: Renal transplantation in French Guiana requires a multidimensional, context-specific approach. Priorities include comprehensive screening for endemic and opportunistic infections, awareness campaigns to promote organ donation, and strengthening local infrastructure for specialised follow-up. These efforts are essential for improving renal transplantation outcomes in this region.

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EP_101 EPIDURAL INFUSION VERSUS CONTINUOUS ERECTOR SPINAE FOR ANALGESIA IN RENAL TRANSPLANT RECIPIENTS

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Background: This study was conducted to compare the efficacy of Erector spinae plane block (ESPB) and continuous epidural infusion (CEI) for pain management in renal transplant recipient under general anaesthesia.

Methods: This was a randomized, double-blinded, controlled trial involving 52 patients, aged 18-65 years undergoing renal transplant surgery comprising of two groups, Group A (n = 26) received CEI with 7.5 ml of 0.25% Bupivacaine bolus whereas Group B (n = 26) received USG-guided continuous ESPB with 20 ml of 0.25% Bupivacaine bolus. Both the groups received an infusion of 0.125% bupivacaine at the rate of 0.1ml/kg/hr following the bolus dose. The primary outcome of the study was to compare NRS scores 24 hours post operatively at rest and movement. Rescue analgesia, duration of hospital stays and patient satisfaction score was also recorded.

Results: NRS score at rest in both the groups was comparable for the first 8 hours postoperatively, however it was superior in ESPB group after 8 hours postoperatively. NRS on movement in both the groups were comparable at all the time intervals. **(Table 1)** Postoperative HR was significantly lower in group ESPB compared to group CEI at all intervals. Post-operative rescue analgesia consumption and patient satisfaction score was comparable between the two groups.

Conclusions: We conclude that continuous ESPB is an effective modality of postoperative analgesia and can be employed as an alternative to continuous epidural analgesia.

Table 1: Comparative analysis of post-operative (VNRS) pain score between the two groups.

Post-operative pain score		Median (IQR)		p-value
		Group CESPB (N = 26)	Group CEI (N = 26)	
At rest	4 hrs	2 (2 - 2.25)	2 (2 - 3)	0.203
	8 hrs	2 (1.75 - 2)	2 (2 - 3)	0.063
	12 hrs	2 (1 - 2)	2 (2 - 2)	0.009
	24 hrs	2 (1 - 2)	2 (2 - 2)	0.010
	48 hrs	1 (0 - 1)	1 (1 - 1)	0.006
On movement	4 hrs	3 (3 - 3)	3 (3 - 4)	0.681
	8 hrs	2 (2 - 3)	3 (2 - 3)	0.064
	12 hrs	2 (2 - 2)	2 (2 - 3)	0.330
	24 hrs	2 (1 - 2)	2 (2 - 2)	0.055
	48 hrs	1 (1 - 1.25)	1 (1 - 2)	0.064

The above table shows the median post-operative pain score at rest and on movement between the two groups.

EP_102 EVIDENCE ON IMPACT OF DIFFERENT EXTRACORPOREAL THERAPIES ON IMMUNOSUPPRESSANTS; A SYSTEMATIC REVIEW

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Background: Extracorporeal therapies (ECT) such as continuous renal replacement therapy (CRRT), extracorporeal membrane oxygenation (ECMO), therapeutic plasma exchange (TPE) and hemoadsorption (HA) are frequently used in the treatment of critically ill patients, but may impact immunosuppressant drug (ID) levels vital for patient outcome. Impact of such therapies on drug levels remain unclear.

Methods: A search of the National Library of Medicine Pubmed database (https://pubmed.ncbi.nlm.nih.gov/), in Clinicaltrials.gov and the Cochrane database was performed. Key terms included: drug removal / drug elimination / drug levels and continuous renal replacement therapy / extracorporeal membrane oxygenation / therapeutic plasma exchange / CytoSorb /Jafron /oXiris / Seraph / PMX-HP. Importance of available in-vivo data were treated as superior over in-vitro data.

Results: Data on potential drug removal was found for 11 different ID, including both *in-vivo* and *in-vitro* studies. For CRRT there was only information regarding rituximab, ECMO only on basiliximab, Jafron HA only on methotrexate, and Seraph HA only on mycophenolic acid and tacrolimus. Information regarding potential drug removal was found for 6 different immunosuppressants in 7 publications with TPE use and for 8 immunosuppressants in 5 publications for CytoSorb HA due to multiple drugs being reported on in one publication. No published data was found regarding potential removal with the oXiris or PMX-HP HA devices (see Table 1). Evaluation of drug removal varied considerably, from systematic blood level testing and comparison of pre- and post-device measurements to clinical evaluations. Most publications were single case reports.

Conclusions: Data on the impact of ECT on ID levels remains scarce with most data being available with TPE and CytoSorb HA. Published reports include in-vitro and in-vivo data with or without direct blood level monitoring. Overall, the level of evidence for the impact of ECT on ID levels is still limited and further research is needed. Drug monitoring, whenever possible, is recommended to support clinical decision making.

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EP_103 A METABOLIC TEST TO TELL MARGINAL FROM POOR QUALITY LIVER GRAFTS DURING MACHINE PERFUSION

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Background: Evaluative measures, helping to decide whether a marginal graft can be used for transplantation or rather be discarded are of utmost importance but yet basically underdeveloped. Recent technical developments allow for the isolated detection of 13C-labeled carbon dioxide in the oxygenator exhaust of an isolated perfused organ. By adding a 13C-labelled substance to the perfusate, its metabolism can be monitored by measuring the increase in 13C carbon in the exhaust air[1]. In the present study this method was investigated for its potential to differentiate between marginal or poor pig livers during machine perfusion and compared to the use of conventional parameters or biomarkers.

Methods: Porcine livers were subjected to 0, 20 or 45 min of warm ischemia (representing healthy, marginal and poor grafts) and cold stored overnight. Evaluative perfusion was done with MPS at 20°C for 3h. After 30 min of equilibration, 13C acetate was injected and its metabolization by the citrate cycle quantified by direct detection of $^{13}CO_2$ at the oxygenator.

Results: Not surprisingly, all conventional parameters (e.g. flow, bile, transaminases, lactate) showed clear differences between healthy and poor livers but no differences were disclosed between marginal and poor livers (flow 1133±298 vs 999±225 ml/min, lactate 1.2±0.7 vs 1.2±0.3 mmol/l, bile 0.4±0.2 vs 0.6±0.5 µl/g/h, AST 591±552 vs 815±339 U/l; mean±SD; n=6, resp.). Only the acetate turnover differed between marginal (41.1±14.9) and poor grafts (20.5±9.9 µmol/30min; p=0.019) and could thus help to recognize usable livers out of the pool of suboptimal grafts. ROC curve analysis for discrimination of marginal vs poor grafts by acetate turnover revealed an area under the curve of 0.89.

Conclusions: Thus, the ^{13}C turnover test appears to have the potential of an objective, quantitative and valuable adjunct in the toolbox for pre-transplant evaluation of questionable liver grafts.

1. Commun Med (Lond).2023;3(1):192.

EP_104 MIDODRINE REDUCES ICU AFTER SIMULTANEOUS BILATERAL NEPHRECTOMY AND KIDNEY TRANSPLANTATION

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Background: - Simultaneous bilateral native nephrectomy with kidney transplantation (BNNKT) for patients with autosomal dominant polycystic kidney disease (ADPKD) is safe, however hypotension requring ICU is needed in about 70% of patients and the need for ongoing vasopressor therapy. Midodrine, an oral alpha-1 adrenergic agonist prodrug, can treat refractory hypotension. The use of midodrine for patients with ADPKD undergoing BNNKT has not been routinely studied. We hypothesized that we would reduce ICU admissions by using routine administration of perioperative midodrine for patients with ADPKD undergoing BNNKT.

Methods: The protocol of midodrine administration (20mg PO q8 hours for 48 hours) was used from March 2023 through March 2024 for ADPKD patients requiring BNNKT. The first dose of midodrine was administered pre-operatively. Our primary outcome of interest was ICU admission rate due to ongoing vasopressor requirements for hypotension. Data from the cohort receiving midodrine was compared to retrospective historical controls for patients who underwent the same procedure without perioperative midodrine use. Patients were excluded from the analysis if they were admitted to the ICU for a reason other than treatment of hypotension with vasopressors.

Results: A total of 115 patients with ADPKD who underwent BNNKT from 2014 through March 2024 were included in the final analysis and of these, 19 received midodrine per protocol from March 2023 through March 2024. Within the midodrine treatment group, 52.2% (12/23) required ICU admission for ongoing vasopressor use compared to 62.0% (57/92) in the historical control group without midodrine use (OR 0.61, 95%CI: 0.24-1.56, p=0.31, NNT:9).

Conclusions: The use of perioperative midodrine for ADPKD patients undergoing BNNKT shows a trend towards decreased vasopressor requirements and need for ICU admission post-procedure compared to a historical cohort. Including midodrine treatment as part of ongoing multidisciplinary enhanced recovery pathway for this unique patient population could be considered to further decrease the need for post-procedure ICU-level cares.

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EP_105 USE OF DRUG ELUTING STENT IN TRANSPLANT RENAL ARTERY STENOSIS

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Background: Following kidney transplantation, the most frequent vascular complication is transplant renal artery stenosis (TRAS). These cases present with a decreasing graft function and hypertension and might also be contributory to loss of the renal allograft.

Methods: We report a case of a 32 year-old male who underwent renal allograft transplantation and who presented with new onset hypertension post-operatively. He had increasing need for antihypertensive medications, decreasing urine output, and a slow graft function in the immediate post-operative period. Imaging revealed a stenosis of the allograft renal artery.

Results: The patient underwent PTA with stenting using a balloon-expandable, drug-eluting coronary stent (Medtronic Resolute Integrity DES). After the procedure, he demonstrated an immediate increase in the urine output, a further decrease in serum creatinine level, and a decreasing dependence on antihypertensives. He was off antihypertensives and discharged improved after 6 post-operative days. He has exhibited normal serum creatinine levels and good urine output on follow-up.

Conclusions: There are several endovascular treatment options available to address TRAS. The best treatment option will depend on a case-to-case basis. There are currently no purpose-made stents for TRAS. This case is reported to highlight the use of DES as a treatment option for TRAS. Long-term safety and efficacy of its use should be validated further.

EP_106 IS AN IMPLANTABLE DOPPLER PROBE USEFUL AS A VASCULAR MONITORING DEVICE IN KIDNEY TRANSPLANT?

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Background: Vascular complications account for 30-35% of the total kidney grafts lost during the first three months after implantation. Early detection of vascular complications allows an opportunity for a prompt intervention that is critical to reducing graft loss. This study aims to evaluate the usefulness of implantable Doppler probes as a vascular monitoring device in kidney transplant patients.

Methods: An implantable Doppler probe is used intermittently for the postoperative monitoring of kidney transplant patients at our centre. We retrospectively described prospectively maintained medical data by comparing the clinical outcomes in kidney transplant patients with postoperative Implantable Doppler probe monitoring against those with standard care clinical observation. The medical data of 472 kidney transplant recipients at the Southwest Transplant Centre between January 2015 and March 2023 was studied and divided into two groups. Group 1 consisted of 264(56%) kidney transplant patients with postoperative Implantable Doppler probe monitoring, while Group 2 comprised 208(44%) kidney transplant patients with standard care clinical observation. The groups were compared regarding the number of vascular complications identified, the number of departmental ultrasound scans required postoperatively, and the 03-month graft loss.

Results: Overall, in all patients, vascular complications were identified in 12.1%, and the resultant graft loss was 12(2.5%). Both groups had similar demographic characteristics. In Group 1, more vascular complications were identified (15.1% vs 8.1%; RR = 1.86), fewer ultrasound scans were requested in the first 24 hours postoperatively (67.8% vs 84.6%; RR = 0.80), and lower graft loss (1.5% vs 3.8%; RR = 0.39) was recorded as compared to Group 2. All probes were removed safely after 72 hours, and no complication related to the device was reported.

Conclusions: The implantable Doppler probe, as a potential adjunct for graft monitoring in kidney transplant patients, could play a crucial role in preventing graft loss. Further controlled studies are warranted to evaluate this device in clinical practice.

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EP_107 EXPLORING THE ROLE OF AN IMPLANTABLE DOPPLER PROBE IN KIDNEY TRANSPLANT: A FEASIBILITY RCT

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Background: Vascular thrombosis is a disastrous postoperative complication, resulting in the loss of 3.5% to 5.7% of all kidney transplants. Blood flow-sensing technology in the early postoperative period may help identify vascular complications crucial to reducing graft loss. This study aimed to assess the feasibility of an implantable Doppler probe as a blood flow-monitoring device in kidney transplant recipients and to evaluate its usefulness in preventing early graft loss

Methods: This 2-arm feasibility randomised controlled trial compared the demographical characteristics and surgical outcomes of kidney transplant recipients who received implantable Doppler probe monitoring (intervention group; n = 30) with those who had standard clinical care (control group; n = 30). Surgical outcomes compared between the groups included the number of early vascular complications identified, the number of departmental ultrasonography scans requested in the first 72 hours postoperatively, and month three graft loss.

Results: Both groups had similar demographic characteristics. In the intervention group versus the control group, fewer ultrasonography scans were requested in the first 24 hours postoperatively (56% vs 91%), and lower graft loss (0% vs 6.6%) was recorded. The results addressed uncertainties around the feasibility study's research methods and required resources for a future pragmatic trial.

Conclusions: An implantable Doppler probe may be a beneficial adjunct for graft monitoring after kidney transplants. This feasibility study provided the necessary preliminary information and filled initial gaps in the evidence that can inform future research. The study's prespecified progression criteria were fulfilled. The study template used can be transferred to other transplant centres across the United Kingdom. A pragmatic large-scale randomised controlled trial is warranted to evaluate the effectiveness of implantable Doppler probes in clinical practice.

EP_108 EFFECTIVENESS OF IMPLANTABLE DOPPLER PROBE VERSUS STANDARD CLINICAL CARE: A SYSTEMATIC REVIEW

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Background: The implantable Doppler probe, a cutting-edge technology, can monitor the patency of vascular anastomosis, thereby facilitating early detection of vascular thrombosis critical to reducing graft loss. This systematic review aims to evaluate the effectiveness of this technology compared to standard clinical care in reducing thrombosis-related graft loss and the requirement for colour duplex ultrasonography in the first 24 hours postoperatively. The objective is to critically appraise, synthesize, and present the best available evidence in medical literature relating to the application of this technology in kidney transplantation.

Methods: A systematic search covered the Ovid Platform databases: MEDLINE, Embase, PubMed, Cochrane Database of Systematic Reviews, JBI Database of Systematic Reviews, and Implementation Reports. The selected papers' critical appraisal, data extraction and meta-analysis using a random effects model were performed using the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-SUMARI). Dichotomous outcomes were expressed as relative risk (RR) or odds ratio (OR) and displayed by a Forest plot as summary statistics of each study and the overall pooled effect estimate with confidence intervals.

Results: The search identified 43 articles. After exclusion criteria, seven (one experimental and six observational) studies were included that comprised a total participant sample of 874 adult kidney transplant recipients with and without blood flow sensing technology. The review findings' certainty of evidence level was rated as moderate. Blood flow sensing technology resulted in a 66% reduction in the risk of thrombosis-related graft loss and a 61% lower probability of requiring colour duplex ultrasonography in the first 24 hours postoperatively compared to standard clinical care.

Conclusions: The evidence from this systematic review demonstrates that blood flow sensing technology can be used as a helpful adjunct in the postoperative monitoring of kidney transplant recipients. However, given the technical limitations, it is emphasized that the signals should be interpreted alongside the traditional clinical assessment techniques.

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EP_109 EXPERIENCES OF PARTICIPATION IN A FEASIBILITY STUDY: AN EMBEDDED QUALITATIVE STUDY

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Background: Kidney transplant survival can be improved with better graft surveillance postoperatively. In the quest to explore new technologies, a trial investigating the feasibility of an Implantable Doppler probe as a blood flow monitoring device in kidney transplant patients was conducted. This qualitative study was embedded in the feasibility trial and aimed to test clinical acceptability and get suggestions for the development of the intervention. The study objectives were to explore the experiences of feasibility study participants and by doing so, identify barriers to the implementation of Implantable Doppler probes in clinical practice (i.e., stakeholder-specific, research-specific, resources, cultural, and organizational).

Methods: Semi-structured interviews containing open-ended questions were conducted with 12 feasibility study participants recruited by purposive sampling. All interviews were audio recorded with verbatim transcription. Thematic analysis of the data was performed at the latent level by an inductive approach using a 6-phase guide by Braun and Clarke in NVivo 12 software.

Results: Three key themes emerged. (1) Perceived value of the intervention in clinical practice: Due to functional limitations and lack of research, the medical professionals revealed clinical equipoise regarding the utility of Implantable Doppler probes. The device was well received by the patients. (2) Challenges and Barriers to implementation of the intervention: Device training for medical professionals and educational sessions for patients were identified. (3) Suggestions for the development of the intervention: Innovative ideas included the insertion of a display screen, a decrease in the size of the monitoring device, the introduction of disposable units to reduce overall cost, and a wireless connection to reduce signal errors and increase patient safety.

Conclusions: There is a wide acknowledgement of the clinical requirement of blood flow sensing technology in kidney transplantation. Implantable Doppler probes may be used as a beneficial adjunct in the early postoperative surveillance of kidney transplant patients. However, the device's technical limitations are the main challenges to its acceptance in clinical practice.

EP_110 HOW TO OVERCOME THE ACHILLES' HEEL OF KIDNEY EXCHANGE PROGRAMS: AN OVERVIEW OF DONOR TRAVEL VERSUS ORGAN SHIPMENT

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Background: Kidney exchange programs (KEPs) allow for optimal living donor kidney transplantation. In multicenter KEPs, either the explanted kidney is shipped or the donor travels to the transplanting center. This review describes the available data on this dilemma and formulates recommendations for clinical practice.

Methods: We systematically searched for articles describing data on organ shipment or donor travel. We analyzed and presented the data in four domains: cold ischemia time, logistics, donor/recipient perspectives and professional perspectives.

Results: Of 547 articles screened, 105 were included (see Figure 1). Our analysis yielded recommendations that are presented in Table 1.

Conclusions: The involvement of different transplant centers imposes challenges for multicenter KEPs. Health care professionals should reduce disincentives for KEP participation. Either by donor travel, organ shipment or combined policy, KEPs should guarantee medical and logistical safety, congruent care for donor and recipient and financial justice for all parties.

Table 1: Recommendations.

Organ shipment	Donor travel
Keep cold ischemia time preferably below 8 hours, given the (potentially) higher risk of delayed graft function.	Ensure a good and comprehensive expense allowance for the donor and a traveling companion.
Exercise caution in highly immunized recipients and in kidneys from older donors.	Consider preference based or travel-distance based allocation, or offer organ shipment to donors unwilling to travel.
Engage with organ procurement organizations to optimize the logistics.	Share protocols for donor evaluation and surgery between the centers.
Mandate conference calls with standardized checklists between surgeons before and after donor nephrectomy.	Review the medical history and test results from the evaluating center, and communicate the proposed match to the donor afterwards.
Guarantee operation room and staff availability, especially during out-of-office hours.	Use donor travel for specific situations, such as limited operating room availability or surgical-technical issues.
Agree with payors on the billing of donor evaluation and procurement costs.	Manage expectations of donors with regard to evaluation and treatment choice in the transplanting hospital.

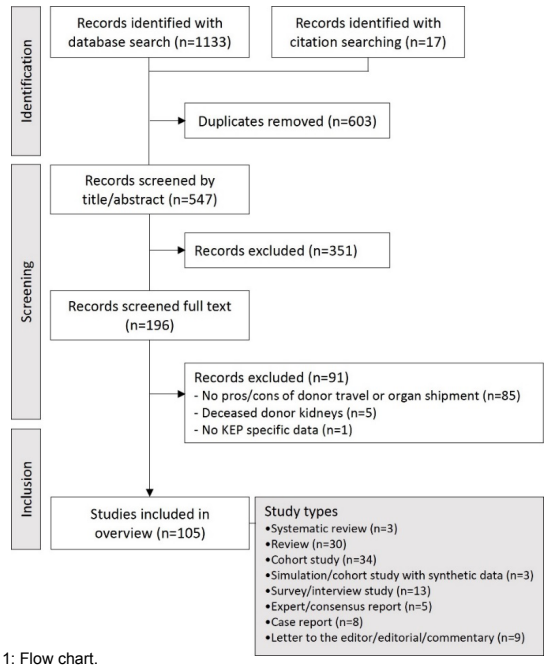

Figure 1: Flow chart.

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Current challenges in transplantation procedures

EP_111 KIDNEY TRANSPLANTATION FROM DECEASED DONORS WITH CANDIDA AURIS INFECTION

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Background: Donor-derived infections are associated with high mortality rates in organ transplant recipients. C. auris is an emerging multidrug-resistant fungal pathogen that poses significant challenges in healthcare settings, particularly among immunocompromised patients. This study presents three cases of kidney transplantation from deceased donors (DD) with C. auris infection.

Methods: Three kidney transplantations from DD with known C. auris infection were performed at the Transplant Unit of Evangelismos Hospital of Athens. A 58-year-old hypersensitized (HS) (PRA> 85%, non-DSA) male with end-stage renal disease (ESRD) received a renal allograft from a 19-year-old male brain-dead donor with a bloodstream infection caused by C. auris, isolated in two different culture specimens, two days apart. The donor received an inhibitor of β (1, 3)-D- glucan synthase antibiotic, echinocandin, for 5 days until procurement. A 58-year-old male and a 51-year-old male with ESRD received a renal allograft from a 57-year-old female brain-dead donor with C. auris isolates in urine sample collections on three consecutive days, without candidemia. The donor received echinocandin for 7 days and amphotericin B for two days until procurement. All recipients received echinocandin, starting one day before surgery, and continuing for 14 days.

Results: Delayed graft function occurred in all three patients, requiring hemodialysis within the first week after transplantation. The HS recipient experienced a mixed-type (AMR/ACR) rejection episode on the 10th day post-transplant, which resolved after treatment with PLEX, IVIG, and ATG. Lymphocele was observed in the three patients, without requiring intervention. All post-transplant cultures were negative for C. auris. There were no side effects due to antibiotic treatment. After a follow-up of 6 months, the first recipient has an eGFR of 43 mL/min/1.73m². Three months post-transplant the two recipients have eGFR 50 mL/min/1.73m² and 45 mL/min/1.73m², respectively.

Conclusions: Kidney transplantation from DD with C. auris infection appears to be successful with appropriate antifungal prophylaxis. The absence of post-transplant C. auris infection in our patients underscores the effectiveness of targeted antibiotic strategies in preventing transmission.

EP_112 POST RENAL TRANSPLANT ANEMIA: DOES ROXADUSTAT HAVE A PLACE? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Post-transplant anemia is a prevalent issue in kidney transplant recipients. Traditional erythropoiesis-stimulating agents (ESAs) face resistance and suboptimal efficacy challenges. Roxadustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), offers a novel mechanism to manage anemia, though its role in post-transplant anemia remains unexplored.

Methods: A systematic review and meta-analysis were conducted, adhering to PRISMA and MOOSE guidelines, to evaluate the efficacy and safety of roxadustat in treating anemia in kidney transplant recipients. Searches in databases including PubMed, Embase, and Cochrane identified randomized controlled trials and observational studies. Data on hemoglobin (Hb) levels, ferritin, glomerular filtration rate (GFR), and adverse events were extracted and analyzed using random-effects models to address heterogeneity.

Results: Four studies with 73 patients (pts), (49.3% male), with a mean age of 46.07±12.9 years, were included. Three pts were ESA-resistant. All pts had stable graft function at a median transplant duration of 7.8 [6,15] years and received roxadustat for 3-9 months. Roxadustat significantly increased Hb levels to a mean value of 3.29 g/dL ($p < 0.0001$), with individual study ranges from 2.02 to 4.56 g/dL. Despite the significant heterogeneity, this increase was consistent across studies ($I^2 = 83.1\%$). The follow-up period across all studies was on average 4.87±2.95 months. Lipid profiles showed mixed results; in two studies that assessed the lipid profile, no consistent reduction in markers was observed, as the results varied. Three episodes of DVT were observed in 3 pts, hypothyroidism in 4 pts, and myocardial infarction in one patient, not related to roxadustat. No significant impact on rejection episodes and graft survival was reported during the follow-up period. GFR remained stable throughout the study periods.

Conclusions: Roxadustat demonstrates potential efficacy in managing post-transplant anemia, particularly in ESA-resistant cases, with a favorable safety profile. However, the short follow-up duration and heterogeneity among studies highlight the need for further research to establish its long-term safety, efficacy, and cost-effectiveness in kidney transplant recipients.

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EP_113 KIDNEY TRANSPLANTATION IN CHILDREN WITH COMPROMISED INFERIOR VENA CAVA

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Background: Previously, such diseases as atresia or IVC obliteration in children with a body weight of up to 20 kg were considered absolute contraindications for renal transplantation in most cases. Since this creates technical difficulties during the operation and greatly increases the risk of venous thrombosis of the nephrotransplant due to insufficient venous blood outflow. Previous surgical procedures on the organs of the abdominal cavity and retroperitoneal space, prolonged presence or repeated insertion of a dialysis catheter into the lumen of iliac veins and IVC, as well as congenital abnormalities of the venous arteries can lead to absolute venous obstruction or obliteration.

Methods: During the period from September 2018 to May 2023, 5 renal transplantations were performed in children with atresia or IVC obliteration. Among them, 4 transplantations were from a deceased donor, 1 was from a live relative donor. The age of the patients was from 1 to 5 years, body weight from 7.8 kg up to 18.2 kg.

Results: The renal transplant was placed abdominally with the formation of a venous anastomosis with an accessible area of the subhepatic section of IVC. The most technically difficult were 2 cases when the transplant was presented from a deceased donor with a right kidney with an elongation of the transplant vein due to the donor's site of IVC. In two cases, a left kidney from a deceased donor was used, which did not require venous reconstruction. In one case, a left kidney transplant from a live relative donor did not require vascular reconstruction. In all the presented transplants, the immediate function of the kidney transplant was noted.

Conclusions: Despite the high surgical risks, renal transplantation to children with atresia or IVC obliteration is a life-saving operation, when it is impossible to create adequate access for renal replacement therapy. Taking into consideration high rate of surgical techniques development, the presence of compromised IVC has ceased to be a contraindication for renal transplantation in children. Comprehensive examination and careful planning of surgical intervention, as well as preventive measures during the postoperative period, reduce the risk of vascular complications, which has a positive effect on the results of renal transplantation to children.

EP_115 ONE-YEAR OUTCOMES OF HEPATIC ARTERY STENOSIS AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: Hepatic artery stenosis (HAS) after pediatric liver transplantation (pLT) can progress to hepatic artery thrombosis, biliary complications, graft failure, and death. However, there is a lack of robust studies investigating outcomes of HAS after pLT. This study aimed to determine one-year graft and patient survival rates and identify risk factors associated with adverse outcomes in patients who develop HAS after pLT.

Methods: We analyzed data from patients who developed HAS after pLT from the HEPatic Artery stenosis and Thrombosis after liver transplantation In Children (HEPATIC) registry. This registry includes data from 24 centers across 20 countries and six continents, spanning a 20-year period during which 8,469 pLTs were performed. Clinical characteristics were examined at three timeframes: pre-transplant, immediate post-transplant, and after HAS diagnosis. Risk factors for graft loss and mortality after HAS were identified using multivariate Cox regression analyses, with model assumptions verified using Schoenfeld residuals.

Results: HAS was reported in 119 patients (estimated 1.4%; 51% female; median age 4.2 years). The overall one-year graft and patient survival rates after HAS diagnosis were 93% (95% CI: 89–98) and 97% (95% CI: 93–100), respectively. Multivariate Cox regression analysis identified dialysis requirement at HAS diagnosis as the sole independent risk factor for both one-year graft loss ($p < 0.01$) and mortality ($p = 0.01$).

Conclusions: HAS after pLT is associated with favorable one-year outcomes, with risk factors for unfavorable outcomes generally lacking. In patients requiring dialysis at the time of HAS diagnosis, other factors are more likely to contribute to multi-organ failure and poor outcomes. Future studies are needed to identify best clinical practice and treatment strategies for pediatric patients with HAS.

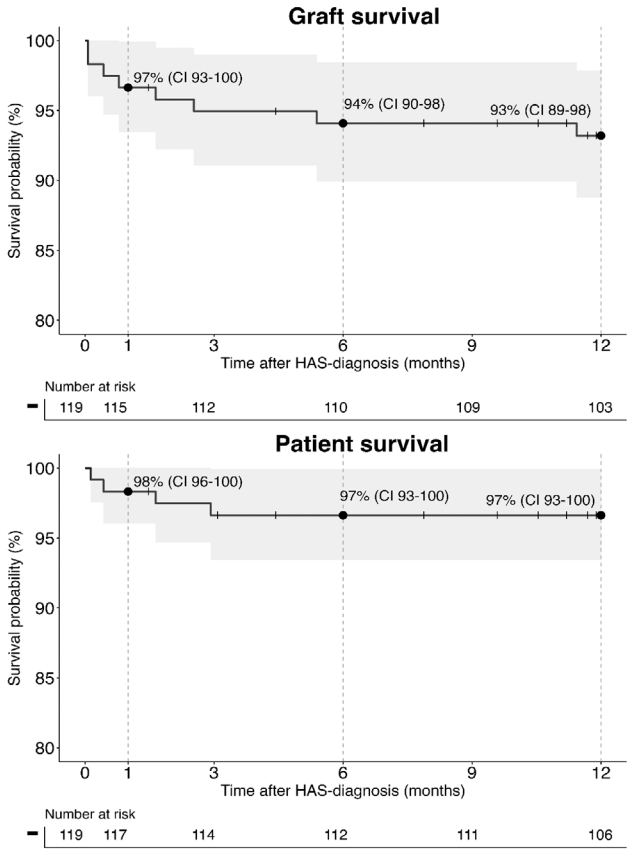

Figure 1. Kaplan-Meier curves displaying the overall graft survival and patient survival within the first year after diagnosis of HAT. Censored cases are depicted with a vertical line, the 95% confidence interval is displayed in grey. Abbreviations – CI, 95% confidence interval; HAS, hepatic artery stenosis.

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EP_116 PULMONARY FUNCTION TESTS AS PREDICTORS OF SURVIVAL AND OUTCOMES AFTER LIVER TRANSPLANTATION

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Background: Pulmonary function tests (PFTs) may be performed ahead of listing for liver transplantation (LT). We aimed to establish whether pre-transplant PFTs correlated with post-transplant mortality.

Methods: A retrospective single-centre study of patients undergoing elective first-graft liver only transplant between 2014 and 2023 was performed. Patients were excluded if PFTs were not performed or available. The primary outcome assessed was all-cause mortality post-LT, and association with PFT parameters (single-breath diffusing capacity of the lung (DLCO SB), forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC and maximum vital capacity (VC max)) using univariable Cox regression. Secondary outcomes included a Spearman's correlation analysis (rho) for correlation of PFTs with ICU length of stay (LOS), advanced respiratory and cardiovascular support days and operation length.

Results: During the study period, 1088 patients underwent LT; 781 met inclusion criteria. 33.2% of patients were female, median age at transplant was 58 years (IQR 50-63 years). 48.9% of patients had never smoked, 40.7% were former smokers, and 10.4% were currently smoking. 13.6% of patients died within the study period, with a median follow-up of 4.6 years (IQR 2.18-6.76). An obstructive pattern of PFTs (FEV1/FVC < 0.7) was seen in 22.4% of patients. **Table 1** shows factors of DLCO SB and FEV1 were shown to be significantly associated with improved post-transplant survival. **Figure 1** shows a difference in survival for those with a below median and above median FEV1. A secondary analysis of patients transplanted between 2019 and 2023 (where PFTs were available for n=263) showed no significant correlation between PFTs, ICU LOS, advanced support days or operation length.

Conclusion: A higher DLCO SB and FEV1 were associated with reduced post-transplant mortality. No association of PFTs and ICU LOS, advanced support days or operation length was found.

Parameter	Median	IQR	HR	95% CI	p
Obstructive	N/A	N/A	1.42	0.92-2.17	0.108
DLCO SB	**6.00 L**	**4.83-7.52 L**	**0.90**	**0.81-1.00**	**0.046**
FEV1	**2.79 L**	**2.24-3.40 L**	**0.70**	**0.55-0.90**	**0.005**
FVC	3.75 L	3.01-4.55 L	0.83	0.70-1.00	0.052
FEV1/FVC	0.76	0.71-0.81	0.13	0.02-1.02	0.052
VC max	3.75 L	3.01-4.55 L	0.87	0.72-1.04	0.124

Table 1: Univariable Cox regression of PFT variables and post-transplant mortality

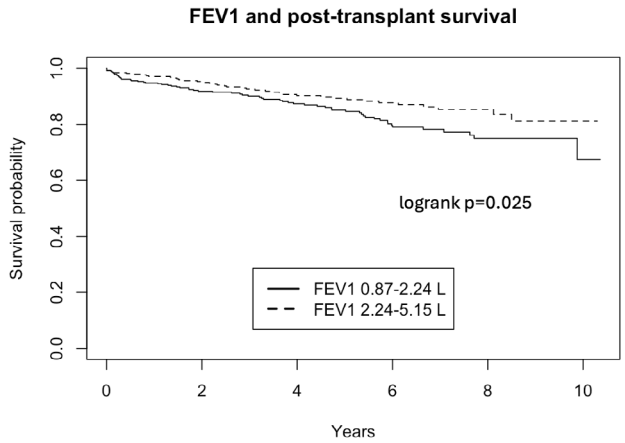

Figure 1:

EP_117 DEVELOPMENT OF ASSESSMENT AND A CONSENTING PROCESS FOR ISLET AUTOTRANSPLANTATION

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Background: Informed consent is crucial in complex surgical procedures such as Total Pancreatectomy with Islet Autotransplantation (TPIAT), a treatment primarily for patients with chronic pancreatitis (CP), recurrent acute pancreatitis and increasingly patients with gene mutations. Given the potential for significant morbidity and mortality, a robust and thorough assessment and consent process is essential to ensure patients are well-informed and appropriately selected.

Methods: This study outlines the assessment and consenting process for TPIAT developed over 30 years by the Leicester Hepatopancreaticobiliary (HPB) Unit. The process is coordinated by a TPIAT Clinical Nurse Specialist (CNS) and involves a multidisciplinary team (MDT) comprising surgeons, gastroenterologists, diabetologists, pain specialists, and psychologists.

Results: Patients referred for TPIAT undergo a multi-step evaluation, beginning with an initial consultation to determine eligibility. Cases are reviewed by the MDT, ensuring a collaborative approach to patient selection. Key features include the ability of any team member to veto a case. The CNS serves as a central contact, providing continuity of care and support. The iterative consent process, involving repeated consultations, ensures patients grasp the procedure's complexities and long-term implications.

Conclusions: The Leicester HPB Unit's model for TPIAT assessment and consent demonstrates the effectiveness of a comprehensive, patient-centered approach. This model may serve as a template for other centres, highlighting the need for continuous improvement and adaptation of modern technologies to enhance patient care.

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Current challenges in transplantation procedures

EP_118 DUAL KIDNEY TRANSPLANTS: WHAT IS THE OPTIMAL TECHNIQUE?

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Background: Although transplantation of dual marginal kidneys dated back to1996, the procedures are still debated. To facilitate the surgical decision, the techniques are reviewed and discussed.

Methods: The sequential approach consists of transplanting one kidney after the other, via one long iliac incision, or two standard iliac incisions. In both cases, the vessels are anastomosed separately to the iliac vessels and the ureters implanted separately, or through a common tunnel. There are 3 simultaneous techniques. 1- the 2 aortic patches are sutured together as a common patch which is then attached to the recipient iliac artery. 2- The renal arteries are connected to a Y iliac artery which serves as inflow to both kidneys. The veins are connected E-S to make a common outflow prior to anastomosis to the iliac vein. 3- The kidneys are reconstructed en bloc by anastomosing the patch bearing the left renal vessels to the aorta bearing the right kidney making the distal aorta the common inflow . The left renal vein is used to cap the proximal vena cava which becomes the venous outflow. Transplantation is performed by connecting both distal aorta and vena cava, respectively, to the iliac artery and vein.

Results: The sequential approach requires multiple vascular anastomoses with increased risks of thrombosis, and requires significantly longer operative time than the other. The tip of the long proximal ureter can be ischemic or compressed by the distal kidney. The simultaneous technique requires one hour of back table reconstruction, but shortens the operation by half, reducing anesthesia time and morbidity for the elderly recipients. Thrombosis has not been observed.

Conclusions: 1 - The sequential technique is obsolete. 2 - The simultaneous techniques are elegant, versatile and suit the multiple vessels organs. 3 - They preserve the other iliac fossa for future transplant. 4 - During procurement, the kidneys are best left en bloc with the intact aorta and vena cava, and the iliac Y graft provided. 5 - The surgeon should familiarize with the different techniques when dealing with the dual transplant offer.

EP_119 MEDIAN ARCUATE LIGAMENT SYNDROME-ASSOCIATED HEPATIC ARTERY THROMBOSIS AFTER LDLT

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Background: Median arcuate ligament syndrome (MALS) can induce hepatic artery thrombosis (HAT) after liver transplantation (LT). The authors experienced a case of MALS associated HAT after living donor liver transplantation (LDLT) that was successfully treated by interventional thrombectomy, balloon dilatation of anastomosis and stent placement at celiac artery.

Methods: A 60 years old male patient underwent LDLT with a modified right liver graft for hepatocellular carcinoma of 5.5cm. Donor was his daughter. GRWR was 1.0. Donor right hepatic artery was 2 mm in diameter and was anastomosed to recipient right anterior hepatic artery (2 mm in diameter) under microscope. Immediate postop AST/ALT was 220/241 IU/L. On Doppler US at postoperative 1 day, hepatic arterial signal could be detected with RI > 0.5. But AST/ALT level rose to 772/844 IU/L next day. On dynamic CT intrahepatic arterial blood flow was visible but faint. HAT was suspected. And MALS was identified, which was not noticed before surgery. Angiography was done. The flow of the gastroduodenal artery (GDA) – common hepatic artery (CHA) is reversed, filling the celiac trunk and splenic artery from the GDA, indicating an obstruction of the celiac trunk orifice. After selecting the obstruction site of the celiac trunk with a guide wire-catheter, the obstruction site was dilated with a 6 mm diameter balloon, after which a 6Fr metallic stent was installed. Thrombotic occlusion of common hepatic artery to the level of the arterial anastomosis was identified. After inducing thrombolysis by infusing 1 mg of tPA with a microcatheter, residual adherent thrombi were removed with a balloon (diameter 2 mm) and suction. Subsequently, angioplasty was performed on the hepatic artery anastomosis stricture site with a balloon (diameter 2 mm).

Results: Finally, the angiogram showed that the HA anastomosis was patent and not stenotic. Hepatic arterial blood flow to the liver graft was significantly improved. On CT scan checked 2 days later, hepatic arterial blood flow was well maintained with good hepatic parenchymal enhancement. AST/ALT level was 90/215 IU/L.

Conclusions: Early identification of MALS-associated HAT after LDLT could be treated successfully by interventional thrombectomy, balloon dilatation of artery anastomosis site and stent placement at celiac artery.

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EP_120 INCIDENCE AND RISKS FACTORS OF BRONCHIAL STENOSIS AFTER LUNG TRANSPLANT; A RETROSPECTIVE ANALYSIS

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Background: Bronchial stenosis following lung transplant is well-documented complications. A retrospective cohort study at Harefield Hospital was conducted to evaluate potential predictors of bronchial stenosis in lung transplant recipients.

Methods: This study involved data from 173 consecutive lung transplant patients operated between 2015 and 2022 at Harefield Hospital, of which 28 patients developed bronchial stenosis postoperatively. Data including age, sex, donor-recipient height mismatch, type of donation (DCD vs. DBD), ischemic time, postoperative ECMO use, primary graft dysfunction grade 3 (PGD3), use of sirolimus, and presence of fungal infection were analysed. Multivariate logistic regression analysis was performed on univariate predictors for bronchial stenosis with an entry criterion of $p<0.05$.

Results: Of the 173 patients, 28 (16.1%) developed bronchial stenosis. There were no significant differences between the two groups regarding age, sex, diagnosis, donor-recipient height mismatch, postoperative ECMO use, and PGD3. Presence of fungal infection and use of sirolimus were strongly associated with bronchial stenosis ($p<0.01$ and $p=0.04$, respectively). Multivariate analysis identified fungal infection and use of sirolimus as the only independent predictors of bronchial stenosis. Whereas cold ischemic time was significantly higher ($p=0.04$) in the control group, the impact of ischemic time on bronchial stenosis was not confirmed in the multivariate analysis ($p=0.135$). Association of bronchial stenosis with DCD donors was seen on univariate analysis, but not seen on logistic regression. There was no difference in 5-year mortality in both groups.

Conclusions: Short-term postoperative complications, such as PGD3 and use of ECMO, may not be associated with bronchial stenosis that remains a detrimental long-term complication. Prevention, aggressive treatment of fungal infection and avoidance of sirolimus may be key factors for prevention of bronchial stenosis.

EP_121 POSITIVE OUTCOME OF LDKT WITHOUT SYSTEMIC HEPARINIZATION DURING DONOR NEPHRECTOMY IN A SINGLE CENTER

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[1]Cha Bundang Medical Center; Hepatobiliary and Pancreas; Transplantation, [2]Cha Bundang Medical Center; Hepatobiliary, Pancreas and Transplantation, [3]Cha Bundang Medical Center; Hepatobiliary, Pancreas and Trasnplantation

Background: Heparin is commonly used during donor nephrectomy to prevent microthrombi formation and improve graft function, but it may pose hemorrhagic risks to the donor. We share our experience of performing living donor kidney transplantation without administering heparin to the donor over the past three years.

Methods: We retrospectively reviewed 22 cases of living donor kidney transplantation performed from January 2019 to April 2023.

Results: In the donor group, 11 patients were male (50%) and 11 were female (50%), with a median age of 52 years (range 23–69). The median operation time was 157 minutes (range 110–195), and median blood loss was 100cc (range 10–550), with no transfusions. The median hospital stay was 8 days (range 7–9). Median hemoglobin levels on postoperative day (POD) 0 and POD 1 were 13.6g/dl (range 11–16.7) and 11.6g/dl (range 11–15.4), respectively. Median creatinine preoperatively was 0.73mg/dl (range 0.5–0.95), and 0.88mg/dl (range 0.44–1.8) on POD 0. Median BUN preoperatively was 12.8mg/dl (range 6.7–18.4), and 12mg/dl (range 7.1–16.3) on POD 0. Median eGFR preoperatively was 98.95 ml/min/1.73m² (range 64.4–116.4) and 79.85 ml/min/1.73m² (range 67–125.7) on POD 0. No major complications occurred in the donor group. In the recipient group, 14 were male (64%) and 8 were female (36%), with a median age of 51.5 years (range 19–61). The median operation time was 455 minutes (range 225–370), and median blood loss was 200cc (range 0–3400). The median hospital stay was 14 days (range 9–28), with no major complications. Median urine output on POD 0 and POD 1 was 6220cc (range 2235–16660) and 4334cc (range 1770–6500), respectively. The median postoperative resistive index was 0.71 (range 0.57–1). Five cases of rejection occurred (2 acute, 3 chronic).

Conclusions: Our experience shows that omitting heparin during donor nephrectomy did not lead to graft loss or hemorrhagic complications. This approach is feasible and safe, with no negative impact on the donor or recipient outcomes.

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Current challenges in transplantation procedures

EP_122 WHEN SHORT RENAL VEIN OF KIDNEY GRAFT: USING AUTOLOGOUS PERITONEUM FOR VEIN EXTENSION

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[1]Cha Bundang Medical Center; Hepatobiliary and Pancreas; Transplantation, [2]Cha Bundang Medical Center; Hepatobiliary, Pancreas and Transplantation, [3]Cha Bundang Medical Center; Hepatobiliary, Pancreas and Trasnplantation

Background: In living donor kidney transplantation (LDKT), the decision of which kidney to use for the graft is typically based on the donor's kidney function. The left kidney is usually preferred due to its longer vein, but in some cases, the right kidney may be selected for the donor's safety. At our institution, we have employed a parietal peritoneal patch to extend the short renal vein of the right kidney graft.

Methods: The donor had normally functioning kidneys, with the left kidney contributing 56.1% of overall function. Therefore, the right kidney was chosen for transplantation, which had one renal artery (5mm) and two short renal veins (10mm and 8mm). During the dissection of the recipient's left iliac fossa, a peritoneal sample was taken. In bench surgery, we combined the two renal veins into one, reshaped the native peritoneum into a tubular structure that matched the vein's width, and lengthened the vein using the peritoneal patch.

Results: A living donor kidney transplant was performed between two siblings. The donor, a healthy 46-year-old female, donated to her 40-year-old brother, who had end-stage renal disease (ESRD) due to minimal change disease (MCD) and hypertension. Immunological testing confirmed ABO compatibility, a full human leukocyte antigen (HLA) match, and negative crossmatch results. The graft weighed 182g, the operation time was 375 minutes, and estimated blood loss was 230ml. The recipient was discharged on postoperative day 11 without complications and maintained good graft function.

Conclusions: The use of autologous parietal peritoneum for venous reconstruction in living donor kidney transplantation is a feasible and effective approach.

EP_123 BEST PRACTICES IN KIDNEY DONATION AND TRANSPLANTATION

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[1]Brown University, [2]Maidstone and Tunbridge Wells Hospital, [3]Paris Transplant Group; Paris Institute for Transplantation and Organ Regeneration (Pitor), Paris, France, [4]Paris Institute for Transplantation & Organ Regeneration; Inserm U970, [5]Paris Institute for Transplantation and Organ Regeneration, [6]Universitaetsklinikum Muenster; Department of General, Visceral, and Transplant Surgery, [7]University Hospital Heidelber; General-, Visceral- and Transplant Surgery, [8]Fondazione Policlinico Universitario Agostino Gemelli Irccs; Renal Transplant Unit, [9]Fondazione Policlinico A. Gemelli; Uosa - Trapianto Rene, [10]-, [11]Imperial College London; School of Medicine, [12]London School of Economics; London School of Economics and Political Science; Department of Health Policy, [13]Imperial College; Transplant Surgery; The West London Renal and Transplant Centre

Background: Kidney donation and transplantation are critical interventions for managing end-stage renal disease. This study explored current clinical practices and how they align with best-practice recommendations.

Methods: A survey tool was designed and validated to collect data on kidney donation and transplantation processes and outcomes. Survey respondents included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: Among 253 survey participants, 46% rated referral systems for potential donors as very effective. Protocols for family consent, donor monitoring, optimization, and organ procurement timing were identified as 'very' to 'moderately' adequate by 83%. Communication training and strategies were identified as areas of improvement, particularly regarding approaching potential deceased donors' families as well as lack of transparency and delays in evaluation. Regional variation in the promotion of living donation was also identified both in the survey responses and in focus groups.

Conclusions: While protocols and referral systems are generally adequate, gaps are evident in communication, living donor promotion, and regional consistency. Both data sets underscore the need for transparent education and standardisation of communication training, which could improve transparency and reduce delays in donor evaluations across all institutions.

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EP_124 BEST PRACTICES IN TRANSPLANT RECIPIENT CARE

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Background: Transplant recipient care is an inherently complex and encompasses post-operative care needs, long-term follow-up, and psychological support. This study examined the differences between current practices and existing guideline recommendations aiming to identify gaps and opportunities for further improvement of transplant recipient care.

Methods: A survey tool was designed and validated to collect data on transplantation processes and recipients' outcomes. Survey respondents included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: Among 253 survey participants, nephrologists were identified as the primary healthcare providers for both short- and long-term care of transplant recipients. While post-operative rehabilitation timing was rated as 'somewhat' or 'very' adequate (61%), follow-up visit frequency decreases significantly after the first three months. Both survey and focus groups data emphasized critical gaps in psychological counselling, patient education, and medication adherence monitoring, underscoring the importance of integrating these aspects into routine care. Support from patient associations was moderate to very effective (71%). Specialist nurses were recognized as crucial for effective follow-up.

Conclusions: Strengthening post-transplant care requires standardized protocols for community care transitions, including referral pathways, enhanced psychological counselling, and consistent patient education. Expanding the role of specialist nurses and patient associations could further improve follow-up care and align practices with best-practice recommendations.

EP_125 THE PERFORMANCE OF SMARTPILOT VIEW VERSUS BISPECTRAL INDEX APPROACH DURING RENAL TRANSPLANTATION

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Background: Renal transplantation is the definitive treatment for end-stage renal disease. Optimal anesthetic depth is crucial to ensure hemodynamic stability and minimize the risk of graft dysfunction.[1-2] The SmartPilot® View system (SPV®) offers a promising assessment of anesthetic depth by predicting the Noxious Stimulation Response Index (NSRI).[3-4] This provides a more comprehensive monitoring modality than the commonly utilized Bispectral Index™ (BIS).[5] In contrast to BIS™, the NSRI accounts for the interaction of hypnotic-opioid agents. Research on this topic in transplant anesthesia is limited.[4,6] This study evaluated the impact of using SPV® alongside BIS™ monitoring versus BIS™ alone for assessing anesthetic depth, hemodynamic control, and recovery outcome in renal transplant patients.

Methods: A prospective, single-center, non-randomized, observational study involving 102 adult patients who underwent living renal transplantation with general anesthesia using sevoflurane between August to November 2024. Participants were conveniently assigned to either SPV+BIS or BIS-only monitoring groups. Standardized protocols ensured uniformity in anesthetic administration. Key outcomes included intraoperative hemodynamic parameters and recovery outcomes. Anesthetic depth based on BIS values, sevoflurane requirement, and other perioperative data were recorded as secondary outcomes. Statistical significance was set at $p < 0.05$.

Results: Patients in the SPV+BIS group exhibited significantly reduced sevoflurane requirement (47.68 ? 13.51 ml vs. 58.05 ? 15.56 ml; p<0.01) and lower BIS values during extubation (41.55 ? 10.73 vs. 47.94 ? 9.73; p=0.001), as shown in Table 1. A marked improvement in hemodynamic stability was observed during reperfusion phase (see Figure 1). However, there were no significant differences noted in recovery outcomes.

Conclusion: The SmartPilot® View (SPV®) system may offer advantages in anesthetic management during renal transplantation by reducing sevoflurane requirement and promoting hemodynamic stability. This study highlights the need for further randomized trials to explore their impact on long-term outcomes.

Table I. Perioperative data and recovery parameters. *Data presented as mean (standard deviation) and frequency (%).*

VARIABLES	SPV+BIS (n=51)	BIS (n=51)	P-value
Baseline Hemodynamic parameters			
Mean Arterial pressure in mmHg (MAP)	110.78 ± 12.11	108 ± 10.29	0.105[1]
Systolic Blood Pressure in mmHg (SBP)	146.24 ± 15.06	144.84 ± 15.4	0.322
Diastolic Blood Pressure in mmHg (DBP)	92 ± 12.16	89.88 ± 9.72	0.074
Heart Rate in bpm, (HR)	86.08 ± 13.78	84.02 ± 12.78	0.219
Intraoperative MAP in mmHg			
Intubation	109.1 ± 21.78	102.96 ± 25.75	0.097[1]
5 minutes post-intubation	98.8 ± 24.31	96.25 ± 20.3	0.283
First surgical incision	96.02 ± 20.63	94.86 ± 20.56	0.219
15 minutes after incision	102.63 ± 16.5	100 ± 19.55	0.232
Reperfusion	98.67 ± 13.58	99.37 ± 15.33	0.378
15 minutes after reperfusion	101.76 ± 11.75	96.88 ± 15.61	0.037**
30 minutes after reperfusion	102.8 ± 13.02	97.69 ± 14.84	0.030**
10 minutes to skin closure	95.49 ± 11.64	96.29 ± 11.38	0.362
5 minutes to skin closure	95.14 ± 12.33	97.18 ± 13.96	0.213
Extubation	109.49 ± 13.08	109.65 ± 17.39	0.480
Intraoperative SBP in mmHg			
Intubation	140.59 ± 33.27	136.8 ± 30.88	0.276[1]
5 minutes post-intubation	133.49 ± 26.42	128.22 ± 25.17	0.151
First surgical incision	130.67 ± 24.19	126 ± 24.52	0.167
15 minutes after incision	136.51 ± 18.1	134.88 ± 24.36	0.351
Reperfusion	137.14 ± 16.43	139.16 ± 19.38	0.300
15 minutes after reperfusion	142.65 ± 17.5	138.63 ± 19.26	0.135
30 minutes after reperfusion	141.96 ± 16.88	138.57 ± 18.76	0.169
10 minutes to skin closure	132.73 ± 14.37	134 ± 13.91	0.025
5 minutes to skin closure	132.69 ± 15.42	135.02 ± 13.76	0.210
Extubation	148.33 ± 17.17	150.9 ± 18.47	0.233
Intraoperative DBP in mmHg			
Intubation	92.02 ± 19.7	86.37 ± 24.15	0.098[1]
5 minutes post-intubation	83.43 ± 19.28	80.22 ± 18.99	0.198
First surgical incision	81.67 ± 19.64	79.35 ± 19.56	0.276
15 minutes after incision	85.71 ± 17.12	82.59 ± 18.44	0.188
Reperfusion	79.29 ± 13.06	79.69 ± 14.65	0.443
15 minutes after reperfusion	81.43 ± 11.25	76.37 ± 15.74	0.031**
30 minutes after reperfusion	83.14 ± 13.14	77.39 ± 14.26	0.017**
10 minutes to skin closure	76.64 ± 11.58	77.71 ± 12.59	0.359
5 minutes to skin closure	76.37 ± 12.08	77.31 ± 13.76	0.357
Extubation	90.08 ± 14.3	90.27 ± 19.93	0.477
Intraoperative HR in bpm			
Intubation	95.96 ± 17.29	94.31 ± 17.18	0.315[1]
5 minutes post-intubation	93.47 ± 18.11	94 ± 19.26	0.443
First surgical incision	91.71 ± 17.22	89.39 ± 19.64	0.359
15 minutes after incision	83.78 ± 15.78	85.63 ± 15.51	0.276
Reperfusion	88.08 ± 16.25	86.25 ± 15.42	0.281
15 minutes after reperfusion	91 ± 15.58	91.6 ± 15.24	0.396
30 minutes after reperfusion	87.75 ± 12.93	88.22 ± 12.28	0.425
10 minutes to skin closure	85.22 ± 13.18	89.53 ± 14.36	0.057**
5 minutes to skin closure	86.53 ± 12.98	90.75 ± 14.68	0.062*
Extubation	93.45 ± 12.97	94.43 ± 13.78	0.356
Bispectral index value (BIS)	36.80 ± 4.53	40.55 ± 4.43	0.0512*
Intubation	95.57 ± 3.87	95.35 ± 4.09	0.399
5 minutes post-intubation	42.57 ± 14.95	39.25 ± 11.8	0.107
First surgical incision	35.84 ± 8.29	36.33 ± 9.06	0.387
15 minutes after incision	37.82 ± 9.14	37.04 ± 7.88	0.320
Reperfusion	37.39 ± 6.67	38.46 ± 6.4	0.233
15 minutes after reperfusion	38.98 ± 7.09	40.35 ± 6.93	0.161
30 minutes after reperfusion	40.12 ± 7.82	41.25 ± 6.95	0.219
10 minutes to skin closure	39.16 ± 6.69	41.22 ± 6.92	0.063*
5 minutes to skin closure	39.39 ± 7.73	43.35 ± 8.92	0.008**
Extubating	41.55 ± 10.73	47.94 ± 9.73	0.001**

VARIABLES	SPV+BIS (n=51)	BIS (n=51)	P-value
Noxious Stimulation Response Index (NSRI)			
Intubation	100 ± 0	-	-
5 minutes post-intubation	32.9 ± 20.56	-	-
First surgical incision	32 ± 18.37	-	-
15 minutes after incision	38.51 ± 13.48	-	-
Reperfusion	39.82 ± 13.11	-	-
15 minutes after reperfusion	46.96 ± 11.48	-	-
30 minutes after reperfusion	45.1 ± 11.78	-	-
10 minutes to skin closure	46.29 ± 11.15	-	-
5 minutes to skin closure	51.04 ± 13.35	-	-
Extubating	56.84 ± 13.67	-	-
Sevoflurane Minimum Alveolar Concentration (MAC)	0.8242 ± 0.089	0.8459 ± 0.096	0.1864
Minimum Sevoflurane MAC	0.73 ± 0.09	0.76 ± 0.09	0.077*
Maximum Sevoflurane MAC	0.93 ± 0.09	0.96 ± 0.09	0.0027*
Sevoflurane consumption (ml)	47.68 ± 13.51	58.05 ± 15.56	<0.01*
Total Propofol Dose (mg)	133.92 ± 43.41	138.16 ± 51.34	0.435
Recovery Outcomes			
Extubation time (minutes)	6.65 ± 3.41	6.35 ± 3.41	0.331
Time of eye opening (minutes)	12.43 ± 5.07	12.78 ± 5.07	0.303
Recovery time (minutes)	8.43 ± 3.91	7.2 ± 3.91	0.055*
Duration in post-anesthesia care unit (minutes)	221.24 ± 76.91	217.25 ± 76.91	0.397
RASS score at recovery room			
+2	0(0%)	1(2%)	0.157
+1	3(6%)	3(6%)	0.323
0	39(76%)	37(73%)	0.433
-1	3(6%)	2(4%)	0.421
-2	7(14%)	8(15%)	0.269
Perioperative data			
Anesthesia duration (minutes)	260.9 ± 64.93	255.16 ± 58.36	0.319
Surgery duration (minutes)	217.24 ± 65.68	219.16 ± 56.88	0.437
Total intraoperative Fluid (ml)	1771.47 ± 414.8	1711.37 ± 419	0.233
Estimated blood loss (ml)	300 ± 149.87	265.82 ± 146.51	0.144
Participants receiving vasopressor	0.92 ± 0.27	0.84 ± 0.37	0.110
Yes	47(92%)	43(84%)	0.109
No	4(8%)	8(16%)	0.109
Vasopressor dosage			
Dopamine dose mcg/kg/min, minimum	0.2 ± 0.69	0.08 ± 0.39	0.146
Dopamine dose mcg/kg/min, maximum	0.45 ± 1.6	0.2 ± 1	0.168
Norepinephrine dose mcg/kg/min, minimum	0.02 ± 0.03	0.02 ± 0.02	0.226
Norepinephrine dose mcg/kg/min, maximum	0.07 ± 0.1	0.1 ± 0.11	0.094*
Dobutamine dose mcg/kg/min, minimum	0 ± 0	0.14 ± 0.75	0.065*
Dobutamine dose mcg/kg/min, maximum	0 ± 0	0.31 ± 1.76	0.102
Ephedrine total dose in mg	12.35 ± 5.76	11.67 ± 10.57	0.367

[1]Independent samples t-test; [2]Chi-square test; *Significant at 10%; **Significant at 5%.

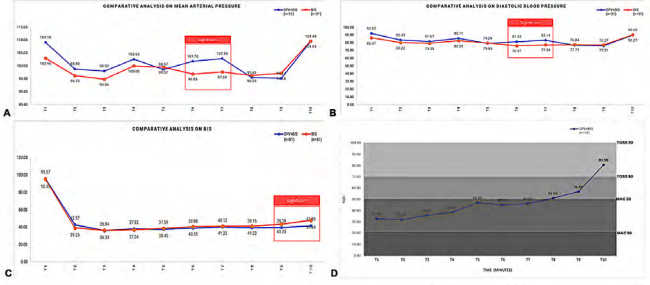

Figure 1. Intraoperative hemodynamic parameters and anesthetic depth plotted against specified time points. (A) Mean arterial pressure. (B) Diastolic Blood pressure. (C) Bispectral index value or BIS. (D) Noxious stimulation response index or NSRI level during the maintenance phase of anesthesia. T1–T2, intubation and five minutes post-intubation; T3, first surgical incision; T4, fifteen minutes after incision; T5, reperfusion; T6 – T7, fifteen minutes and thirty minutes after reperfusion; T8–T9, ten and five minutes to skin closure; T10 extubation; TOSS 50, Tolerance of Shake and Shout 50; TOSS 90, Tolerance of Shake and Shout 90; MAC 50, Minimum alveolar concentration 50; MAC 90, Minimum alveolar concentration 90.

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Current challenges in transplantation procedures

EP_126 KIDNEY TRANSPLANTATION IN CHILDREN WITH BARDET BIEDL SYNDROME A SURGICAL CHALLENGE

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Background: Bardet biedl syndrome (BBS) is a rare autosomal recessive multi-system disorder caused by defects in genes encoding for proteins that localize to the primary cilium/basal body complex. The clinical phenotype is extremely variable and includes: obesity, renal disease, bladder dysfunction, hypogonadism, retinal dystrophy, polydactyly and developmental delay.The prevalence of renal disease in BBS has been estimated to be as high as 53-82% and around 8% will deteriorate to ESRD, most of them in early childhood. Given their comorbidities: obesity, genitourinary abnormalities and type 2 diabetes, kidney transplantation (Ktx) poses a higher risk as well as a surgical challenge. We will describe our single center experience with kidney transplantations of a cohort of children with BBS.

Methods: A retrospective cohort study including all pediatric BBS transplants performed during the years 2011-2024. In Schneider Children Medical Center. Data was abstracted from the medical charts and included: Demographics, comorbidities, BMI, urogenital defects, diabetes and complications following Ktx and graft and patient survival.

Results: During the study period 8 kidneys were transplanted in 5 children. The mean age at transplantation was 13.1 ±3.9 years. Mean BMI was 27.2 ± 6.9 kg/m^2. 7 transplantations were from a deceased donor and one from a non-related living donor. Post-surgical complications included- recurrent UTI (4 children), late rejection in 2 children and one patient with obstruction of the ureter and re operation (uretero- pelvic anastomosis).Among the 5 patients 3 received a second transplant secondary to graft loss (at 2,5,10 yrs.) All the 3-second transplants are still functioning after 2, 2 and 5 years follow up respectively. Average GFR of functioning grafts was 66 ±34 ml/min/1.73m2. Patient survival was 100%.

Conclusion: kidney transplantation in patients with BBS is a complicated but doable procedure. Few cases of these patients are reported and this is a relatively large cohort of these rare patients. Given the risks associated with transplant and their comorbidities it is important to perform a comprehensive pre-transplant evaluation that includes: urogenital assessment and intervention weight management and treatment psychosocial assessment to gain a better long term outcome.

EP_127 PORTAL MODULATION IN ADULT LIVING DONOR LIVER TRANSPLANT: FOR ACHIEVING BETTER OUTCOMES

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Background: Living donor liver transplantation (LDLT) was firstly introduced as an alternative to deceased donor liver transplantation. In adult LDLT (ALDLT), it is inevitable that the graft would be smaller than the native liver. However, if the graft function is not sufficient to satisfy the metabolic needs of the recipient, small-for-size syndrome (SFSS) can be encountered. Elevated portal vein pressure (PVP) is believed to be a main contributor in the pathophysiology of the SFSS. Therefore, we analyzed the potential impact of PVP on the outcomes in ALDLT in this study.

Methods: Data was gathered prospectively for patients who underwent ALDLT with PVP monitoring during the period between June 30th, 2018, and June 30th, 2020, in Kyoto University Hospital. As a result, 36 patients were enrolled in our study. Modulation was done by splenectomy when graft weight to recipient spleen volume ratio was ≤ 0.7 gm/ml or PVP after graft reperfusion was > 15 mmHg when graft was obtained from older or ABO incompatible donors.

Results: With this modulation strategy, SFSS was not encountered, overall survival was 100%. High final PVP tended to be encountered in smaller graft weight, lower donor BMI and left lobe grafts. GSVR <0.64 gm/ml was an independent risk factor for high PVP after graft reperfusion. Splenectomy was safely done with no difference in complications, postoperative platelet count was higher and daily ascites amount was lower in patients who underwent splenectomy

Conclusions: PVP monitoring and modulation is a necessity for good outcomes after ALDLT

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EP_128 MANAGEMENT OF BILIARY STRICTURE AFTER ADULT LIVING LIVER TRANSPLANTATION

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Background: Biliary stricture was a common problem after living donor liver transplantation (LDLT), it represents an independent risk factor for post-transplant morbidity and mortality; so The aim to study the management options for post-transplant biliary strictures after LDLT for adult recipients and its efect on outcome.

Methods: This cohort study was conducted on adult recipients of LDLT who suffered post operative biliary stricture from January 2015 to end of October 2023. Including 67 adult patients Recipients were divided into two groups based on post-operative biliary stricture: Group A, which had 29 patients without stricture, and Group B, which had 38 patients with stricture. Comparative Analysis of multiple variables was done to identify the possible risk factors for development of Biliary stricture

Results: Out of 67 adult recipients. 38 recipients had suffered post operative biliary stricture. They were as 32 (84.2%) males and 6 (15.8%) females. The mean onset of biliary stricture was (7.97 months ± 5.5). ERCP ballon dilatation and stent insertion was done in 29 patients (76.3%) and failed in 4 patients (10.5%). Percutaneous transhepatic dilatation and stenting (PTD) was done in 16 patients (42.1%) with Randeveau technique (PTD with ERCP) was done in 9 patients (23.6%).10 patients (26.3%) underwent surgical intervention (hepatico-jejunostomy) after failed endoscopic and percutaneous intervention. There was a statistically significant difference regarding; multiple bile ducts, increased donor age, the increased time of arterial anastomosis, usage of biliary stent as well as increased cold and warm ischemia time, which may be considered a potent risk factors for development of postoperative biliary complications.

Conclusions: Management of biliary stricture is multidisciplinary team approach. Most of cases were successfully treated by nonsurgical approaches via endoscopic (ERCP) or interventional radiology (PTD). When both (ERCP) and (PTD) fail, surgical intervention in the form of Reux-en-y hepaticojejunostomy was done.

EP_129 DONOR SAFETY IN LIVING DONOR LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE IN FIRST 300 CASES

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Background: Several large centers have reported outstanding outcomes of LDLT to decrease waiting list mortality. However, the safety of donor in LDLT is a curial issue.so the aim to Identify and evaluate the safety of the surgical outcome of living donor liver transplantation.

Methods: This retrospective study included 300 consecutive living liver donors who underwent operations at our center from April 2003 to November 2017. We evaluated the safety of donors with regard to three aspect complications were recorded prospectively and stratified by grade according to Clavien's Gradient system (Grade 1 to Grade

Results: They were 190 Males (63.5%) & 110 Females (36.5%) with donor's mean age 28.2±6.5 y with average of 18-45 years. Adult recipients were 242 (80%) and pediatric recipients 58 (20%). There was one donor mortality in our center and the overall morbidity rate was in 98 donors (32.5%). A total 109 complications were recorded, biliary complication in 48donors (16%), non-biliary complication occurred in 50 donors (16.5%) while in 11 donors (3.6%) had both biliary and non-biliary complications. According to Clavien grading complication system there were Grade 1 40 (36.5%), Grade III A 59 (54%), Grade III B7 (6.5%), Grade IVA 1(0.9%), Grade IVB 1(0.9%), Grade V 1(0.9%).

Conclusions: with carful donor selection and specialized patient care donor hepatectomy is a relatively safe procedure, when performed by a dedicated & well trained team. A prompt diagnosis and meticulous intervention is considered a first priority whenever a donor complication expected

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EP_130 IMPACT OF DONOR BILIARY ANATOMY ON THE OUTCOME OF ADULT LIVING LIVER TRANSPLANT RECIPIENTS

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Background: Living related liver transplant is an excellent treatment for patients with end stage liver disease. Published reports suggest that 9–38% of patients after LDLT develop biliary complications. The reported complication rate does not seem to improve significantly with experience. Despite major advances in the field of liver transplant, biliary complications remain a major source of morbidity and mortality. So The aim of this study to analyze the outcome of the variant biliary types in the donor and their impact on adult recipient's outcome

Methods: This is a longitudinal retrospective study carried out on 107 patients underwent adult LDLTs in National Liver Institute, Menoufyia university , Egypt in the period from June 2010to the end of December 2015. Donor selection was done thorough full assessment. MRCP was routinely performed to evaluate the anatomy of the donor biliary anatomy. MRCP was performed by 1.5 T magnets using breath-hold heavily T2-weighted sequences in axial and coronal thin sections, and variable-thickness rotating slabs.

Results: The patients were 97 males (90.7%) and 10 females (9.3%) and their age ranged from 22 to 63 years old. Biliary variations according to MRCP using Varotti classification into four types revealed Biliary variations in 27(25.2%) out of 107 cases 5 of them of type 2 14 of type 3a and 8 of type 3b. There were statistically significant differences between recipients who had biliary complications and those who did not have, regarding type 1 with short stump and warm ischemia time. Biliary complications occurred in 53 out of the 107 recipients included in this study (49.5%). The complications included bile leak in 40 cases (37.5%), biliary strictures in 13 cases (12.1%) and concomitant biliary stricture and bile leak in 17 cases (15.9%). Biliary complications contributed to the death of 11 recipients. They represent 10.2% of the total number of recipients and 25.58% of total number of mortalities

Conclusions: Biliary variations in the donor are associated with different incidences of biliary complications in the recipients of LDLTx. Frequency of biliary complications was higher among patients who received right lobe grafts from donors with MRCP findings of Type 1 with short stump right duct.

EP_131 HOW COULD WE HAVE ESTABLISHED THE TOTALLY LAPAROSCOPIC DONOR HEPATECTOMY IN SMALL VOLUME CENTER?

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Background: With the technical improvement and accumulation of experiences, laparoscopic donor hepatectomy for living donor liver transplantation has increased worldwide. However, it is still performed by experienced surgeons at a limited number of large-volume centers. In this study, we introduce the outcomes of donor hepatectomy and experiences of establishing laparoscopic donor hepatectomy for living donor liver transplantation programs in small-volume centers.

Methods: Between Mar 2010 and Oct 2022, 66 donor hepatectomies for LDLT were performed at our center. We had a transition period applied laparoscopy-assisted donor hepatectomy (LADH) between open donor hepatectomy (ODH) and pure laparoscopic donor hepatectomy (PLDH). Sixty-six donors were enrolled and grouped into ODH, LADH, and PLDH groups. We reviewed the medical records of these donors and compared preoperative demographics and outcomes of donor hepatectomy between each surgical procedure.

Results: ODH, LADH, and PLDH were performed for 39, 16, and 11 donors, respectively. There was no difference between groups in preoperative demographics. Open conversion during laparoscopic surgery was performed for 1 donor in each LADH and PLDH group due to bleeding. Operation time was significantly longer in PLDH than ODH and LADH (451 min vs 327 and 380 min, $p<0.001$), although there was no difference in the incidence of transfusion. The incidence of postoperative complications was similar in each group (25.6%, 18.8%, and 18.2% in ODH, LADH, and PLDH groups, $p=0.794$).

Conclusions: Pure laparoscopic donor hepatectomy can be established in small volume centers with constant efforts to overcome the learning curve and appropriate selection of indications. The transition period applying laparoscopic-assisted donor hepatectomy could be helpful for the safe establishment of pure laparoscopic donor hepatectomy in small volume centers. However, pure laparoscopic donor hepatectomy should be performed by an experienced surgeon because of the complexity of surgery and donor safety.

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EP_132 PERITONEAL ACCESS REMOVAL AFER KIDNEY TRANSPLANTATION: TIMING AND OUTCOMES

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Background: Many end-stage kidney disease patients awaiting kidney transplantation (KT), utilize peritoneal dialysis (PD) for kidney replacement therapy. After successful KT, the peritoneal dialysis catheter (PDC) used for PD is typically removed to prevent complications such as infections, mechanical issues, or discomfort. The optimal timing for PDC removal post-transplant remains a subject of debate. While early removal minimizes infection risks and facilitates healing, delayed removal allows a safety net in case of delayed graft function (DGF) or transplant failure, enabling patients to resume PD seamlessly if needed. Balancing these factors is crucial for enhancing post-transplant outcomes and ensuring patient safety. This study aims to report the time for PDC removal and outcomes.

Methods: We reviewed data from PD patients who underwent KT at HRH Princess Maha Chakri Sirindhorn Medical Center during 2018-2024. The time interval for PDC removal was calculated from the date of KT to the date of catheter removal. In addition, the study reported on the incidence of PDC-related infections and DGF requiring PD during the post-transplant period.

Results: Among the 25 patients, 14 (56%) underwent living donor KT, while 11 (44%) received deceased donor KT. The cohort comprised 16 males (64%) and 9 females (36%), with a mean (SD) age at PDC insertion of 36.38 (14.35) years and a mean age at KT of 40.09 (14.35) years. The average waiting time for KT was 3.18 (2.20) years. In all cases, the PDC was left in situ post-KT. The mean (SD) time to PDC removal after KT was 3.65 (1.19) months. Two cases (8%) developed DGF, necessitating PD post-transplant. No infections related to PD were observed while the PDC remained in situ during the post-transplant period.

Conclusion: The findings indicate that leaving the PDC in situ for an average of 3.65 months post-KT is both practical and safe. Despite the occurrence of DGF in 8% of cases, the PDC effectively supported the resumption of PD without contributing to catheter-related infections. These results suggest that this approach provides a viable strategy for balancing the risks and benefits of delayed catheter removal.

EP_133 MACHINE PERFUSION PARAMETERS TO PREDICT GRAFT INJURY OR EARLY FUNCTION AFTER LIVER TRANSPLANTATION

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Background: Pushing the limits of acceptance criteria for donor organs requires tools to support the surgeon with appropriate estimation of the quality of organ grafts.

Methods: As part of a randomized controlled trial, we evaluated a variety of biomarkers during machine perfusion as potential candidates to predict the ulterior fate of the graft after transplantation. The latter had been defined either by morphological injury to the graft as represented by maximal release of transaminases during the first 3 days after transplantation (TA max), or early functional recovery determined as maximum liver function capacity (LiMAx-test) during mechanical ventilation on postoperative day one. 20 livers from extended criteria donors, previously accepted for transplantation, were subjected to machine perfusion with MPS solution for at least 90 min. Temperature was increased from 10°C to 20°C during the first 60 min. Data were obtained after 90 min of perfusion.

Results: Significant correlations with peak transaminase levels after transplantation were found for perfusate levels of glucose, tissue inhibitor of metalloproteinase2 (TIMP2), AST, pH and lactate, with best correlations being evident for the product of TIMP2 and lactate (r^2=0.82; p<0.001). No significant correlation was found for cold ischemia time, donor risk index, perfusate flow or release of flavin mononucleotides. Most interestingly, early liver function (LiMAx) after transplantation did not significantly correlate with either of the above parameters. The best prognostic factor was again the product of TIMP2 and lactate which calculated a correlation factor of r^2=0.15 (p=0.10). Hepatic functional recovery (LiMAx values) actually did not correlate with readout of morphological reperfusion injury (peak transaminase levels) with a computed coefficient of only r^2=0.15 (n.s.).

Conclusions: Function might not easily be prognosticated by predominantly non-functional injury parameters. The development and refinement of functional investigations of the organ during machine perfusion might hence be recommended.

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Current challenges in transplantation procedures

EP_134 LIVER TRANSPLANT IN UNRESECTABLE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE BILE DUCT

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Background: Intraductal papillary mucinous neoplasm of the bile duct (IPMN-B) is one of the main precursors to biliary carcinoma (invasive carcinomas in 40-80%), with increased risk of recurrent biliary obstruction and complications such as cholangitis. Surgical resection is the mainstay of treatment. When perihiliar and intrahepatic bile duct are involved, bile and liver resection is needed, and liver transplant remains an exceptional therapy for cases not suitable for resection.

Methods: We present a case of a 73-year-old male with recurrent cholangitis. Labs significant for elevated total alkaline phosphatase. An abdominal ultrasound showed common bile duct dilation, and subsequent endoscopic ultrasound showed bile duct obstruction from an intraductal soft tissue lesion. Histologic findings were consistent with low-grade intraductal papillary neoplasm (no evidence of cholangiocarcinoma); magnetic resonance showed enhancing soft tissue extending into the right and left intrahepatic ducts (Bismuth IV). A laparotomy with hiliar lymphadenectomy, cholecystectomy and intraoperative Spyglass was performed and confirmed unresectability. Finally, the patient was listed and application for Model for End-Stage Liver Disease (MELD) exception points was requested and granted.

Results: A staged orthotopic liver transplant was performed. Due to firm adhesions to the cava vein, classic cavectomy technique with choledoco-jejunostomy is needed, preventing the usage of a piggyback; postoperative course was complicated by transitory renal failure and abdominal hypertension (temporary closure of the abdominal wall with a surgical mesh). The explant pathology demonstrated a high grade intraductal papillary mucinous neoplasm of the bile duct (high grade dysplasia), affecting bilateral secondary and tertiary bile ducts.

Conclusions: IPMN-B is a rare disease with widely varied presentations. Surgical treatment follows similar rules applicable to cholangiocarcinoma. When intrahepatic biliary system is affected and surgical resection is not possible, liver transplantation becomes a solution. We must be aware of the difficulty when previous surgery is performed; it´s advisable a laparoscopic or robotic approach to avoid adhesions that alter the anatomy in case of a subsequent liver transplant.

EP_135 AGE AS A LIMITING FACTOR IN LUNG RETRASPLANTATION

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Background: Lung retransplantation (LR) accounts for 5% of worldwide lung transplants (LT) and has lower survival rates than first LT. The main factors contributing to mortality within a year of surgery include early-onset chronic graft dysfunction (CLAD) of a restrictive phenotype (RAS), older donor age and the need for prior mechanical ventilation (NIV). The aim of the study is to analyse the characteristics of LR patients at our centre and to evaluate whether the survival rate varies by age at the time of LR.

Methods: A retrospective study of patients who underwent LR at Vall d'Hebron University Hospital between 1990 and 2024 was conducted. We evaluated variables including: reason for LR, hospital and ICU stay, comorbidity and need for previous NIV. Qualitative variables were expressed as frequencies and percentages, and quantitative variables were expressed as mean values and standard deviations. Survival was analysed using Kaplan-Meier curves. Cox regression was used to compare patients over and under 45 years of age.

Results: 27 patients undergoing LR were included in the study; 21 (78%) were female and six (22%) were male, with a mean age of 28 years at first LT and 34 years at LR. Indications for LR included: CLAD due to bronchiolitis obliterans (BOS) in 19 (71%) patients, RAS in 7 (26%) patients and mixed in 1 (3%) patient. CLAD developed 4 years after the first LT in 26 patients and in the first year in 1 patient. Only 2 (7%) patients required NIV as a bridge to LR. The average duration of ICU and hospital stay following a LR was 31 and 39 days, respectively. The most prevalent comorbidity was renal failure (9 patients, 29%), followed by liver failure and heart failure, both present in one patient each (4%) (Figure 1). The median survival time for patients over 45 was 1,341 days (95% CI: 228 - 2,453 days), while for patients younger than 45, the median was recorded as 2,142 days (95% CI: 1,384 - 2,900). There was no significant difference in mortality between the two groups (hazard ratio 0.696, 95% CI 0.187-2.585, p=0.588) (figure 2).

Conclusions: The primary cause of reTP identified in our study is CLAD phenotype BOS. No increased mortality risk was observed between the groups of patients over and under 45 years old.

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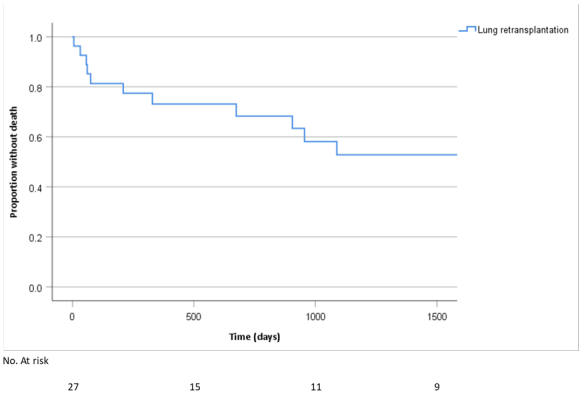
First lung transplant (N= 27)		Lung retransplantation	
Reason			
ILD	9 (33%)	CLAD BOS	19 (71%)
COPD	1 (4%)	CLAD RAS	7 (26%)
PH	2 (7%)	CLAD mixta	1 (3%)
CF and BQ	15 (56%)		
Type of transplant			
Bilateral	24 (89%)	Bilateral	22 (82%)
Unilateral	3 (11%)	Unilateral	5 (18%)
Ischemia time			
Left	4:27h	Left	5:31h
Right	4:15h	Right	5:40h
Transplant bridge NIV			
No	27 (96%)	No	25 (93%)
Yes	1 (4%)	Yes	2 (7%)
ECMO bridge transplant			
No	27 (100%)	No	23 (85%)
Yes	-	Yes	4 (15%)
Grade of acute rejection			
A1	4 (31%)	A1	3 (43%)
A2	2 (15%)	A2	3 (43%)
A3	6 (46%)	A3	1 (14%)
A4	1 (8%)	A4	-
Antibody-mediated rejection			
No	22 (82%)	No	27 (100%)
Yes	2 (7%)	Yes	-
Not reported	3 (11%)		
Improved lung function			
FVC	2874 mL±787 (75,7 ±15,9)	FVC	2436 mL ± 748 (64% ± 19%)
FEV1	2407 ± 777 (75,8 ± 18,3)	FEV1	FEV1 2003 mL ± 658 (63,6% ± 20%)
Repeated infections ≥3			
No	18 (67%)	No	24 (88%)
Yes	9 (33%)	Yes	3 (12%)
Comorbidities			
Renal insufficiency	9 (29%)		
Hepatic insufficiency	1 (4%)		
Heart failure	1 (4%)		
No	17 (63%)		
Cause of death			
Infection	7 (50%)		
Chronic allograft dysfunction	1 (7%)		
Surgical complications	5 (36%)		
Neoplasia	1 (7%)		

Figure 1. Patient characteristics



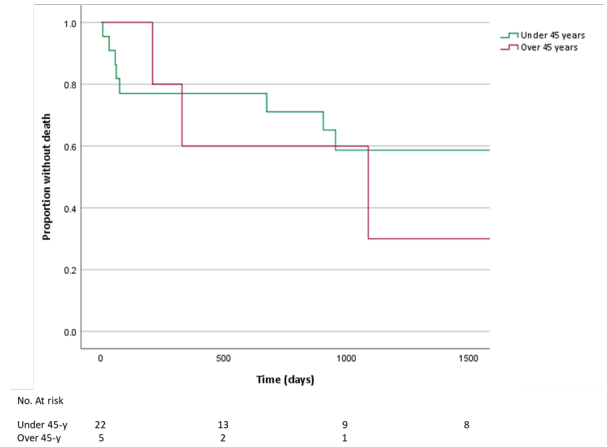


Figure 2. Survival in LR patients and according to age at LR

EP_136 LONG-TERM OUTCOMES OF RIGHT VS LEFT PAEDIATRIC KIDNEY TRANSPLANTS OVER A 33-YEAR PERIOD IN THE USA

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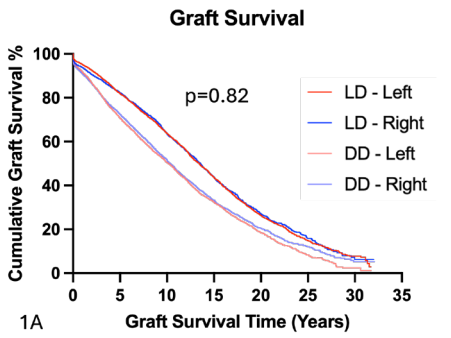
Background: Right kidneys have shorter renal veins than left kidneys. This may make the transplant surgery more challenging although there is no evidence supporting this in paediatrics. We reviewed the use of right versus left kidneys transplanted in children over a 33-year period in the USA.

Methods: Data were retrieved and analysed on right versus left kidney transplants performed in paediatric recipients from 1987-2020, from the United Network for Organ Sharing. Data were compared using chi-square test, t-tests and Kaplan-Meier survival analysis.

Results: Overall, 38% (n=9,160) of kidney transplants in children were done using right kidneys, with right kidneys being used more often in organs coming from deceased donors (DD) (42% of DD kidneys, and 25% of living donor (LD) kidneys, p<0.01). Right kidneys had significantly more delayed allograft function than left kidneys (11.1% vs 7.5%, p<0.01) even when accounting for donor type (5.8% vs 4.6% p=0.01 in LD transplants, and 15.0% vs 12.8% p<0.01 in DD transplants). However, there was no significant difference in primary non-function (p=0.37). In DD transplants, right kidneys were more likely to develop a thrombus (1.8% vs 2.6%, p<0.01). Kaplan-Meier analysis also showed that right kidneys had a worse allograft survival (median survival 11.3 years vs 12.2 years, p<0.01). However, when accounting for donor type and transplant era, this difference is no longer significant (Figure 1A). The same findings were found for patient survival (Figure 1B).

Conclusions: Left kidneys are more frequently used in LD as the choice of a longer renal vein makes transplantation easier. Using right kidneys for transplantation, where the vein is shorter and may require extension, carries an increased risk of delayed allograft function and thrombus formation. However, when adjusted for donor type there was no significant difference in allograft or patient survival when using right kidneys compared to left kidneys even in LD.



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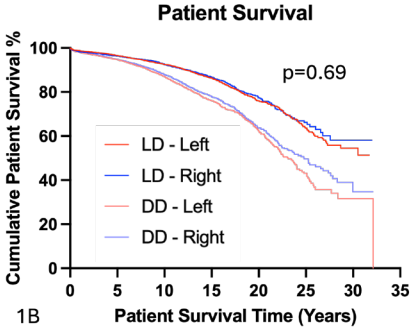

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Current challenges in transplantation procedures

EP_137 TRANSPLANT URETERIC STENT REMOVAL USING ISIRIS IN AN AMBULATORY OUTPATIENT SETTING

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Background: The intraoperative insertion of ureteric stents reduces urological complications after kidney transplantation however timely removal is critical to reduce the risk of secondary complications such as infection. Transplant ureteric stent removal (TUSR) is traditionally undertaken with flexible cystoscopy in a theatre environment. Isiris® is a single-use flexible cystoscope with integrated grasper. We aim to analyse TUSR using Isiris® in an ambulatory setting in terms of acceptability, efficacy and cost-effectiveness.

Method: A retrospective analysis of a contemporaneously maintained database at a single centre from 01/2021 to 06/2022 was carried out. TUSR was performed using Isiris® in an outpatient advanced nurse practitioner (ANP)-led clinic or on the ward by both surgical trainees and ANPs. Demographics, operative details and stent removal details (including time to removal and patient refusal rates) were collected. Descriptive statistics and a cost analysis was performed based on equipment costs and NHS tariffs.

Results: 345 consecutive patients were included in analysis. The median age was 54 years (range 19-81), M:F 1.3:1, with 81.6% having received their first transplant. A single ureteric anastomosis was present in 99.1% of cases with a total of 348 stents removed. 98.8% of stents were successfully removed using Isiris® (refusal rate of 1.2%) resulting in 86 theatre sessions freed to allow other surgical activity. 86.3% were removed in clinic, the remainder on the ward. The median dwell time was 34 days (25.75-43) with 73.8% removed within 6 weeks. The cost-saving per stent was £545.00 amounting to a total saving of £154,021.00.

Discussion: TUSR using Isiris® is acceptable and effective. Transferring TUSR to an ambulatory setting is not only associated with financial savings but is coupled with an increase in theatre capacity thus reducing the burden on stretched resources.

EP_138 PARATHYROIDECTOMY OR CINACALCET FOR PRE-TRANSPLANT HYPERPARATHYROIDISM: WHAT IS THE BEST OPTION?

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Background: Secondary hyperparathyroidism is a common consequence of end-stage renal disease. Despite the efficacy of kidney transplantation in treating renal failure, many transplant recipients still suffer from persistent or tertiary hyperparathyroidism. Furthermore, the impact of secondary hyperparathyroidism therapy choices on other renal transplant outcomes is poorly understood.

Methods: We retrieved the data registry of 334 patients who received a kidney allograft between January 2007 and December 2014 at the Sheffield Teaching Hospitals, NHS Foundation Trust, United Kingdom. We identified three groups: the parathyroidectomy group (34 patients), which included patients who had parathyroidectomy before transplantation, and The Cinacalcet group (31 patients), which included patients who received cinacalcet before transplantation. Finally, the control group (269 patients) includes patients transplanted in the same period but with no evidence of hyperparathyroidism. We reviewed all groups' demographic data, biochemical parameters, and graft survival.

Results: We found that patients who underwent parathyroidectomy before transplantation had significantly better calcium and parathyroid hormone levels than the cinacalcet group (p-value 0.003). Short—and long-term graft survival was comparable in all groups. In addition, the cinacalcet medicine was more cost-effective, with a median price of £ 2714 compared to £ 6256 for a parathyroidectomy.

Conclusions: Renal allograft survival was comparable in all groups. Tertiary hyperparathyroidism was less likely to occur in patients who underwent parathyroidectomy than those who took cinacalcet. However, cinacalcet therapy was more cost-effective than parathyroidectomy.

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Current challenges in transplantation procedures

EP_139 RATIONALIZATION OF ARTERIOVENOUS FISTULA TRAY: A SUSTAINABILITY QUALITY IMPROVEMENT PROJECT

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Background: This project aims to reduce the number of unused instruments in the AVF surgical tray to reduce unnecessary waste, minimize environmental footprints, and improve staff satisfaction. Currently, large numbers of items are embedded in AVF trays, which are not used and create the problem of increased and unnecessary costs, environmental impacts during surgery, and delayed turnaround time. **Objective:** To measure the utilisation rate of provided equipment in the standard AVF tray and subsequently assess the impact of the elimination of superfluous items. Assessed outcomes are efficiency, personnel workload, procedural costs, and environmental footprint related to CO2 emissions.

Methods: A prospective audit of 25 AVF surgeries was carried out using a tracking form to document unused instruments. Data was presented in the form of a heat map, showing items that are frequently unused. A reduced surgical tray was designed following consultation with surgical and theatre staff. The carbon footprint of the reduced surgical tray was calculated using the methodology described by Rizan et al. Feedback was sought from staff regarding how this rationalization could affect workflow and satisfaction

Results: Results indicated that 24 from 52 instruments can be removed without affecting the quality of the procedure. Initial data analysis shows a reduction in set-up time, sterilization needs of instruments, and overall cost per procedure. The reduction in the carbon footprint of the new tray has been calculated at 203.3 kg CO2 per year, estimating 119 AVF procedures annually. Monetary costs shown significant savings as well. A repeat staff survey is underway to review satisfaction with the reduced set.

Conclusions: A simple SusQI analysis can be applied to surgical trays to reduce environmental impact significantly. This is primarily through a reduction in sterilisation energy and related emissions. Reducing the size of the tray through consultation with surgeons and theatre staff can also have a positive impact on finances and staff satisfaction.

Standard Tray Before Reduction

Backup Tray

New Tray

EP_140 120 PEDIATRIC LIVER TRANSPLANTS: DONOR OUTCOMES AT A SINGLE CENTER IN ARGENTINA

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Background: Pediatric living donor liver transplantation (P-LDLT) is crucial in Latin America due to the limited availability of pediatric cadaveric donors. This study examines outcomes of 120 living-related liver donors for 118 pediatric recipients over a decade (2015–2024) at an Argentine center.

Methods: A retrospective study evaluated donor outcomes, including anthropometric data, perioperative anesthesia management, and complications classified using the Clavien-Dindo system.

Results: Donors were predominantly female (59%), with a mean age of 31 years and BMI of 25.3. Most were parents, with many originating from neighboring countries. The “fast track” protocol with early mobilization and regional anesthesia, using an epidural catheter in most of the cases, allowed for management in general wards. Liquid diet was initiated 8 hours postoperatively. Open left lateral sectionectomy was the most common surgical approach, with 8 cases that required graft hyper-reduction. An ultrasonic dissector was used in nearly all cases from 2017. Mean surgery duration was 248 minutes. A cell saver system recovered 310 mL of blood on average, and only 3 donors needed transfusions. Normal arterial anatomy was found in 75% of cases. The average hospital stay was 4.9 days, with drainage duration in uncomplicated cases averaging 6.5 days. The donor complication rate was 7.5%, with no deaths. Grade III complications (5%) required percutaneous or surgical treatment for biliomas (5 cases) or bile peritonitis (1 case). Grade IV complications (2.5%) included ICU admissions for pneumonia (1 case), septic shock from biliary fistula (1 case), and post-surgical respiratory depression (1 case). Minor complications (17 cases) were self-limiting biliary leaks or wound infections.

Conclusions: The “fast track” protocol, including early mobilization, regional analgesia, and early diet, significantly reduced morbidity in donors, with no mortality, highlighting the safety and effectiveness of P-LDLT in the region.

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Current challenges in transplantation procedures

EP_141 EIF5A INHIBITION ENHANCES HYPOXIA TOLERANCE AND IMPROVES ISLET TRANSPLANTATION OUTCOMES

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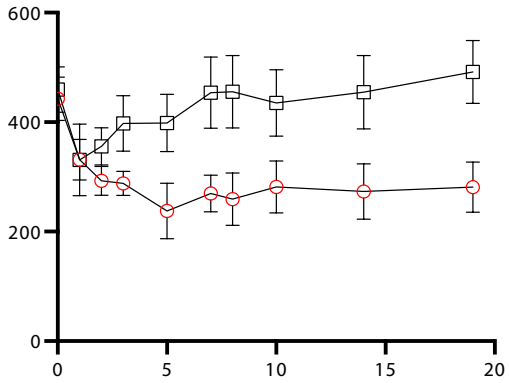
[1]Monaco Hospital, [2]Lp2m Laboratory

Background: Pancreatic islet transplantation is an alternative for patients with Type 1 diabetes (T1D) but is limited by the number of islets available. Indeed, many islets are lost during the procedure from preparation to transplantation, mainly due to ischemia/reperfusion injury. In addition, a recipient requires three successive islet transplants, thus necessitating several donors. We have shown that GC7 (N1-guanyl-1,7-diaminoheptane), an inhibitor of eIF5A hypusination, improves the resistance of various cells and tissues to ischemia/reperfusion, including a pancreatic beta cell line. We therefore investigated the effect of GC7 on the quality and quantity of mouse pancreatic islets when used during the isolation procedure, and then on the functional recovery of these islets when transplanted into mouse models of T1D.

Methods: Pancreatic islets were obtained by digesting mouse pancreases with a collagenase/GC7 mixture. We then analyzed their short- and long-term survival, morphology, function and resistance to ischemia/reperfusion. Finally, a suboptimal number of these islets (~150) were transplanted under the renal capsule of T1D mice with severe hyperglycemia.

Results: Islets conditioned with GC7 showed improved survival at 24h and 72h and better protection against ischemia/reperfusion injury. T1D mice transplanted with a sub-optimal number of these islets showed better glycemic control with a -35% variation in blood glucose at D20 (vs. +6% for control islets) demonstrating better functionality and survival than control islets.

Conclusion: GC7-conditioned islets showed improved survival at 24 and 72 h and better protection against ischemia/reperfusion injury.



EP_142 FIRST SUCCESSFUL SIXTH KIDNEY RE-TRANSPLANTATION IN SLOVAK REPUBLIC. ONLY THIRD KNOWN CASE REPORT WORLDWIDE

Stefan Hulik[1], Tatiana Baltesová[2], Rastislav Kalanin[3], Igor Gaľa[4], David Adandedjan[5], Diana Tomasurova[4], Zuzana Lukacova[4], Janka Katuchova[3], Luboslav Bena[4]

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Background: We present the first successful sixth kidney re-transplantation in the Slovak Republic, performed in the University Hospital of L. Pasteur Kosice, only the third known case worldwide.

Methods: A 57y.o. female with 5th kidney graft failure. Living donor an ABO and HLA-incompatible (HLA MM A/B/DR - 2/2/1, IK 17, historically positive antibodies (B44). Desensitization protocol: Rituximab, 3x Immunoadsorption, Thymoglobulin. Kidney procurement by HARSLDN - WIT 1min 50s. Transplantation orthotopically through a midline incision, after splenectomy and left native kidney nephrectomy. End to end anastomosis of graft vein on preserved recipient renal vein, arterial anastomosis end to side on splenic artery. Immediate production of urine after reperfusion. Second WIT less then 30min and CIT 8h 30min. End to end uretero–uretero anastomosis on 28cm long double-J-stent, ultrasound control of correct position. 2 abdominal drains around the graft.

Results: Immediate Graft Function. Spontaneous JJ stent dislocation and obstruction with urinary leak successfully managed by urologist, exchange of double J stent for longer one 30cm followed by surgical team re-laparotomy. Spontaneous bleeding into the sublingual soft tissue causing airway obstruction required tracheostomy by ORL specialist. Spontaneous bleeding from peripheral artery branch on colon transversum required re-laparotomy. Mild pancreatitis successfully managed conservatively with Octreotide added to the treatment. Thrombosis in peripheral veins of forearm successfully managed conservatively with angiologists and hematologists. Impaired consciousness with non-convulsive status epilepticus - we attributed to PRES, successfully managed by neurology team. Hepatopathy in critically ill patients combined with potential hepatotoxicity of treatment medication successfully managed with hepatologists. The patient was discharged on POD 34, with normal creatinine level.

Conclusions: Despite significant postoperative complications, the graft demonstrated immediate graft function (IGF), reflecting the success of the multidisciplinary approach. This report underscores the potential of individualized surgical and immunological strategies in addressing the challenges of extreme retransplantation cases.

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Current challenges in transplantation procedures

EP_143 REVITALIZING A TRANSPLANT PROGRAM: THE FIRST 45 SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTS

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Background: Simultaneous pancreas-kidney transplantation (SPK) is a transformative solution for patients with end-stage renal disease (ESRD) and insulin-dependent diabetes. Despite its success, excellent outcomes are hindered by challenges such as donor selection, surgical techniques and long-term graft survival.

Methods: We retrospectively reviewed all SPK cases performed at our institution from June 2021 through December 2024, analyzing donor and recipient characteristics, advancements in surgical protocols, and perioperative management strategies. Outcomes of interest included patient and graft survival, metabolic parameters, and postoperative complications.

Results: We analyzed 45 SPK recipients with a median age of 43 years (28-62). 51.2% were male, 51.1% had Type 1 diabetes mellitus and 88.8% were on dialysis. All cases were performed using a standardized technique. The median operative time was 292 minutes (207-500) with a median blood loss of 200 ml (50-800). 36 cases (80%) were Pancreas-first implantation. The median pancreas and kidney warm ischemia was 25 (17-36) and 30 minutes (20-50), respectively. The median postoperative stay was 6 days (4-30), with delayed kidney function in 6 cases (13.3%), and no dialysis requirements. 30-day relaparotomy and hospitalization rates were 4.4% and 41%, respectively. There were no ureteral strictures, arterial or venous graft thrombosis. Enhanced immunosuppressive regimens lead to low acute rejection rates (4.4%), with a 1-year median HbA1C of 5.4. Survival was 100% at 1 and 3 years, with kidney and pancreas graft survival rates of 100% and 97% at 1 year and 100% and 91% at 3 years. Persistent challenges include re-admissions for gastroparesis exacerbations and managing complex comorbidities.

Conclusions: SPK continues to be a highly effective therapy for diabetes-related ESRD, with advancements in surgical techniques, donor preservation, and immunosuppression driving improved outcomes. Our experience demonstrates that by addressing ongoing challenges with standardized procurement, optimized implantation and post operative management, and multidisciplinary collaboration, excellent recipient outcomes are attainable.

EP_144 INTRA-OPERATIVE SALINE CHOLANGIOGRAPHY - AN ALTERNATIVE TOOL FOR BILE DUCT DIVISION IN LDLT

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Background: Intraoperative cholangiography with contrast medium is the gold standard procedure to identify the biliary anatomy and to locate the appropriate division point to transect the bile ducts in living donor liver transplantation. However, it is associated with an increasing in operation time, added cost, inherent risk of bile duct injury associated with contrast medium, radiation exposure and the need for additional equipment and personnel. Moreover, we can only see the bile duct on monitor instead of direct vision.

Methods: We use normal saline instead of contrast medium for intraoperative cholangiography, which we call it intraoperative saline cholangiography. With the help of intraoperative saline cholangiography, we can have a direct visual intuition over the hilar plate and design the cutting line of the bile duct without additional equipment and personnel.

Results: Starting from 2005 July to 2021 October, there are 618 LDLT operations performed at our institution, we exclude 9 left lobe donors, 609 LDLT right lobe hepatectomy operations are performed. Among them, 252 donors use contrast medium for IOC and 17 donors end up with biliary complication, the complication rate for contrast medium group is 6.7%. On the other hand, 357 donors use normal saline for IOC and 13 donors experience biliary complication, the complication rate for saline group is 3.6% (p=0.081). Although there is no statistical difference, but we can see the decreasing trend in intraoperative saline cholangiography group. Biliary complications for those LDLT right lobe donors are minor bile leakage and biliary stricture; and most of them are managed with endoscopic retrograde biliary drainage, only 2 donors need further operation for their biliary complication.

Conclusions: In our institution, IOC is routinely performed for donor hepatectomy operations, but with the replacement of normal saline over contrast medium, we can see the bile duct with direct eye vision and make the appropriate transection point for right hepatic duct without additional equipment and personnel. Therefore, intraoperative saline cholangiography is a simple, fast, safe and reproducible procedure with equipment present in an ordinary hepatobiliary operating theater.

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EP_145 NURSES EXPERIENCE WITH GIVING POST-TRANSPLANT EDUCATION TO IMMIGRANT KIDNEY TRANSPLANT RECIPIENTS

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Background: About 20% of kidney transplant recipients (KTRs) in Norway are immigrants, of whom more than half need an interpreter. To maintain good health post-transplant the KTRs follows 8 weeks of postoperative patient education (PE) which tailor theoretical and practical transplant knowledge. The PE program was developed in a Norwegian context and has not been evaluated in the context of immigrant KTRs. The objective of the present study was to explore nurses' experiences with giving PE to immigrant KTRs as part of developing an intervention to increase health literacy and learning outcomes in immigrant KTRs, and health literacy sensitivity and cultural competence in transplant nurses.

Methods: Twenty-nine nurses from three different wards participated in five focus group interviews. The interviews were transcribed and analyzed using Clarke and Brauns' thematic analysis.

Results: Three main themes were generated: *1) Communication barriers and lack of competence in using an interpreter:* The nurses found PE using an interpreter challenging and lacked appropriate communication tools to uncover possible barriers in the communication-chain. The nurses also lacked structured training in PE using an interpreter; *2) Cultural insecurity in patient education:* The nurses were afraid of offending the patient, for example when bringing up sensitive themes. Sexuality following transplantation were perceived as culturally inappropriate, especially in the presence of an interpreter; *3) Limited time window for patient education and communication:* The interpreter session represented a window for communication where PE were often one of several activities. Having a fixed time with an interpreter could strengthen the prioritizing of PE, but it could also challenge the patients' needs, as the patient were not always ready and susceptible for PE.

Conclusions: The study shows that the nurses lacked communication tools and systematic training in PE to immigrant KTRs using an interpreter. Cultural insecurity and lack of cultural competence left the immigrant KTRs in a vulnerable situation with potential less resources and knowledge to take care of their health post-transplant. The study provides important data in the development of an intervention to strengthen equity in post-transplant follow-up.

EP_146 INDIA'S FIRST SUCCESSFUL REDO-DOUBLE LUNG TRANSPLANTATION: IN FAVOUR OF A SECOND CHANCE

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Background: According to Spanish proverb, 'Hope' is the last thing we lose as human beings, it helps us to face our difficulties and stand up to adversity. Here is a case review of 34yr old gentleman who underwent India's first successful Redo-double lung transplantation after waiting for 119 days on VVECMO as a bridge to transplantation.

Methods: **Case report**: A 34yr old young gentleman with post covid lung fibrosis with type 2 respiratory failure underwent successful double lung transplantation in April 2021. In January 2024 he was diagnosed with antibody mediated rejection (AMR) which was treated as per our protocol. Initially he responded to therapy, but later gradually his clinical condition worsened, declining lung functions and chest scan showed bronchiolitis obliterans syndrome (BOS) changes and decided to give a benefit of extracorporeal photopheresis (ECP)therapy. During his hospital stay, he developed respiratory distress, initially managed with NIV, later intubated and placed on ventilator as NIV failed. Subsequently VVECMO was initiated on 27th June 2024 in view of persistent hypercapnia despite of maximum ventilator support. His repeat single antigen bead (SAB)1 and 2 titers were elevated and treated with plasmapheresis, IVIG, carfilzumab (AMR protocol). His blood culture grew klebsiella pneumonia, candida auris treated as per culture sensitivity reports. maximum medical therapy, we failed to wean him off from life supports and decided to register him for Redo double lung transplantation after multidisciplinary transplant meeting considering his age and preserved other organ functions. Finally, he underwent successful Redo-double lung transplantation on 25th October 2024. His postoperative period was uneventful, recovered and improved with aggressive pulmonary rehabilitation and was discharged from hospital on 21st November 2024.Currently he is under our closed follow up, celebrating his new lease of life.

Results: Positive outcomes with Redo lung transplantation depends on various factors like younger patients with CLAD-BOS, transplant team's expertise and patient family's support.

Conclusions: Redo lung transplantation is a real option that is both necessary and useful in highly selected recipients.

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EP_147 PSEUDO-ANEURYSM OF THE RENAL ARTERY FOLLOWING TRANSPLANTATION: DIAGNOSI AND TREATMENT OPTIONS

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Background: Pseudo-aneurysms of the renal artery (PSARs) are rare complications following kidney transplantation. Their etiology can be attributed to infectious causes or vascular surgical damage. Pseudo-aneurysms can lead to graft loss and patient death due to rupture or sepsis. Timely diagnosis is imperative for the choice of an interventional or medical approach, although the best strategy remains controversial to date.

Methods: Six kidney recipients with conspicuous PSARs arising after transplantation: one case of a living donor kidney, two cases of combined liver and kidney, one case of a double kidney, one single kidney from donation after brain death, one single kidney from donation after cardiocirculatory death. In 50% of cases, onset with hemorrhagic shock, whereas in other cases, an occasional finding within the first month following transplant. In two cases, allonephrectomy following angiographic placement of graft-excluding stent, in two other cases direct allonephrectomy. In the two cases of combined liver and kidney transplantation, we performed allonephrectomy and consequent re-transplantation of the same renal graft after vascular debridement and toilette with intersection of vascular Homograft; in one out two cases, the graft was removed due to recurrence of pseudo-aneurysm after one month of graft functioning, whereas the second kidney is still functioning after 10 years.

Results: Allonephrectomy in 100% of patients, 50% of failure due to early recurrence in one out two cases of consequent allonephrectomy and re-transplantation. Over 80% (5/6) graft loss, one case of fungal septicemia, but no death. In (84%) 5/6 the cause of PSAR was fungal versus (16%) 1/6 bacterial with massive primary non function of the graft. In the case of the double kidney, exclusion by stenting of the first affected graft, but allonephrectomy extended to both the grafts due to intra-operative finding of silent involvement of the second kidney.

Conclusions: Pseudo-aneurysms of the renal artery are burdened with high rates of graft loss and patient morbidity and mortality, as they most commonly initiate with rupture and hemoretroperitoneum. The surgical approach of consequent allonephrectomy and re-transplantation of the same graft after vascular debridement and toilette is possible in highly selected cases.

EP_148 DONOR-RECIPIENT MISMATCH IN LUNG TRANSPLANTATION: THE ROLE OF GRAFT SIZING IN CLINICAL OUTCOMES

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Background: Lung transplant (LTX) is a life-saving procedure for patients with end-stage lung disease, but donor-recipient (D/R) size mismatch can lead to complications like primary graft dysfunction (PGD) or chronic lung allograft dysfunction (CLAD).

Methods: This retrospective study included patients who underwent LTX at the University Hospital of Siena (2013-2023). Patients requiring graft resizing due to size mismatch were assigned to the Sizing Group (S); those without resizing to the Non-Sizing Group (NS). Donor-recipient characteristics (sex, height, BMI) were analyzed. The primary endpoint was identifying predictive factors for graft resizing; secondary endpoints included survival, PGD, CLAD, ischemia time, and mechanical ventilation. Group S was stratified by characteristics such as age, sex, lung disease, type of graft resection to assess differences in outcomes like PGD, CLAD, and acute kidney injury (AKI).

Results: The study included 146 patients: 17 in Group S and 129 in Group NS. A significant difference was found in recipient height (164 cm in S vs. 169 cm in NS, $p = 0.004$). More bilateral LTX were performed in S (82.3%) compared to NS (76.0%, $p = 0.02$). Group S had a higher Lung Allocation Score (31 vs. 20, $p = 0.668$), but no significant differences in comorbidities or preoperative lung function were observed. The D/R height ratio was the sole predictor for graft resizing ($p = 0.02$). Postoperative outcomes showed no significant differences, although there was a trend toward higher incidence of PGD3 (53% vs. 29.7%, $p = 0.13$) and prolonged mechanical ventilation in S. Stratification of Group S revealed that male patients had a higher incidence of CLAD (50% vs. 0%, $p = 0.015$) and AKI (50% vs. 0%, $p = 0.016$). In patients over 50, PGD was observed in all cases (100%). Those undergoing anatomical resection had a higher rate of AKI (45% vs. 0%, $p = 0.018$). Overall survival did not differ between the groups ($p = 0.625$).

Conclusions: D/R height mismatch plays a critical role in determining the need for graft resizing. While resizing is a feasible solution, it may lead to worse short-term outcomes such as higher PGD rate and prolonged mechanical ventilation, particularly in older male patients with obstructive pulmonary disease. These findings highlight the importance of carefully assessing mismatches before LTX.

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EP_150 GOOD RESULTS OF SALVAGE LIVER TRANSPLANTATION CASES FOR THE HCC PRESENTED ADVANCED BCLC STAGES

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Background: Hepatocellular carcinoma (HCC) is a leading cause of liver-related morbidity and mortality, especially in patients with chronic hepatitis B. Advanced HCC with portal vein tumor thrombosis (PVTT) and distant metastasis is challenging to manage. This case series evaluates the outcomes of three patients with chronic hepatitis B-related HCC, treated with surgical resection, adjuvant therapies, and liver transplantation (LT).

Methods: Patient 1: A 46-year-old male with chronic hepatitis B presented with a 6 cm tumor and PVTT. He underwent left hepatectomy and tumor thrombectomy. Postoperatively, a metastatic nodule was treated with percutaneous ethanol injection (PEI), followed by wedge resection of pulmonary metastases. Nine years later, he developed decompensated cirrhosis without recurrence, and underwent living donor liver transplantation (LDLT). The patient remains recurrence-free and stable three years after transplantation. **Patient 2:** A 56-year-old male with chronic hepatitis B had a 10 cm HCC with PVTT. After right hemihepatectomy and TACE for intrahepatic metastases, he underwent LDLT. Post-transplantation, he has remained recurrence-free and stable for 30 months. Patient **3:**A 56-year-old male presented with a 6.5 cm HCC and satellite nodule. He underwent hepatectomy, RFA, and several rounds of PEI for recurrent lesions. Four years later, a mass with PVTT was treated with radiotherapy. He developed decompensated cirrhosis and underwent LDLT, surviving one year post-transplantation without recurrence.

Results: All patients had favorable outcomes post-transplantation, with stable liver function and no recurrence of HCC after liver transplantation. Aggressive management, including hepatectomy, PEI, TACE, and radiotherapy, helped control disease progression in these advanced cases.

Conclusions: Surgical resection, adjuvant therapies, and liver transplantation are effective for managing advanced HCC, even in cases with PVTT and metastasis. Liver transplantation offers long-term survival with stable liver function, even in patients with severe liver dysfunction due to cirrhosis. Regular follow-up and monitoring are essential to detect recurrence and ensure optimal outcomes.

EP_151 THE CASE I WILL NEVER FORGET

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Background: Kidney transplantation is the treatment of choice for a minority of patients with end-stage renal disease (ESRD). Despite big variety of techniques, surgical complications are still big problem for kidney transplant recipients.

Methods: The 44-year-old patient with diabetes mellitus type 1, on peritoneal dialysis 3 years. The donor's left kidney was transplanted. Urine output was observed within the first few minutes. Only after reperfusion, it was noticed that the transplant had been sutured in reverse, with the renal pelvis positioned upward instead of downward. After mapping we decided to rotate the graft as much horizontal as possible to allow proper orientation of the pelvis, avoiding any kinking. This was also aimed to reduce the risk of necrosis of the ureter due to kinking. After final positioning, the bladder was opened. Transparent fluid was obtained, identified as the saline. An anastomosis was performed between the ureter and the bladder using a stent. At the end of the operation, a Doppler ultrasound was performed, all regions being well perfused. The 40 minutes after the operation, due to the cessation of urine output, suspicion arose of an anastomotic insufficiency. Ultrasound examination revealed a significant amount of fluid in the abdominal cavity. The patient was transferred to the operating block. The retroperitoneal space was reopened, and no significant exudate was observed around the transplant. The "ureter-bladder" anastomosis was examined. Sutures were removed, revealing an anastomosis between the ureter and the peritoneal cavity. Approximately 1–1.5 liters of urine were drained from the cavity. The bladder was located and isolated again. This time, the bladder was distended with saline mixed with brilliant green dye to aid in visualization. An anastomosis between the ureter and the bladder was performed using a stent. One hour later, 1 liter of urine was obtained. The patient was discharged from hospital at o/p day 11.

Results: Patient was discharged from hospital at p/o day 11. Creatinine level was 91. Stent was removed after month simultaneously with PD catheter.

Conclusions: Rotating graft up and horizontally and using ureteral stent can save donor kidney from losing and can have good function without any complication.

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EP_152 SURGICAL COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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Background: Kidney transplantation is the best therapeutic option to replace renal function in patients with end-stage kidney disease. Despite advances in surgical techniques, the surgical procedure itself is associated with a risk of postoperative complications, the incidence of which ranges between 5-25%. The most common surgical complication is ureteral stenosis. The aim of this retrospective analysis was to identify risk factors for surgical complications after kidney transplantation over a 11-year period.

Methods: Baseline characteristics of the recipients (age at the time of transplantation, sex, and type of donor) and factors influencing the development of surgical complications (type of induction therapy, diabetes mellitus, BK positivity) were recorded in the cohort. The study included all 283 patients who underwent kidney transplantation at University Hospital Martin between 2013 and 2023. Patients who developed a surgical complication (bleeding, lymphocele, ureteral stenosis) were identified and investigated in relation to the observed independent risk factors for the development of surgical complications.

Results: Surgical complications occurred in 15.8 % of patients (n = 45). The most common was ureteral stenosis (60 % of all surgical complications). The average duration from the onset of a surgical complication was between 5,4 and 8,6 months. By using Cox proportional-hazard regression multivariate analysis, none of the parameters that were looked at were found to be independent risk factors for the development of surgical complications (end point: surgical complications itself, bleeding, ureteral stenosis, lymphocele/lymphorrhea).

Conclusions: Kidney transplantation significantly improves quality of life and survival in patients with end-stage kidney disease. It is important to prevent technical complications at all stages of the transplantation process (from donor nephrectomy to transplantation of the transplanted kidney to the recipient). We consider a multidisciplinary approach to the patient and a close collaboration between the nephrologist and the surgeon as a key point.

EP_153 CLINICAL OUTCOMES OF KIDNEY TRANSPLANT IN OBESE RECIPIENTS: A RETROSPECTIVE STUDY

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Background: The prevalence of obesity worldwide has steadily increased in recent decades. The impact of recipient obesity on kidney transplant outcomes is not clear. The study aims were to determine the effect of recipient obesity on surgical and graft outcomes.

Methods: A single-institution retrospective study was performed on adult kidney transplant recipients from 01/2000 to 12/2023. Recipients were classified based on body mass index (BMI) at the time of transplantation: obese (BMI ≥ 30 kg/m2) and nonobese recipients (BMI < 30 kg/m2). The analysis included surgical complications, delayed graft function (DGF), and 1-year estimated glomerular filtration rate (eGFR).

Results: Overall, 941 recipients were studied, including 153 (16.3 %) with BMI ≥ 30 kg/m2. Mean age was 52 years, mean BMI was 24.9 kg/m2, 627 (66.6%) were men, and 362 (38.5%) received a kidney from a living donor. Obese patients had comparable postoperative major complication (Clavien > 3a) rates (26.6 vs 33.3%, p=0.221) and mean comprehensive complication index (21.9 vs 20.2, p=0.092). DGF (20.0% vs 14.0%, p=0.082) and eGFR (52 vs 51 ml/min/1,73m2, p=0.541) were not statistically different in obese and nonobese recipients.

Conclusions: Postoperative surgical outcomes and 1-year graft function were comparable between obese and nonobese recipients. Consequently, kidney transplantation should be considered in obese recipients.

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EP_154 AI-ASSISTED REAL-TIME 3D BILE DUCT REGISTRATION FOR LAPAROSCOPIC DONOR HEPATECTOMY

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Background: To guide the surgeon for precise and safe bile duct division during laparoscopic living donor hepatectomy, image-guidance such as ICG camera is utilized. However, a limitation exists in using ICG as the right hepatic duct, the target for division, is embedded inside the Glissonean capsule and liver parenchyma. Thus, a pre-reconstructed 3D model could aid in guiding the surgeon to select the appropriate division point. Still, there is a discrepancy between the 3D model and the surgical view from the camera, limiting its practical use.

Methods: To address this challenge, we developed a 3D model registration tool using Unity engine to facilitate better registration for augmented reality surgery. Additionally, we built an automated registration model to automate the 3D model registration on the surgical video. A ResNet model was employed for deep learning, with the outcome target being the position and rotation scales of the 3D model compared to the ground truth developed by surgeons specializing in donor hepatectomy. The dataset consisted of 944 images from 37 videos, and a 3:1 training and validation split was performed.

Results: The MSEs (mean squared error) were 1.17 and 1.83 for the training and validation sets, respectively. The RMSEs (root mean square error) were 0.41 and 2.03, respectively. The Dice similarity coefficient (DSC) scores were 0.677±0.227 for training and 0.688±0.216 for validation.

Conclusions: The deep learning model showed promising potential for developing an automated 3D registration model. However, further research is required to develop the model for real-world application in surgery.

EP_155 SUCCESSFUL REDUCED-SIZE LIVER TRANSPLANTATION OF LARGE-FOR-SIZE FROM DONATION AFTER CARDIAC DEATH

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Background: Large-for-size (LFS) liver grafts pose significant clinical challenges, including abdominal compartment syndrome, inadequate liver perfusion, and compression induced parenchymal damage, which may lead to delayed graft function or even graft loss. We report a successful case of ex vivo reduced liver transplantation in an adult patient with a LFS graft.

Methods: A 66-year-old female with hepatitis C-related cirrhosis and recurrent hepatocellular carcinoma was evaluated for liver transplantation. Her preoperative computed tomography (CT) scan showed a maximum anterior-posterior diameter of 12.8 cm in the thorax. The donor was a 47-year-old male with hypoxic brain damage secondary to a suicide attempt (BMI 40.4, blood type AB). The donor was classified as donation after cardiac death (DCD, Maastricht type III). Due to unstable donor vital signs, a CT scan of the liver graft could not be performed. During surgery, the total graft weight was 3,530 grams, with a maximum graft thickness of 17 cm. To prevent complications from graft size mismatch, the right lobe was resected ex vivo, preserving the middle hepatic vein and left lobe for transplantation. The right lobe weighed 1700 grams, and the left lobe, which was used for transplantation, weighed 1830 grams. The cold ischemia time was 151 minutes, while the functional warm ischemia time was 20 minutes. No ascites were present, and blood loss was 6,500 ml.

Results: Postoperatively, the recipient's hepatic function recovered well, and she was discharged 20 days after surgery. One-year follow-up confirmed stable liver function with no complications.

Conclusions: In conclusion, this case study underscores the importance of anthropometric matching, particularly the recipient's maximum right anterior-posterior (RAP) diameter, in optimizing outcomes for LFS grafts. Tailored surgical strategies and split liver transplantation offer effective solutions to mitigate complications and enhance graft utilization, particularly in resource-limited settings, thereby maximizing the benefits of liver transplantation.

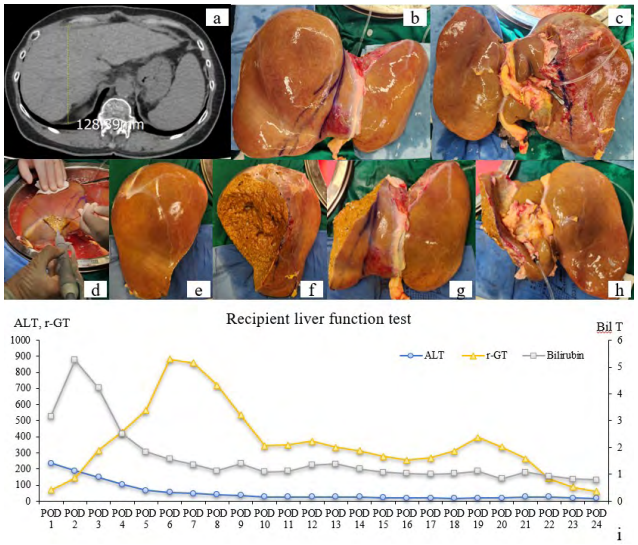

FIGURE 1. (1a) Preoperative CT scan of the recipient showing RAP of 128.39 mm. **(1b, 1c)** Donor's whole liver. **(1d)** Ex vivo liver reduction procedure. **(1e, 1f)** Right lobe of the liver. **(1g, 1h)** Preserved left lobe and middle hepatic vein.

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EP_157 FATIGUE AFTER HEART TRANSPLANTATION-A LONGITUDINAL FIVE YEAR FOLLOW-UP

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Background: This study reports one of very few longitudinal five-year follow-ups after heart transplantation (HTx). Fatigue is a distressing and common symptom after HTx, which might constitute a barrier to performing necessary ily life activities. As accomplishment is the most important driver of self-efficacy, it highlights the necessity of exploring the magnitude of fatigue among heart recipients (HTRs) and its possible impact on their self-efficacy. The aim was to explore self-reported fatigue from time on the waiting list to five years after HTx and its association with sleep problems and self-efficacy.

Methods: This multicenter, longitudinal cohort study includes 48 HTRs, 12 women and 36 men, with a median age of 57 years followed from pre-transplant to five years post-transplant. Fatigue was explored by the Swedish version of the Multidimensional Fatigue Inventory-19, which includes five dimensions: General Fatigue (GF), Physical Fatigue (PF), Reduced Motivation (RM), Reduced Activity (RA) and Mental Fatigue (MF). The Self-efficacy for managing chronic disease 6-Item Scale was used to measure self-efficacy. Sleep problems were measured The Organ Transplant Symptom and Well-being Instrument (OTSWI).

Results: Fatigue was significantly reduced in all areas 3 months after HTx compared to pre-HTx except for MF; GF (p≤.001), PF (p≤.001), RA (p≤.001), RM (p=.001) and MF (p=.244). Physical fatigue further improved between 3 and 6 months (p=.26) as did reduced activity (p=.05). General fatigue decreased from 6 months to one year (p=.042). However, there were no significant changes between one and two years or two- and three-years post HTx. From three to four years motivation significantly increased (p=.020), while mental fatigue became worse (p=.020). Finally, from four to five years motivation was reduced (p=.033). Sleep problems were moderate and persistent over the five years. No gender differences were identified in any variable. The relationship between self-efficacy and fatigue is strong. The greater the fatigue, the lower is self-efficacy.

Conclusions: Fatigue improves in all areas except for mental fatigue after HTx. Hence mental fatigue remains a prominent issue during recovery from HTx.

EP_158 SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATIONN: MORE THAN THREE DECADES OF EXPERIENCE AT BOCHUM UNIVERSITY HOSPITAL

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Background: Simultaneous pancreas and kidney transplantation (SPK) is the only method that can enable patients with type 1 diabetes mellitus (DM1) and end-stage renal disease to live a life free of insulin and dialysis. The aim of this study is to present and to evaluate the 31 years of experience of primary SPK in Bochum University Hospital.

Methods: This retrospective analysis covers all primary SPKs performed from 1994 to 2024. Demographic data, diabetes and dialysis history, surgical techniques, postoperative morbidity and mortality, as well as long term outcomes were assessed.

Results: Of 693 pancreatic transplantations, 640 (92%) were SPKs, 33 (5%) – pancreas after kidney transplantations (PAK) and 20 (3%) – pancreas transplantations alone (PTA). Of the 640 SPKs, 28 were retransplantations and 612 – primary SPKs. The primary SPKs were analyzed further. Of the 612 recipients, 42% were female. The mean duration of dialysis was 2.8 ± 2.2 years, while the mean duration of diabetes was 29.7 ± 8.5 years. In 16.8% of the recipients, a portal venous drainage of the pancreas was chosen, in 69.8% a central venous drainage. Exocrine drainage was to the small bowel in 88.6% of cases and to the urinary bladder in 8%. Postoperative morbidity was 52.8% and included bleeding (23.7%), pancreatitis (17.0%) and graft thrombosis (14.3%), while postoperative mortality was 1.8 %. The functional duration of the kidney transplants was 14.2 ± 0.7 years, with 1-, 5- and 10-year functional rates of 88.7%, 81.4% and 67.5% achieved. The pancreas transplants functioned for 11.9 ± 0.6 years, with 1-, 5- and 10-year rates of 73.6%, 65.9% and 56.2%. The survival time of the recipients was 15.0 ± 0.6 years, with 1-, 5- and 10-year survival rates of 96.1%, 87.8% and 74.2%.

Conclusions: SPK is the effective gold standard of treatment for patients with DM1 and end-stage renal disease. Our results of over three decades show excellent survival rates, a long functional duration of the grafts and acceptable postoperative morbidity. These results underline the importance of specialized centers for this complex procedure. Future developments should focus on reducing postoperative complications and extending the functional life of the grafts.

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Current challenges in transplantation procedures

EP_159 HOW DOES SURGICAL TECHNIQUE AFFECT THE INCIDENCE OF EARLY BILIARY COMPLICATIONS AFTER LIVER TRANSPLANT?

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Background: Biliary complications are a major cause of morbidity after liver transplantation. It has been suggested that technical factors such as suture size, anastomotic technique (continuous versus interrupted), and anastomotic adjuncts may affect the rate of early biliary complications (EBC) such as bile leak and anastomotic stricture. The aim of this study is to evaluate whether technical features of the duct-to-duct anastomosis are related to the development of EBC after liver transplantation.

Methods: This single-centre retrospective analysis includes all patients who underwent liver transplantation in 2022 and 2023 with duct-to-duct anastomosis. EBC were defined as those diagnosed within 90 days post-transplant. The relationship between anastomotic factors and EBC was explored.

Results: 157 liver transplants were included, out of which EBC occurred in 15 cases (10.6%). Demographical and graft variables as well as anastomotic variables, like suture size and suture material, were not found to be associated with EBC. Only the suture technique for biliary anastomosis was found to be statistically correlated to EBC incidence (p value 0.013): out of 15 EBC patients, in 10 of these cases continuous suture technique was used for biliary anastomosis (66.7%). No EBC were recorded in the biodegradable stent group, although this finding was not statistically significant due to small numbers.

Conclusions: Identifying surgical techniques that reduce the incidence of EBC is necessary to reduce the morbidity associated with liver transplantation. The use continuous technique appears to be associated with higher incidence of EBC, warranting further investigation with a larger study to ascertain whether suture size and material, and biodegradable stents can contribute to lower EBC rates.

EP_160 MAKE IT EASIER: A NOVEL APPROACH TO ESTABLISH ORTHOTOPIC RIGHT LUNG TRANSPLANTATION IN RATS

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Background: Although the left lung transplantation (LTx) model in rats is widely utilized, the right lung remains less common due to anatomical complexity and technical challenges. Notably, the right lung accounts for about 70% of total lung function in rats, making it a more representative indicator of transplantation outcomes and an essential step toward establishing a bilateral rat lung transplantation model. In this study, we developed a novel orthotopic right LTx model in rats, incorporating several innovations to enhance accessibility for beginners and provide a more feasible and reliable platform for basic research.

Methods: Twenty consecutive orthotopic right LTx were performed on Sprague-Dawley rats by a single surgeon using our modified techniques. The duration of each procedure, ischemia time, post-surgery complications, and survival rate at two weeks were recorded.

Results: The key innovations of our novel model mainly include extending the donor's right pulmonary vein by ligating the left branch, improving the visibility by integrating anterior and posterior surgical fields of the right pulmonary hilum, and modifications to the incision of vessels. All transplantations were successfully completed without bronchial or vascular tearing, twisting, or folding. The heart-lung block retrieval, donor lung preparation, cold ischemia, warm ischemia and total operation time were 7.5±0.3 min, 22.6±1.8 min, 38.3±1.6 min, 20.2±1.3 min and 76.1±2.2 min, respectively. During the follow-up, only two rats (10%) succumbed to complications related to atelectasis and infection.

Conclusions: Our novel technique streamlined the learning process for rat right LTx and yielded reliable outcomes, suggesting a feasible option for basic research in lung transplantation.

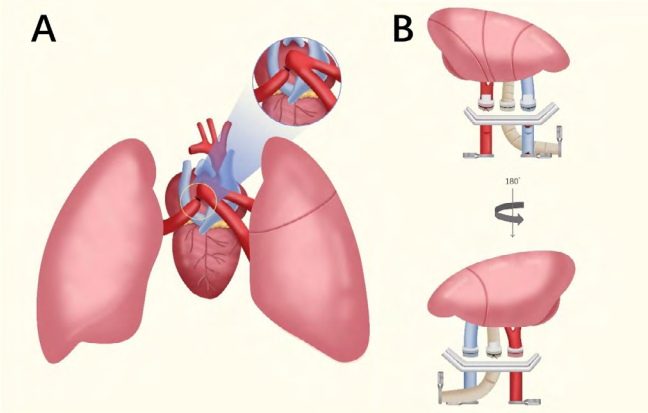

Fig1. Schematic drawing of modified orthotopic right lung transplantation technique.

(A) During donor preparation, the left pulmonary vein is dissected, ligated at its proximal end, and then transected distally at the point of ligation.

(B) Recipient Procedure includes sequentially anastomosing the pulmonary vein and pulmonary artery from the anterior aspect, followed by anastomosis of the bronchus from the posterior aspect. Thereafter, a transverse incision was made at the distal end to allow for the drainage of blood.

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Current challenges in transplantation procedures

EP_161 TREATMENT OF REFRACTORY ANEMIA WITH ROXADUSTAT IN RENAL TRANSPLANT RECIPIENTS

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Background: Roxadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, stimulates erythropoiesis by addressing inflammation and regulating iron metabolism. These properties suggest its potential to treat refractory anemia in renal transplant recipients effectively.

Methods: This prospective observational study enrolled renal transplant recipients diagnosed with refractory anemia, defined as hemoglobin (Hb) levels below 10 g/dL despite receiving the maximum recommended doses of erythropoiesis-stimulating agents (ESAs) for three months. Baseline parameters, including Hb, ferritin, iron saturation index (ISI), folic acid, vitamin B12, glomerular filtration rate (GFR), and C-reactive protein (CRP) as an inflammatory marker, were measured. Follow-up assessments were conducted at 1, 2, and 3 months after initiating Roxadustat at doses per standard recommendations. The primary endpoint was the proportion of patients achieving Hb levels >11 g/dL at three months. Secondary endpoints included changes in Hb, ferritin, ISI, CRP, and the documentation of any adverse events.

Results: en renal transplant recipients (5 male, 5 female) with a median age of 67.5 years (IQR: 60.7–72.7) and a median time post-transplant of 87 months (IQR: 24.0–216.0) were included. Median baseline GFR was 15.5 mL/min/1.73 m² (IQR: 13.25–30.25). The immunosuppresion consisted of tacrolimus 2, sirolimus 3 and tacrolimus with sirolimus in 5 recipients. The median initial dose of Roxadustat was 70 mg three times weekly. At three months, all patients (100%) achieved Hb levels >11 g/dL. Median Hb increased significantly from 9.35 g/dL (IQR: 8.72–9.75) to 11.50 g/dL (IQR: 11.13–12.15), with a median change of +2.95 g/dL (IQR: +2.30–+3.18, p=0.0001). Ferritin levels decreased by a median of 142.5 ng/mL (IQR: −539.25 to −52.00, p=NS), and ISI showed a median change of −5.65% (IQR: −10.15 to −2.82, p=NS). CRP levels demonstrated a non-significant change (median: −0.70 mg/L, IQR: −0.90 to +0.80, p=NS). No adverse events were observed, and no significant changes in GFR occurred during the study.

Conclusions: Roxadustat is an effective and safe treatment option for managing refractory anemia in renal transplant recipients, achieving significant improvements in hemoglobin levels.

EP_162 ALLOGRAFT BIOPSY UNDER INTRAVENOUS OR ORAL SEDATION: WHICH IS THE BEST OPTION FOR PEDIATRIC RENAL TRANSPLANT RECIPIENTS?

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Background: Renal allograft biopsy is a routine procedure in the diagnostic work up of kidney transplant recipients. As it is a minimally invasive procedure, it can be performed by administering oral sedation or intravenous sedation. We examined differences in safety, efficacy and renal findings between biopsies performed under intravenous sedation and oral sedation in paediatric and adolescent renal transplant recipients

Methods: We retrospectively analyzed the biopsies performed at our Center from 2009 to 2024. Differences in length and composition of the core, number of glomeruli, biopsy- and sedation-related complications, and achievement of a renal pathology diagnosis after percutaneous biopsy performed under oral sedation or intravenous sedation were evaluated. A cost-effectiveness analysis was also performed.

Results: The study included 711 biopsies (251 patients), with intravenous sedation administered in 77.1% of cases. Intravenous sedation was associated with significantly longer cortical samples (median 1.8 cm vs. 1.5 cm, p<0.001) and more glomeruli (16 vs. 8, p<0.001) than oral sedation. Diagnostic success was higher with intravenous sedation (88.5%), compared to oral sedation, (75%, p <0.001, OR 2.6). Complication rates were similar between the groups, with biopsy-related complications occurring in 12.9% of cases. Sedation-related complications occurred in 4.9% of intravenous sedation procedures. The cost per successful diagnosis was similar for intravenous sedation and oral sedation.

Conclusions: Our study suggests that allograft biopsy under intravenous sedation in pediatric renal transplant recipients can offer better diagnostic success without additional cost or risk.

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Current challenges in transplantation procedures

EP_163 MINIMAL INGUINAL INCISION VERSUS CONVENTIONAL HOCKEY STICK ACCES TO THE ILIAC FOSSA IN KIDNEY TRANSPLANTATION

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Background: The most common incision for kidney transplantation (KT) is an inverted J-shaped incision. However, demands for minimally invasive surgery in KT are increasing as in other various field of surgery. Minimally invasive surgery (MIS) has been in use in Solid Organ Transplantation for the last three decades. However this approach is generally favoured for the donor surgery rather than for the recipient's. We evaluated retrospectively short-term outcomes between minimal inguinal access (MIA) and conventional hockey-stick access (HSA) to the iliac fossa in a series of 168 recipients.

Methods: Between January 2018 and May 2022, a consecutive series of 168 patients performed by a single senior surgeon where enrolled, 61 patients in the MIA group vs 107 patients in the HSA. The minimally invasive surgical procedure involves an inguinal incision restricted to 6 cm, whereas the aponeurosis receive an 8 cm J shape para-rectal dissection from the pubic tubercle. Vessels and nerves of the abdominal wall are spared, and the dissection to create a retroperitoneal pouch is minimal. The kidney meticulously prepared at bench table is suspended ex-situ during the vascular anastomosis time, and can be concurrently cooled to reduce the warm ischaemia, whereas the Lich-Gregoir technique is used for the uretheral anastomosis. We compared the baseline clinical characteristics and post operative results between two group. Student's t-test was used for the comparison of averages. The Chi-square test and Fischer's exact test were used for the comparison of categorical variables versus cases/controls. A p-value<0.05 was considered statistically significant. All data were processed using Spss version 2024 for Windows

Results: The MIA group had less delayed graft function (5%vs16,8%, χ^2 0,027, OR 0,26), and post operative pain (35 % vs 67,6% χ^2 0, OR 0,258), with the higher scale of NRS scale in the HSA group (16,7% vs 25%). Re-intervention where major in the conventional group 1,7% vs 11,1%, χ^2 0,006, so as need of blood trasfusion (6,7% vs 21,30%, χ^2 0,023, OR 0,26)

Conclusions: This study has limitations in providing strong evidence. However, minimal inguinal incision seems to be safe approach for KT, with a benefit in terms of functional recovery, reduced complication rates (re-interventions, transfusions) and post-operative pain.

EP_164 UROLOGICAL COMPLICATIONS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Background: Urological complications can affect the outcome of kidney transplantation. The aim of this study was to evaluate the occurrence of urological complications and their management in a cohort of pediatric kidney transplant recipients.

Methods: A retrospective analysis on 178 patients who received a renal transplant at our Pediatric Kidney Transplant Center between 2011 and 2023 was conducted. Demographic and clinical data were analyzed. Urological complications were categorized as early, intermediate, or late based on their onset time.

Results: Out of 178 patients, 28 (15.7%) experienced urological complications. Most patients (61%) had a pre-existing uropathy. Early complications (7-30 days) were all obstructive, namely, ureterovesical junction obstruction and perirenal collections. Intermediate complications (1-3 months) comprised ureteral stenosis, symptomatic vesicoureteral reflux (VUR), and obstructive lymphocele. Late complications (>3 months) included symptomatic VUR and ureteral stenosis, with one case leading to ureteral rupture. Early complications were often detected due to acute graft dysfunction, while late ones were mainly identified during routine clinical, laboratory, or ultrasound follow-up. Urological complications requiring surgical or endoscopic therapy were 13.4%. Most ureteral stenoses were treated with initial endoscopic stents, followed by definitive surgery. VUR was treated with endoscopic correction with a high success rate (75%), while open surgery was reserved for cases where initial treatments failed or complications recurred. No clear correlations were found between patient characteristics and risk of urological complication. Urological complications required multiple diagnostic procedures and therapeutic interventions (+2.5 admissions in mean and approximately +EUR 24,000) compared to an uncomplicated post-transplant course. However, they did not significantly impact transplant outcomes, with a graft survival rate comparable to that of the control group.

Conclusions: Regular post-transplant follow-up is crucial, especially for patients with known risk factors, to allow for timely detection and treatment of urological complications, avoiding detrimental effects on graft function and improving transplantation outcomes.

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Current challenges in transplantation procedures

EP_165 POLYPHARMACY, THERAPEUTIC INERTIA AND ADHERENCE OF HEART RECIPIENTS TO DRUG THERAPY

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Background: Currently, the "gold standard" treatment for end-stage heart failure remains heart transplantation. Lifelong use of immunosuppressive and adjuvant therapy requires constant medical supervision in order to optimize treatment regimens and increase the adherence of heart transplant recipients to the treatment. The aim is to study and adapt a method for systematically assessing the complexity of the treatment regimen using the MRCI index, and its relationship with long-term prognosis in heart transplant recipients.

Methods: The results of the study were obtained by analyzing the data of heart transplant recipients observed in the consultative and diagnostic department at the National Medical Research Center for Transplantology and Artificial Organs. To evaluate drug therapy, the "complexity index" of the medication regimen was used MRCI. In our study, "polypharmacy" was defined as the use of five or more drugs, and the concept of "high-risk polypharmacy" was the use of more than eight drugs. Heart transplant recipients were divided into two groups based on the amount of medications they received daily.

Results: the study included patients observed in the consultative and diagnostic department from January 2008 to December 2017. The indicator of the number of medications used by the patient by the fifth year of observation was 9.2±4.2. During the data analysis, the average total MRCI score was 48.72 ± 19.15 (range 32 to 70); medications to treat comorbidities accounted for 42.9% of the total MRCI score, and immunosuppressive therapy accounted for 28.7%. The total MRCI score in the high-risk polypharmacy group was 58.49±17.41; 50.27% of the total MRCI score was accounted for by medications used to treat comorbidities. The analysis revealed a correlation between the total MRCI score and the frequency of hospitalizations.

Conclusions: Patient adherence to prescribed treatment is a predictor of a favorable prognosis for long-term survival without adverse events, however, low adherence and therapeutic inertia are accompanied by a decrease in quality of life, an increase in the frequency of hospitalizations and increases the risk of adverse events.

EP_166 ASSESSIG LONG-TERM OUTCOMES OF HEART TRANSPLANT RECIPIENTS

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Background: Heart transplantation is an established treatment method with proven effectiveness of patients with terminal heart failure. In recent years, the number of operations performed has been steadily growing, and therefore, number of patients requiring outpatient monitoring increasing. the aim is to carry out retrospective analysis of heart transplant recipients observed in consultative and diagnostic department and educe complications that arise in early, and late period of outpatient observation.

Methods: the research included 1436 patients come upon outpatient observation from January 2008 to December 2022. The characteristics of recipients were used for the analysis, including data laboratory and instrumental examination methods and also the nature and frequency complications that arise on different stages of observation.

Results: The survival of recipients amounted to: 96.5%; and 88.0% at 1 and 5 years of follow-up. During the first year hypertension was diagnosed in 34.87% cases, after 5 years in 48.65%. Post-transplant diabetes mellitus was detected in 7.24% cases. By the 5th year of observation the average GFR decreased on 17%. Vasculopathy of heart transplant was determined in 286 cases and required percutaneous coronary operation in 47% of cases. Malignant neoplasms were developed with 61 patients.

Conclusions: Dynamic outpatient monitoring of heart transplant recipients focused on timely diagnosis of complications arises after transplantation hearts.A personalized approach of post-transplant assistance will improve patient's survival and quality of their lives.

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Current challenges in transplantation procedures

EP_167 INCISIONAL HERNIA AFTER LIVER TRANSPLANTATION. OUR EXPERIENCE WITH TRANSVERSUS ABDOMED RELEASE FOR REPAIR

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Background: Incisional hernia is a common complication after liver transplantation (LT). Wall defects in this population are often complex due to extended incision and immunosuppression. Posterior Component Separation (PCS) with Transversus Abdomis Release (TAR) has been reported in limited series in LT recipients with good results.

Methods: We applied this technique at our center to treat complex incisional hernia in LT patients. From December 2023 to December 2024, 19 patients previously transplanted at our center underwent TAR with PCS (M = 17, F = 2). Fifteen patients had a previous Mercedes incision while 4 had a Makuuchi incision. Hernia have been classified according to the European Hernia Society Classification. Ten patients had both median (M) and lateral (L) defects. 12 had a width (W) > 10 cm and 7 had multiple “swiss cheese” W1 and W2 defects. Everolimus based immunosuppression was discontinued at least 15 days before surgery.

Results: In all the cases a 45 x 60 cm or 30 x 45 cm prothesis was placed over the posterior fascia (3 polipropilene and 16 polyvinylidene fluoride PVDF). Eight cases required an additional dual mesh prothesis due to the impossibility to close the posterior fascia while 2 required an additional polyglycolic acid prothesis reinforcement due to the thinness of the posterior fascia. We routinely placed 4 drainages on the prothesis that have been removed with an output <50 cc. All patients underwent an enhanced recovery protocol. Median in-hospital length of stay was 6 days. Complications were: 1 seroma, 1 bleeding treated conservatively, 1 prolonged ileus, 1 ascites. We did not have hernia recurrencies.

Conclusions: Our experience shows this technique can be safely used in LT patients with low incidence of complication and no recurrent hernia.

EP_168 IMMUNOBIOMARKERS AS EARLY PROGNOSTIC PREDICTORS AFTER LIVER TRANSPLANTATION

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Background: The use of biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR) and the neutrophil-to-platelet ratio (NPR), has shown promise in evaluating early outcomes after medical, interventional, and surgical treatments. NLR has emerged as an indicator of systemic inflammation and physiological stress. NPR has emerged as a potential indicator of inflammation and thrombotic risk in the context of surgical and radiological procedures. The aim of our study is to analyze the correlation of NLR and NPR with the development of post-LT early complications after stratification for HCC diagnosis.

Methods: Consecutive patients undergone LT between January 2019 and December 2023 were enrolled. Data regarding the concentration of hemoglobin and the differential leukocyte count on postoperative days (POD) 0, 1, 3, and 5 were collected.

Results: The dataset included 161 consecutive patients undergone LT. Clavien-Dindo IV-V complications had a good correlation with NLR I POD (p=0.05), NLR III POD (p<0.001), NLR VII POD (p<0.001), NPR III POD (p<0.001). In addition, the NPR ratio on POD III correlated with the onset of 30-day hemorrhage (p=0.009). Finally, 30-day mortality had a significant association with the NLR I POD (p=0.03) and with NLR VII POD (p=0.004), while NPR had a significant correlation with 30-day mortality in NPR VII POD (p=0.004).

Conclusions: The analysis of NLR and NPR are strictly correlated with Clavien-Dindo IV-V complications and 30-day post-LT death.

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Current challenges in transplantation procedures

EP_169 BILIARY COMPLICATION AFTER KEHR T-TUBE REMOVAL: PROGNOSTIC FACTORS AND RISK STRATIFICATION

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Background: The Kehr T-tube (T-tube) is a drainage placed inside the biliary tract during surgery. Subsequent removal can be performed by applying heterogeneous protocols with consequent variable complication rates. In our Center, there is a significant case history of T-tube placement and subsequent removal after liver transplantation (LTx). The aim of the work is to evaluate the prognostic factors of biliary complications after T-tube removal.

Methods: A retrospective analysis of patients who underwent T-tube placement and subsequent removal after LTx from January 2018 to May 2024 at our Center was performed. The clinical-demographic data of donors and recipients, transplant data, T-tube characteristics, and removal timing were collected. The endpoints analyzed were choleperitoneum requiring percutaneous drainage, choleperitoneum requiring endoscopic treatment (with ERCP), and hospitalization after T-tube removal.

Results: We analyzed 197 consecutive patients who underwent LTx. In 181 cases, the T-tube was positioned and subsequently removed. A post-removal biliary complication was recorded in 12% of cases, with an 8% rate of need for ERCP. The cohort of complicated patients had, compared to the uncomplicated patients, a longer median latency to T-tube removal (182 days vs. 166 days, p-value 0.04), a longer cold ischemia time after LTx (580 minutes vs. 420 minutes, p-value 0.038), and a higher rate of diagnosis of diabetes mellitus (42% vs. 24%, p-value 0.02).

Conclusions: The use of a T-tube is a practice still used in liver transplantation, with a variable rate of complications following its removal due to the different protocols adopted in the Centers. The identification of factors related to biliary complications after T-tube removal can determine an improvement of the Center protocols and promote a more rigorous follow-up in patients at risk of complications.

EP_170 SURGICAL COMPLICATIONS OF LIVING KIDNEY DONATION WITH DIFFERENT SURGICAL TECHNIQUES IN GERMANY

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Background: Safety and reduced physical impairment of the living donor is the main concern of surgeons and physicians treating living kidney donors.

Methods: We analyzed perioperative complications of different surgical techniques from the German living donor registry SOLKID-GNR including data from 1020 donors. Laparoscopic donor nephrectomy (LDN) was the most common technique (58%), followed by retroperitoneoscopic (RDN, 21%) and open retroperitoneal (ORN, 16%) donor nephrectomy. An open abdominal (OAN) approach was rare (5%).

Results: Perioperative complications within the first three months after donation occurred in 14.3, 9.8, 13.1 and 17.1%. This was not statistically different. Most common surgical complications were wound complications with 3.1%, followed by bleeding complications (2.6%). Bleeding with need for transfusions was more common in OAN (5.7%) compared to LDN (2.0%) and 0% in ORN and RDN (p=0.01), while complications according to anesthesia or positioning were more common in ORN (3.5%) compared to 0-0.7% in the other techniques (p=0.02). 3.3% of the donors experienced complications not related to the surgical technique. The only risk factor identified for perioperative complications was active or former smoking (p=0.04) while gender, age, BMI, side of nephrectomy and surgical technique had no impact on perioperative complications.

Conclusions: We conclude that with a complication rate of 13.3% living donor nephrectomy is a safe but not a complication-free procedure. All techniques used in Germany have comparable complication rates with former or active smoking being the main risk factor for a higher rate of complications.

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EP_171 INTESTINAL TRANSPLANTATION: AN UNDERUTILIZED PROCEDURE WITH OUTCOMES COMPARABLE TO OTHER SOLID ORGAN TRANSPLANTS

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Background: Intestinal (ITx) and multivisceral (MvTx, liver/stomach/pancreas/bowel) transplantation were traditionally reserved for patients with irreversible intestinal failure (IF) and severe complications from parenteral nutrition. The criteria for MvTx have broadened. These now include indications such as benign tumour excision requiring evisceration, need for liver transplantation with associated portomesenteric thrombosis, ... Although ITx is surgically and immunologically challenging, they remain the only life-saving option for well-selected patients. Herein, we analyzed the ITx results at a single-center between 10/2000-11/2024.

Methods: Continuous variables are reported with median (min-max). The study cohort includes 32 patients, with median follow-up of 5.03 (0.09-21.73) years. Categorical variables are reported in proportions (%) and compared with Fisher. Kaplan-Meier curves are used for survival rates, compared by Log-rank test.

Results: Of the 32 ITx, median age was 42 (2-62) years (5 children,16%), and sex ratio 1/1. Causes of IF were short bowel syndrome (SBS) (44%), dysmotility (22%), splanchnic thrombosis (16%), reTx (9%), microvillus inclusion (3%), tumor (3%), and liver Tx/frozen abdomen (3%). Graft types were 12 (38%) isolated intestine, 9 (28%) liver/intestine, 10 (31%) MvTx, and 1 (3%) modified MvTx (stomach/pancreas/bowel). Median ICU/hospital stay: 14 (2-70)/105 (55-680) days; acute rejection (AR): 47% (15/32); 1-/5-/10-yr patient and graft survival: 81%/74%/57% and 71%/67%/56%, respectively. In the last 10 yrs, 65% of ITx included liver (13/20 *vs.* 6/12 before, p=0.474). Liver-inclusive (LI) grafts (*vs.* non LI) had less AR (42% *vs.* 54%, p=0.720), no graft loss due to rejection (acute or chronic) (0% *vs.* 31%, p=0.02), and a 1-/5-/10-yr patient and graft survival of 73%/73%/64% (*vs* 92%/75%/45%, p=0.948) and 73%/73%/64% (*vs* 69%/61%/45%, p=0.525), respectively (Fig.1). The current waiting list counts 5 MvTx (no isolated intestine).

Conclusions: Outcome after ITx has become comparable to other life-saving organ Tx. Over the years, we observed an increase in liver-inclusive grafts, which appear to offer improved long-term outcome.

EP_172 ATTITUDES AND ACCEPTANCE AMONG LIVER TRANSPLANT RECIPIENTS FOR SELF-MEASURING WITH HOME-MONITORING (LASER-STUDY)

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Background: Liver transplant recipients (LTR) require lifelong aftercare, with frequent monitoring in the first year after transplantation. A home-monitoring system was introduced as part of standard aftercare with focus on self-measuring. Our objective was to investigate the LTR perspectives (attitudes, expectations and experiences) prior to initiation of home-monitoring and to assess the level of patient activation.

Methods: This prospective cohort study included all consecutive LTR between 1-6-2023 until 31-05-2024. Data from the baseline was analyzed for this study. LTR did not participate if there was language barrier or technical capability, or no informed consent was given. LTR were recruited during hospital admission after transplantation and prior to the introduction of the home-monitoring system. Participants were sent an online questionnaire based on Unified Theory of acceptance and use of Technology (UTAUT-32) and Patient Activation Measure (PAM-13) that was answered using a 5-point Likert scale (*0 = strongly disagree, 4 = strongly agree*). Socio-demographic and medical data were obtained from participants medical records. Correlation analysis was performed on both questionnaires.

Results: In total, 51 participants were included, of which 25 (*49%*) were female and median age was 56 years (*IQR 43-65*). 44 participants (*86%*) completed the baseline questionnaire. UTAUT-32 was divided into 7 domains: Expected load (*M=2.79±0.39*), Facilitating conditions (*M=3.08±0.49*), Social influence (*M=2.00±0.41*), Fear (*M=1.28±0.39*), Data Security (*M=1.5±0.24*), Self-Efficacy (*M=2.02±0.29*), Behavioral intention to use (*M=3.14±0.47*), and Informed & engaged (*M=2.29±0.44*). Patient activation was positively correlated with UTAUT-32 subscales Expected load, Facilitating conditions, Social influence, Behavioral intention to use, and Informed & engaged *r = .47 - .57, p <.001 (table 1)*. Between 1-4 measurements per day was seen as acceptable.

Conclusions: Prior to use LTR felt informed well and expressed willingness to use self-measuring for home-monitoring. Overall scores showed high trust and low fear. Prospective data collection is ongoing and will assess how use over time influences perspective.

Table 1: Pearson correlation: PAM-13 compared to UTAUT-32 domains

Baseline		Informed & Engaged	Behavorial intention to use	Fear	Data Security	Facilitating conditions	Social Influence	Expected Load
PAM-13	Pearson Correlation	0,522	0,558	0,027	0,124	0,545	0,468	0,576
	Sig. 2-tailed	<0,001	<0,001	0,862	0,421	<0,001	0,001	<0,001
	N	44	44	44	44	44	44	44

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Current challenges in transplantation procedures

EP_173 KIDNEY AUTOTRANSPLANTATION: INTEGRATING COMPREHENSIVE LITERATURE INSIGHTS WITH SINGLE-CENTER EXPERIENCE.

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Background: Kidney autotransplantation (KAT) is an advanced surgical solution for complex renal and ureteral pathologies, offering favorable outcomes and improved symptom relief in cases where conventional treatments fail to address anatomical or functional challenges effectively. Recent advancements in robotic surgery have expanded KAT's indications, enhancing patient outcomes. This study combines a literature review with a single-center cohort analysis to evaluate KAT's clinical utility, safety, and therapeutic outcomes.

Methods: This review of current literature focused on KAT's indications, surgical innovations, and outcomes, emphasizing renal function preservation, symptom resolution, and complications. A retrospective analysis of 13 patients treated at the University of Florida was conducted. Indications included ureteral disorders (62%), reflux-related pain (23%), renal tumors (8%), and Nutcracker syndrome (8%). Manifestations included acute kidney injury, hydronephrosis, recurrent infections, flank pain, and urosepsis. Laterality of the transplants predominantly involved the left side, accounting for 77% of procedures. Robotic-assisted nephrectomies were performed in 23% of cases, while laparoscopic nephrectomies constituted the remaining 77%.

Results: The literature supports KAT as effective for renovascular hypertension, complex ureteral injuries, and selected oncological cases. In our cohort, stable renal function was seen postoperatively in all patients with ureteral strictures and tumors. Nutcracker syndrome symptoms resolved completely, and 67% of chronic-flank pain cases showed significant improvement. Complications occurred in 31% of patients: Clavien-Dindo I (8%), II (15%) and IIIb (8%). These rates are lower than those reported in similar studies. 69% of patients experienced no postoperative complications. Notably, there was no 30-day mortality.

Conclusions: KAT is a safe and effective option for complex renal pathologies, achieving favorable outcomes and symptom relief in carefully selected patients. Multicenter studies are essential to refine patient selection, standardize protocols, and analyze long-term outcomes to enhance KAT's role in clinical practice.

EP_174 STAPLED VERSUS SUTURED SIDE-TO-SIDE INFERIOR VENA CAVA ANASTOMOSIS DURING ORTHOTOPIC LIVER TRANSPLANTATION

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Background: Stapled side-to-side cavo-caval anastomosis (STSCCA) during OLTx is a novel approach that is an evolution of a sutured side-to-side cavocavostomy. The technique is feasible which was shown in animal studies and small series in human but experience is limited. This study aims to assess safety and early postoperative outcomes of the study cohort and matched subjects transplanted with sutured STSCCA. This is the largest series of patients with stapled inferior vena cava (IVC) anastomosis to date.

Methods: A retrospective analysis was performed among patients selected form a cohort of 562 recipients who underwent OLTx between January 2022 and September 2024 at the Department of General, Transplant and Liver Surgery, Medical University of Warsaw. 110 patients who underwent OLTx with preservation of the IVC and stapled STSCCA were identified and matched to patients with sutured anastomosis. Propensity score matching with 1:1 case to control ratio was done for reduction of bias. Patients after conventional IVC anastomosis and retransplantations were excluded from the study. Perioperative and early postoperative outcomes were analyzed using Mann-Whitney U test for continuous variables and chi2 test for categorical variables, and $p<0.05$ were considered statistically significant.

Results: No intraoperative complications related to the use of stapler were observed. Median IVC clamping time was 9.5 (1.5-45) minutes. Stapled and sutured groups did not differ significantly in median warm ischemia time (68 vs 65 minutes, p 0.96), postoperative mortality (1.8% vs 6.3%, p 0.09), reoperation rate (18.2% vs 24.8%, p 0.24), endoscopic interventions for bile leak (12.7% vs 16.6%, p 0.4), anastomotic venous outflow alterations on the first postoperative day (12.7% vs 11.8%, p 0.9) and Clavien-Dindo score >2 (57.2% vs 52.7%, p 0.5). A decrease of IVC clamping time and ischemia time was noted during the development of the technique.

Conclusions: Stapled side-to side cavocavostomy is as safe and reliable as traditional sutured anastomosis. Refinement of the technique results in shorter implantation time and improved quality of the anastomosis which may positively influence outcomes of OLTx and make stapled IVC anastomosis a resonable alternative to the standard technique.

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EP_175 UTILITY OF THE REVISED CARDIAC RISK INDEX FOR PERI-OPERATIVE RISK ASSESSMENT AFTER KIDNEY TRANSPLANTATION

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Background: The revised cardiac risk index (RCRI) was designed for peri-operative risk assessment before elective major non-cardiac surgeries, but it is unclear if it allows differentiation of risk after kidney transplant surgery.

Methods: Data was retrospectively extracted from hospital informatics systems for all kidney transplant recipients at a single centre between 2007-2020. Electronic patient records were manually searched, and records linked to various sources (e.g., NHS Blood and Transplant, Hospital Episode Statistics, national death registry). RCRI scoring was based upon six variables: 1) pre-operative ischaemic heart disease, 2) pre-operative stroke, 3) pre-operative heart failure, 4) pre-operative insulin dependent diabetes, 5) major surgery, and 6) creatinine >2g/dl (177 mmol/l). By default, kidney failure patients undergoing kidney transplant surgery score 2/6 as a minimum. Summary statistics were obtained of the study cohort. Logistic regression (for length of stay and emergency re-admission within 90-days) and Cox regression (post-op MACE and post-op mortality) was utilised to explore the relationship of RCRI with post-op outcomes adjusted against age, sex, ethnicity, time on waiting list and donor type.

Results: Data was extracted for 2,041 kidney allograft recipients. In our cohort, 68 post-operative MACE events were observed during the index admission after kidney transplant surgery – from these 42 (61.8%) died during subsequent follow up compared to only 14.4% experiencing death in the cohort not experiencing post-operative MACE. In multivariable analysis, RCRI was associated with length of stay (Odds Ratio 4.17, 95% CI 2.00-8.70, p<0.001), post-op MACE (Hazard Ratio 1.50, 95% CI 1.29-1.74, p<0.001) and post-op mortality (Hazard Ratio 1.52, 95% CI 1.31-1.77, p<0.001) but not emergency re-admission rates within 90-days of surgery (Odds Ratio 1.17, 95% CI 0.97-1.41, p=0.107).

Conclusion: The RCRI identified kidney transplant candidates at increased risk for post-surgery MACE. However, the utility of the RCRI as a tool to identify high-risk kidney transplant candidates as a sum greater than its individual component parts is unclear in a real-world setting.

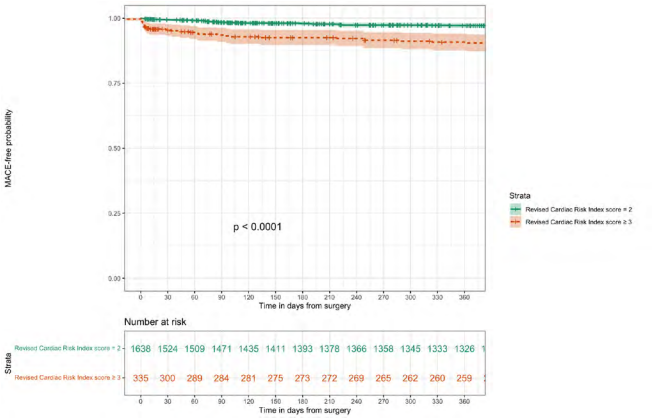

Figure. Unadjusted Kaplan-Meir plot of survival post kidney transplant stratified by baseline RCRI score

EP_176 INCIDENCE OF, PREDICTORS FOR AND OUTCOMES FOLLOWING PRIMARY GRAFT DYSFUNCTION AFTER CARDIAC TRANSPLANTATION

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Background: Failing function of the newly transplanted heart is the leading cause of early morbidity and mortality after heart transplantation (HTx). This condition can affect the left, right, or both ventricles, with varying degrees of severity. This study aimed to determine the incidence of primary graft dysfunction as defined by the International Society for Heart and Lung Transplantation (ISHLT) criteria and identify predictors and impact of PGD on both short-term and long-term outcomes in a single center.

Methods: A total of 830 consecutive patients that underwent a HTx in our center between 1984 and 2021 were retrospectively reviewed. After exclusions for age <18 years, (n=103) or missing data, n=60) the main analysis included 667 (80.4%) adult patients. Medical records were examined for pre-, intra- and post-operative data with focus on the 24 hours post transplantation and long-term survival. The ISHLT primary graft dysfunction classification criteria were applied except for mild PGD.

Results: Of the 667 patients, 70 (10.5%) fulfilled criteria for PGD whereof 41 (6.1%) had left ventricular (LV) PGD and 29 (4.3%) right ventricular (RV) PGD. Among those with PGD-LV, 5 cases (12%) exhibited moderate PGD-LV, while 36 cases (88%) demonstrated severe PGD-LV. Patients with PGD were younger (46 vs 50 years, p=0.03), and more often had pretransplant dialysis, a ventricular assist device (VAD) or previous cardiac surgery. No donor factor was associated with PGD but duration on by-pass during the transplant procedure was. Patients with PGD had longer post-operative duration of mechanical ventilation and ICU stay. This cohort also more frequently had a postoperative mechanical circulatory support, continuous renal replacement therapy, repeated surgery and sepsis. Mortality or re-transplant occurred more frequently in patients diagnosed with PGD both at 30 days (n=30 [45%]) vs without PGD (n=19 [3%]) and after one year (n=34 [51%]) vs (n=44 [8%]) (HR for 1-year follow-up 6.89 (95% CI 4.01 to 11.83), p<0.0001).

Conclusions: In this single center experience, primary graft dysfunction following HTx was related to poor prognosis in terms of both 30-day and 1-year survival. Recipient related risk factors such as age, pre-transplant VAD, and previous cardiac surgery were related to PGD while donor related variables were not.

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EP_177 PROLONGED COLD ISCHEMIA TIME IN PANCREAS TRANSPLANTATION YIELDS SIMILAR OUTCOMES COMPARED WITH STANDARD OF CARE OUTCOMES

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Background: Overall number of deceased donor pancreas transplant have decreased overtime, and the rate of nonuse pancreas have reached its highest at 28.6% in 2022. There are many reasons for nonuse pancreas, with newer allocation schemes, broader organ sharing, increase ischemia times, decrease risk tolerance and lack of center/surgeon expertise playing a role. We aim to evaluate our single center experience on the use of pancreas with prolonged cold ischemia time (CIT) and outcomes. Standard of care is to place the pancreas within 12 hours(hrs) of CIT. We report our single-center experience in the use of pancreas with over 12hrs of CIT.

Methods: Single center retrospective review of all simultaneous kidney/pancreas (SPK) and pancreas transplant alone (PTA) from January 2014 to September 2023 with at least 6m of follow up. Pancreas graft failure was defined as allograft pancreatectomy or recipients' fully dependency of insulin and/or c-peptide levels <2.0 ng/ml.

Results: We had 190 SPK/PTA recipients during the study period, we divided them by less or more than 12hrs of pancreas CIT.Table1. Shortest CIT was 3.5hrs and longest was 23hrs, significantly higher among the groups (p<0.001). Enteric-drained recipients were more likely to have CIT<12hrs and bladder-drained more likely to have >12hr CIT (p<0.00001). Table2: Mean follow-up was longer in the group with >12hrs CIT, 5yrs vs 2.8 yrs (p=0.03). Patient survival was lower among the group with CIT>12hrs (p=0.007). However, there were no difference in pancreas graft survival among the groups. A1C, c-peptide and fasting blood glucose was similar up to 5yrs of follow-up.

Conclusions: In the current environment of high nonuse rate for pancreas transplantation, allowing longer pancreas CIT and total pancreas preservation time, may increase the rates of pancreas transplantation. We are evaluating our outcomes with regards to post-op complications, enteric leak, intra-abdominal abscess and length of stay, between both groups, under and longer than 12hrs CIT.

Table 1: Baseline Characteristics.

	Pancreas CIT <12 hours (n = 155)	Pancreas CIT >12 hours (n = 35)	P values
Recipient Mean Age	42	43	0.977
Male n (%)	**81 (52.3%)**	**25 (71.4%)**	**0.0394**
Race/Ethnicity n (%)			
Black	36 (23.2%)	9 (25.7%)	0.757
Hispanic	81 (52.3%)	17 (48.6%)	0.697
White	38 (24.5%)	9 (25.7%)	0.881
Mean (range) **CIT Pancreas (hours)**	**8.7** (3.5 - 12)	**16** (12 - 23)	**<0.001**
Mean (range) **Total Pancreas Preservation time (hours)**	**9.17** (3.90 - 13.13)	**16.29** (8.52 - 23.48)	**<0.001**
Recipient Mean C-peptide	1.04	0.884	0.282
Recipient Mean A1C (%)	7.8	7.6	0.176
Recipient Mean BMI	25.25	25.99	0.102
Drainage Type			
Enteric	**133 (85.8%)**	**8 (22.9%)**	**<0.00001**
Bladder	**22 (14.2%)**	**27 (77.1%)**	**<0.00001**

Table 2: Recipient Post Transplant Characteristics.

	CIT <12 hours	CIT >12 hours	P value
Mean (range) **follow up (years)**	**2.8** (0.5 - 8.8)	**5** (0.5 - 9.0)	**0.030**
Patient Survival	**95.5%**	**82.9%**	**0.007**
Pancreas Graft Survival	93.5%	100%	0.124
Mean A1C (%) at 3 months	5.0	5.2	0.318
Mean C-peptide at 3 months	4.21	4.00	0.635
Mean FBG at 3 months	90	89	0.808
Mean A1C (%) at 6 months	**5.0**	**5.7**	**0.088**
Mean C-peptide at 6 months	3.96	3.59	0.986
Mean FBG at 6 months	95	93	0.931
Mean A1C (%) at 1 year	5.0	5.5	0.217
Mean C-peptide at 1 year	3.77	3.14	0.141
Mean FBG at 1 year	93	90	0.650
Mean A1C (%) at 5 years	5.8	5.4	0.197
Mean C-peptide at 5 years	**2.54**	**4.30**	**0.008**
Mean FBG at 5 years	90	97	0.188

*FBG = Fasting Blood Glucose

EP_178 DACRON VASCULAR GRAFTS: A LONG-TERM SOLUTION FOR SHORT RENAL VEIN CHALLENGES IN LIVING DONOR KIDNEY TRANSPLANTATION

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Background: In living donor kidney transplantation, short renal veins pose significant technical challenges during graft placement and vascular anastomosis. Many surgeons have traditionally avoided using artificial grafts for vein extension due to concerns of infection and thrombosis. However, we share our experiences using Dacron vascular grafts (Hemagard, Maquet, Germany) for renal vein extension with long-term safety and efficacy.

Methods: We retrospectively reviewed cases of living donor kidney transplantation performed at Seoul National University Hospital from 2016 to 2024 where Dacron vascular grafts were employed for renal vein extension. Patient demographics, comorbidities, and laboratory data were evaluated. The size of Dacron grafts was selected based on the anatomical requirements. Patients were postoperatively prescribed antiplatelet therapy to support vascular patency. Imaging follow-up using sonography was performed before discharge.

Results: A total of 11 patients underwent renal vein extension using Dacron vascular grafts. Among them, 5 were male and 6 were female, with a mean age of 50.1±16.2 years and a mean BMI of 24.7 ± 3.2 kg/m^2. Nine cases involved the donor's right kidney, while two involved the left kidney. The average diameter of the used Dacron graft was 12 mm. At the time of discharge, the mean serum creatinine (Cr) level was 1.19±0.3 mg/dL, and the mean estimated glomerular filtration rate (eGFR, CKD-EPI) was 63.6±7.9 mL/min/1.73m^2. The average follow-up duration was 42.5±28.5 months. One case required reoperation on postoperative day 2 due to bleeding unrelated to graft. No additional complications were reported in the remaining cases. All patients underwent imaging follow-up within the first postoperative week, without thrombosis or stenosis. Vascular patency was excellent in all cases during follow-up periods, except for one patient who died of pneumonia 18 months postoperatively and another who experienced graft failure due to IgA nephropathy recurrence 46 months after transplantation.

Conclusions: The usage of Dacron vascular grafts for short renal vein extension is a reliable and effective technique in living donor kidney transplantation, with favorable long-term safety and efficacy.

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EP_179 THE OUTCOMES OF THE DECEASED DONOR KIDNEY TRANSPLANTTION IN THE PATIENTS WITH THE HEART DISEASE

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Background: Patient with end stage renal disease (ESRD) have various heart diseases. The result of deceased donor kidney transplantation (DDKT) performed in these patents are difficult to predict. Therefore, we would like to investigate the results of DDKT performed in ESRD patients with heart disease.

Methods: Between March 2011 and Sep. 2024, 111 patients underwent DDKT at the department of surgery at Konyang university hospital, Daejeon, Korea. We compared two groups according to heart disease history: no heart disease group (n=83), heart disease group (n=28). The following characteristics were evaluated retrospectively through the medical records.

Results: The 5-year patient survival in the no heart disease group was higher as 95.6% compared to 85.2% of the heart disease group (P = 0.037). But, the 5-year graft survival were 94.8% and 92.9% in the no heart disease group and heart disease group (P = 0.900) retrospectively. The eGFR level by period of recipients was significantly differentiated between both groups (1week: 60.3±27.2ml/min vs. 48.2±27.7ml/min, P=0.027, 36 months; 81.2±23.6ml/min vs. 68.2±21.0ml/min, P=0.021). However, hospital stays day, operation time and complication rates were not significantly differentiated between the two groups.

Conclusions: According to the results of this study, kidney transplantation in patients with heart disease should be decided after careful consideration of the patient's condition before surgery.

EP_180 OBESITY IS NOT A BARRIER TO DECEASED DONOR RENAL TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Background: Obesity rates in end-stage renal disease (ESRD) are increasing. There is no national consensus in the UK limiting body mass index (BMI) for renal transplantation (RT) however, the perception of increased adverse outcomes and technical difficulty may limit access to RT for those with the highest BMIs. We aimed to analyse outcomes from a high BMI recipient cohort to add to the discussion surrounding optimal patient selection in this high-risk demographic

Methods: Retrospective analysis was performed comparing adult deceased donor (DD) RT recipients with a BMI cut off at 35 kg/m^2 at a single centre (2022-2023). Recipient, donor, outcome and survival data were analysed using non-parametric tests and Kaplan Meier analysis.

Results: Of the 345 DD recipients who underwent RT, 36 (11.7%) had BMI > 35 kg/m^2 (range 35-41). Recipient demographics were comparable, with the high BMI group receiving less expanded criteria donor (ECD) kidneys (33% vs 50%). The high BMI group had a longer anastomosis time (49 minutes (41-59, IQR) versus 43 minutes (36-50, IQR) p<0.001, and were more likely to require critical care admission (p=0.022) but had similar complication rates (Table 1) with only wound infection (p=0.009) being significant. Graft survival (p=0.7, logrank) and patient survival (p=0.4, logrank, Fig.1A) were statistically equivalent. Our high BMI cohort included 11 (30.5%) aged > 60 years who all received ECD kidneys. There were no significant differences in early complications, with a non-significant reduction in survival compared to recipients > 60 years with a BMI < 35 kg/m^2 (p=0.09, logrank, Fig.1B).

Discussion: This study highlights that obesity is not a barrier to successful transplantation if combined with careful donor and recipient selection and with effective perioperative support in place. With the advancement of robotic assisted techniques, transplantation for morbidly obese patients may become more accessible in the future. Further studies including frailty and comorbidity parameters will help us better understand the feasibility of transplantation, especially in elderly, obese cohorts.

Characteristic	BMI < 35, N = 309	BMI > 35, N = 36	p-value
Admission to Critical Care	33 (11%)	10 (28%)	**0.022**
Length of Stay	9 (6, 15)	10 (6, 16)	0.8
Primary Function	152 (49%)	17 (47%)	0.8
Primary Non-Function	10 (3.2%)	1 (2.8%)	>0.9
Delayed Graft Function	145 (47%)	18 (50%)	0.7
Duration of DGF	9 (6, 14)	10 (7, 10)	0.8
30-Day Mortality	4 (1.3%)	0 (0%)	>0.9
1-Year Survival	293 (95%)	34 (94%)	>0.9
30-Day Graft Loss	12 (3.9%)	3 (8.3%)	0.4
1-Year Graft Survival	280 (92%)	31 (89%)	0.5
Graft Thrombosis	2 (0.6%)	0 (0%)	>0.9
Bleed/Haematoma	40 (13%)	5 (14%)	0.8
Re-Exploration	15 (4.9%)	2 (5.6%)	0.7
Wound Infection	5 (1.6%)	4 (11%)	**0.009**
Wound Dehiscence	3 (1.0%)	1 (2.8%)	0.4
Collection	4 (1.3%)	2 (5.6%)	0.12
Urine Leak	1 (0.3%)	0 (0%)	>0.9
Ureteric Stricture	3 (1.0%)	0 (0%)	>0.9
Renal Artery Stenosis	9 (2.9%)	2 (5.6%)	0.3
Incisional Hernia	11 (3.6%)	2 (5.6%)	0.6

Median (IQR); n (%)
Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Table 1: Outcomes following deceased donor kidney transplantation compared by recipient BMI (cut off 35 kg/m^2)

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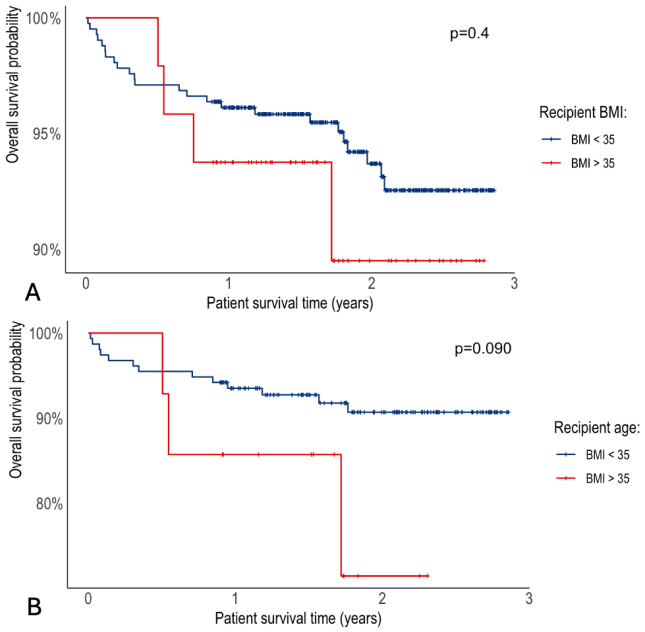

Figure 1: Kaplan Meier analysis of patient survival comparing deceased donor kidney transplant recipients stratified by BMI - (A) entire cohort, (B) recipients aged > 60-years.

EP_181 IMPACT OF INCORRECT VOLUMETRY ON RECIPIENT OUTCOME AFTER LDLT - HIGHER ACCURACY BY USING VOLUMETRY-ASSIST SOFTWARE

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Background: Liver transplantation (LT) is an established treatment for patients with end-stage liver disease. Due to the shortage of suitable organs living donor liver transplantation (LDLT) has emerged as an alternative. Assessing the size of the liver graft through preoperative volumetry is essential for the outcome after LDLT. While the current standard is manual CT-volumetry (MV), the use of volumetry-assist software (VS) may replace the previous routine. In this study, we analyzed whether VS is superior to MV in terms of accuracy and thus may improve postoperative outcomes.

Methods: We conducted a retrospective analysis of 133 LDLTs, which were performed at University Hospital Regensburg from 2004 to 2021. Recipients were assigned to a pediatric (age < 15 years) and an adult (age ≥ 15 years) cohort. Both cohorts were then subdivided by graft-recipient-weight-ratio (children: GRWR ≤ 4 vs. > 4, adults: GRWR < 0.8 vs. ≥ 0.8) to compare postoperative outcomes. Additionally, volumetric assessment by VS using Syngo.via Liver Analysis (Siemens Healthineers) was performed blinded. For both pediatric and adult LDLTs, we investigated whether an unfavourable GRWR, not detected by preoperative MV, could have been accurately represented by VS.

Results: In children (n = 100), significantly higher rates of abdominal compartment, delayed wound closure, postoperative sepsis and extended treatment period were seen for a GRWR > 4 (n = 34). This was due to an underestimated MV in 13 cases (38.2%), whereas in 69.2% of these a correct result would have been achieved using VS. In contrast, a significant increase in hepatic artery thrombosis, portal vein thrombosis and liver failure was observed in adults (n = 33) with a GRWR < 0.8 (n = 6). Four cases (66.7%) were caused by an overestimated MV, of which 50% would have been measured correctly with VS. Overall, MV was correct in 35.3% of the cases (n = 47), while VS measurement achieved an accurate result in 66.9% of the cases (n = 89).

Conclusions: Our study confirmed a higher accuracy by using VS compared to currently common MV. This approach may reduce the incidence of postoperative complications, particularly due to underestimated volumes in children resulting in a large-for-size graft with a GRWR > 4 and overestimated volumes in adults with a GRWR < 0.8 representing a small-for-size transplantation.

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Current challenges in transplantation procedures

EP_182 NOVEL APPROACH OF SPLIT LIVER ON HOPE

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Background: Liver splitting is an integral part of liver transplant training and essential for a pediatric liver transplant program. Prolonged static cold ischemia for the right lobe is a constant challenge and may lead to inferior graft outcomes.

Methods: We present our simplified technique of splitting the liver (through video demonstration) and share our experience of splitting the liver on Hypothermic Oxygenated Machine Perfusion (HOPE)

Results: Total of six liver were transplanted after resection on HOPE. We performed 3 Splits and 1 reduction. One right lobe graft was rejected by another center in term of prolonged cold ischemia time. Splitting can be done in 6 simple steps 1) Identifying hepatic vein anatomy 2) Identify hepatic artery and division of left hepatic artery 3) Bile duct anatomy and division 4) parenchymal division 5) Caudate resection 6) Cut surface check and portal vein division. All 6 grafts did very well in post-transplant period with no post-reperfusion syndrome. Median peak ALT was 683 IU/L with median ICU stay for 13 days. None of the grafts encounter any biliary or vascular complications. We did not encounter any graft loss or patient loss during this case series

Conclusions: Splitting liver of HOPE can be easily done using our standard and simple technique. HOPE- Split leads to good patient and graft survival.

EP_183 ADULT-TO-ADULT RIGHT LOBE GRAFT LIVING DONOR LIVER TRANSPLANTATION FOR VIETNAMESE ACUTE-ON-CHRONIC LIVER FAILURE

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Background: Acute-on-chronic liver failure (ACLF) has a high mortality rate, and liver transplantation is considered a definite treatment for patients with this condition. This study aims to evaluate the outcomes of living donor liver transplantation (LDLT) in ACLF patients in a single centre in a lower middle-income country, Vietnam.

Methods: This was a retrospective study at the 108 Military Central Hospital (Hanoi, Vietnam), enroling 51 patients diagnosed with ACLF based on Asian Pacific Association for the Study of the Liver (APASL) criteria who underwent LDLT with a right lobe graft from December 2019 to December 2022. The authors utilize the model for end-stage liver disease (MELD) and APASL ACLF Research Consortium (AARC) scores to evaluate and stratify the severity of ACLF.

Results: The average age of all patients was 47.27±13.61, with 88.24% being male. The average BMI was 22.78±2.61. The most common underlying liver disease was chronic viral hepatitis B (88.2%). The average MELD score of the patients was 34.90±5.61, with 33.3% having MELD score greater than or equal to 40. In terms of ACLF severity, five patients (9.8%) had grade I ACLF, 35 patients (68.6%) had grade II ACLF, and 11 patients (21.6%) had grade III ACLF. The average AARC score was 9.43±1.68. The duration of treatment in the ICU was 8.59±7.27 days, and the length of hospital stay was 28.02±13.45 days. The most common post-transplant complication was biliary complication (19.61%). Death occurred in 7 patients (13.7%). The survival rates at 6 months, 1 year, and 3 years were 84%, 81.7%, and 81.7%, respectively.

Conclusion: Living donor liver transplantation for ACLF patients is safe and has a high post-transplant survival rate. Multidisciplinary care before, during, and after surgery, and the decision to do a liver transplant early, is essential in saving the lives of ACLF patients.

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Current challenges in transplantation procedures

EP_184 SINGLE ORIFICE OUTFLOW RECONSTRUCTION IUN RIGHT LOBE GRAFT LIVING DONOR LIVER TRANSPLANTATION

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Background: Outflow reconstruction is one of the key requirements of a successful living donor liver transplantation. The aim of study is to evaluate the technical characteristics and outcomes of single orifice outflow reconstruction in living donor liver transplantation using right lobe graft in a center in Vietnam.

Methods: The prospective study was performed on 52 cases of living donor liver transplantation using right lobe graft at 108 Military Central Hospital from January 2019 to December 2020. Polyester prostheses were used in reconstructing the MHV when the remnant liver volume was less than 35% of the donor liver volume. Venous branches with diameter ≥ 5mm were preserved and anastomosed to the prosthesis.

Results: There were 42 cases of using the extended lobe living donor liver transplant (80.8%) and 10 cases of the modified right lobe graft. We conjoined the MHV and RHV as a single orifice hepatic vein. A total of 15/52 accessory right inferior HV with diameter > 5 mm were anastomosed directly to inferior vena cava (IVC) in an end-to-side fashion in recipient (28.8%). There were 1 cases of middle hepatic vein obstruction (1.9%). The mortality rate of hepatic venous outflow obstruction was 1,9%. The caliber of HV anastomosis (< 30 mm) was an independent risk factor for hepatic venous outflow obstruction.

Conclusions: The single orifice hepatic vein reconstruction in LDLT using a right lobe graft is a simple and feasible surgical technique, and it does not require cadaveric vessels.

EP_185 COMPARATIVE STUDY OF LIVING DONOR KIDNEY TRANSPLANTS: RIGHT VS LEFT

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Background: Transplant teams often hesitate to use the right kidney (RK) in living donor (LD) transplants due to the complexities of anastomosing the short, thin-walled right renal veins, which can potentially lead to graft loss or graft dysfunction. Nevertheless, circumstances may arise where selecting the RK over the left kidney (LK) is unavoidable. Consequently, it is crucial to thoroughly examine the implications of such a choice on the overall transplant outcome.

Methods: We retrospectively analyzed data from adult patients who received LD kidney transplants involving meticulous patient selection and surgical techniques at our center from January 2020 to December 2023. We included all kidney donors who were over 18, fit to donate, and had undergone diethylenetriamine pentaacetic acid split function and/or computed tomography based volumetry. The variables examined comprised donor and recipient demographics, and outcome measures included technical graft loss (TGL), delayed or slow graft function (SGF), and post-transplant serum creatinine (SC) trends. We used a logistic regression model to assess the likelihood of adverse outcomes considering the donor kidney side.

Results: Of the 250 transplants performed during the period, 56 (22%) were RKs. The recipient demographics and transplant factors were comparable for the right and LKs, except that the donor warm and cold ischemia time were shorter for RKs. TGL and SGF each occurred in 2% (n = 1) of RKs and 0.5% (n = 1) of LKs, the difference being insignificant. These complications, however, were not related to the venous anastomosis. One RK (2%) developed delayed graft function after 48 hours, which was attributable to postoperative hypoxia rather than the surgical technique. The post-transplant SC trend and mean SC at the last follow-up were similar across both kidney sides

Conclusions: The donor kidney side has little impact on post-transplant adverse events and graft function in LD transplants, provided that careful patient selection and precise surgical techniques are employed.

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EP_188 MANAGEMENT OF A ACUTE COMPLICATION OF A BRACHIOCEPHALIC ARTERIOVENOUS FISTULA IN AN ADOLESCENT

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Background: The primary arteriovenous fistula is the standard vascular access for end stage renal disease (ESRD) patients requiring long term hemodialysis (HD). The Primary fistulas suggested in AVF include radiocephalic fistula (RCF), brachiocephalic fistula, (BCF) and basilic vein transposition (brachial-basilic) fistula. A major problem with these AVFs is the high frequency of primary failures, either due to lack of maturation or early thrombosis. We are describing the management of an acute complication of the braciobasilic AVF with transposition in an adolescent.

Methods: A 14year female with ESRD was on MHD via left radiocephalic AVF. She presented to us with left RCF thrombosis. After thorough clinical and radiological evaluation, it was found that left cephalic vein was thrombosed. Left basilic vein diameter was around 2.8mm at albow. Left brachiobasilic avf with basilic vein transposition was done with good thrill till axilla. On next day morning, there was no thrill or bruit. Color doppler showed no flow in basilic vein and a thrombus in basilic vein from elbow for 5cm, there was 1cm thick subcutaneous hematoma.

Results: On re-exploration, a large hematoma in subcutaneous space around basilica vein (Fig. 1a) evacuated. Basilic vein showed thrombus (Fig. 1b). Brachial artery control taken proximally and distally. A small venotomy done on basilica vein. Using 3Fr fogarty catheter, thrombectomy done and vein irrigated with heparin saline. Proximal clamp released temporarily to check flow. There was free flow of blood from venotomy site. Venotomy closed with 7-0 prolene. Clamps released, there was thrill present in basilica vein. Incision closed in layers. Once this vein matured, she was started on MHD through this access.

Conclusions: A timely postoperative diagnosis and management can save the vascular access from such complications.

Figure 1 a) A large subcutaneous hematoma around basilica vein. b) A thrombus in the basilic vein

EP_189 BUILDING BRIDGES BETWEEN AUTHORITY AND HEALTHCARE PROFESSIONALS - A KEY TO DEVELOPING NATIONAL GUIDELINES

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Background: In 2023, the Swedish National Board of Health and Welfare received a government assignment aimed to ensure that education and knowledge regarding the organ donation process were consistent across the country, regardless of hospital size or location. The target group for the national guideline was healthcare professionals working in hospitals where potential organ donors could be identified.

Methods: The project applied a Participatory Action Research (PAR) approach as an implementation strategy, emphasizing the value of experiential knowledge to address practical challenges and facilitate change. PAR involves the active participation and leadership of those directly affected by an issue, generating new knowledge and driving improvements in systems and practices. Throughout 2024, the project team worked at national, regional, and local levels to identify key action points and address challenges faced by healthcare professionals in the organ donation process. The initiative included six national meetings, 18 regional face-to-face meetings, and two national congresses with broad representation. Additionally, a referral process involving approximately 150 stakeholders provided valuable feedback before the final publication. All input was carefully evaluated and adapted to meet the specific needs of healthcare professionals.

Results: On December 9, 2024, the National Board of Health and Welfare launched “Donationsguiden,” a digital platform for organ donation available both as an app and a web solution. “Donationsguiden” implemented itself after a soild anchoring during the project period and created more than 1500 downloads at Appstore during the first week, and the platform had an activity with around 1200 actions per day – without any further publicity.

Conclusions: It seems that the key point were the bridges that were built in an early stage and throughout the project. Next step in Sweden will be to publish a National Action plan for both organ- and tissue donation – managing the same principal – with cooperation and participation at all levels during the project time. These two measures will hopefully lead to more lifesaving transplantations in Sweden through more identified organ donators.

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Current challenges in transplantation procedures

EP_190 IMPACT OF RENAL ARTERY NUMBER ON EARLY AND MID-TERM OUTCOMES IM LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Multiple renal arteries in kidney grafts present technical challenges in living donor transplantation. This study aimed to evaluate the impact of single versus multiple renal arteries on early and mid-term postoperative outcomes

Methods: A total of 245 living donor kidney transplant recipients from June 2022 to December 2024 were analyzed. Patients were divided into two groups: single artery (n=190) and multiple artery (n=55). Demographic characteristics, creatinine levels, GFR, dissection time, warm ischemia time, and SGF rates were compared between the groups. Statistical analysis included the Independent t-Test for normally distributed variables and the Mann-Whitney U Test for non-normally distributed variables. A p-value of <0.05 was considered statistically significant.

Results: The single artery group comprised 125 females and 65 males, with a mean age of 42.31 ± 14.3 years, BMI of 27.72 ± 4.5, and follow-up of 10.24 ± 8.67 months in recipient. The multiple artery group included 19 females and 36 males, with a mean age of 42.6 ± 14.8 years, BMI of 26.5 ± 5.8, and follow-up of 9.81 ± 8.52 months in recipient. No significant differences were found between the groups in 5th-day creatinine levels, final creatinine levels, 5th-day GFR, final GFR or SGF rates (p>0.05). However, warm ischemia time and donor surgical dissection time were significantly higher in the multiple artery group (p=0.0001).

Conclusions: Our study demonstrates that the presence of multiple arteries does not adversely affect early and mid-term postoperative outcomes, and the technical challenges associated with multiple artery grafts can be effectively managed without compromising graft function in the early postoperative period. Therefore, the presence of multiple renal arteries should not be considered a contraindication for living donor kidney transplantation, provided that the surgical team is experienced in handling these complex cases.

EP_191 FACTORS INFLUENCING DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANTATION A FIVE-YEAR ANALYSIS

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Background: Delayed graft function (DGF) is a frequent complication in kidney transplantation, particularly among recipients of deceased donors, that can adversely affect graft survival. This study analyzed kidney transplantations performed at a single center over a five-year period, to investigate factors associated with the occurrence of DGF.

Methods: A single-center retrospective cohort study included 139 deceased donor (DD) and living donor (LD) kidney transplants performed between 2019 and 2024. Data collected included donor and recipient characteristics, HLA compatibility, time on dialysis, cold ischemia time (CIT), and hematological indices, such as Absolute Neutrophil Count (ANC), Absolute Lymphocyte Count (ALC), and Absolute Monocyte Count (AMC), before and one-day post-transplant. Statistical methods, chi-square tests, and logistic regression were employed to identify risk factors associated with DGF.

Results: A total of 139 kidney donors with a median age of 55.5 [46.9, 63.3] were included. Deceased donors accounted for 79.1% (110/139). The recipients' median age was 53 [45, 59]. DGF was significantly more prevalent among DD kidney recipients (68.2%), compared to LD recipients (chi-square, p=0.003). Each additional year of substitution therapy before transplantation increased the risk of DGF by 11.9% (p=0.022). Logistic regression also identified prolonged CIT as a key determinant, with each additional hour increasing the DGF risk by 9.4% (p=0.006). The hematological indices differed significantly between recipients of DD and LD grafts. ALC and AMC were significantly lower in recipients of DD kidneys (p=0.019 and p=0.038, respectively). Among DD recipients, those with DGF exhibited higher ALC compared to those without DGF, although the difference was not statistically significant.

Conclusions: In our population time on dialysis and CIT were critical determinants of DGF risk. Post-transplant ALC and AMC levels, vary between graft sources and may influence recovery, warranting further investigation.

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Current challenges in transplantation procedures

EP_192 MECHANICAL BOWEL OBSTRUCTION AND APPENDICITIS DUE TO HERNIATION IN TO THE EXTRAPERITONEAL SPACE OF A KIDNEY GRAFT

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Background: A 37-year-old male patient underwent renal transplantation, including a left nephrectomy for the donor and transplantation on the right side for the recipient. The patient was discharged on postoperative day 5 without complications, with normal laboratory parameters, including a white blood cell (WBC) count of 9,000 and a C-reactive protein (CRP) level of 9. He subsequently presented on day 14 post-op with abdominal pain, nausea, vomiting, inability to defecate, and inability to pass flatus. Clinical examination prompted the insertion of a nasogastric tube, and laboratory investigations revealed a WBC count of 11,000 and CRP of 9. Radiological evaluations, including an erect abdominal X-ray and oral contrast-enhanced CT, demonstrated air-fluid levels and proximal intestinal distension, suggesting ileus. The imaging showed a possible bridge ileus, though the cause remained unclear. Given the retroperitoneal location of the transplanted kidney and the peritoneal nature of the suspected adhesion, an exploratory laparoscopy was deemed necessary.

Methods: Case Report.

Results: Exploratory laparoscopy revealed three distinct peritoneal defects, each 2 to 3 cm in diameter, an unexpected complication, as peritoneal integrity is usually intact during renal transplantation. The herniation of the appendix, ileum, and omentum through these defects caused inflammation and ileus. The omentum showed necrosis, while the intestines demonstrated positive peristalsis without ischemia or necrosis. The peritoneal defects were partially repaired with 2.0 V-Loc suture, though complete restoration was not possible due to fragile tissue. An appendectomy was performed to reduce the risk of recurrent herniation into the retroperitoneum.

Conclusion: This case highlights a rare complication of renal transplantation—peritoneal defects leading to organ herniation and intestinal ileus. It emphasizes the need for careful inspection of the peritoneum during and after renal transplantation to ensure its integrity. Surgeons should maintain a high index of suspicion for organ herniation in patients presenting with ileus post-transplant, even when retroperitoneal organs are involved.

EP_193 IMPACT OF DONOR HEPATECTOMY TIME ON EARLY ALLOGRAFT DYSFUNCTION AND LONG-TERM OUTCOMES IN LIVER TRANSPLANTATION

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Background: Donor hepatectomy time (DHT) has been shown to influence graft viability and post-transplant outcomes. Although several studies have investigated the impact of DHT, its effect on early allograft dysfunction (EAD) remains unclear.

Methods: We analyzed all liver transplant recipients from deceased donors at our center between January 1, 2019, and December 31, 2023. DHT was defined as the time elapsed from liver flushing with ice-cold preservation solution to the completion of donor hepatectomy, when the liver is placed on ice or the back table. The primary aim was to determine whether prolonged DHT (>60 minutes) is associated with increased EAD.

Results: During the study period, 358 liver transplants from deceased donors were performed, with DHT data available for 144 cases: 66% (95) were donation after brain death (DBD) and 34% (49) were donation after circulatory death (DCD). The median follow-up was 3.1 years (1–5.9 years). The median DHT for the cohort was 56 minutes (11–155 minutes), and the median cold ischemia time was 6.26 hours (3.1–10 hours). Patients with DHT ≤60 minutes comprised 93 cases (65%), while 51 cases (35%) had DHT >60 minutes. INR levels were slightly elevated in the prolonged DHT group (1.42 mg/dL [0.85–4.5] vs. 1.12 mg/dL [0.84–1.79]), but other laboratory parameters, including AST (1,543 U/L [267–7,697] vs. 1,540 U/L [276–5,291]), ALT (1,204 U/L [142–4,169] vs. 1,198 U/L [194–3,936]), and bilirubin (2.1 mg/dL [0.2–9.8] vs. 2.1 mg/dL [0.4–8.8]), were comparable. EAD was observed in 25% of cases in both groups, primarily driven by elevated transaminase levels. Among those, liver biopsy findings post-reperfusion showed mild changes in 59.45% of cases, moderate in 21.62%, and severe in 5.4%. The CCI was marginally higher in the prolonged DHT group (26.3 vs. 24), and the median hospital stay was longer (17.11 days vs. 15.8 days). Graft survival rates were significantly better in the DHT ≤60 minutes group, with 1-, 3-, and 5-year survival rates of 95%, 93%, and 87%, respectively, compared to 90%, 86%, and 74% in the DHT >60 minutes group.

Conclusions: Prolonged donor hepatectomy time does not appear to adversely impact early allograft dysfunction but strongly influences long-term graft survival rates. Efforts should be made to minimize DHT, particularly in cases with additional risk factors.

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EP_194 MATCHMYKIDNEY, AN ALGORITHM-DRIVEN, COST-EFFECTIVE PAIRED DONATION PROGRAM FOR EXPANDING TRANSPLANT OPPORTUNITIES

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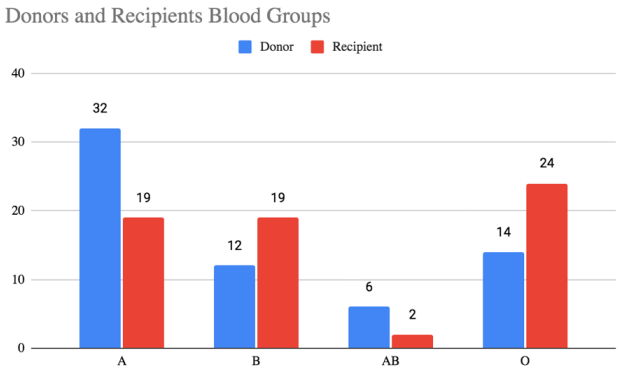
Background: Paired donation is the best solution for increasing success rates, ensuring better compatibility, and expanding access to kidney transplantation. The smart algorithm-driven "Match My Kidney" program, launched in January 2023, is a useful tool facilitating paired kidney donations by allowing better matches compared to the previous eras where matches were planned without any computer program.

Methods: The program evaluated 64 donor-recipient pairs, achieving 8 successful matches through paired donation at Florence Nightingale Hospital in Turkey. Blood group analysis revealed a predominance of type A among donors (32 cases) and type O among recipients (24 cases). To prioritize matches, the program integrates immunological risk factors, including recipients' HLA antibody MFI levels, HLA compatibility, and donor age. It matches up to 4 couples and requires only an internet connection, making it highly accessible for clinics with limited resources. It supports national and international multicenter collaborations with strict data privacy and security protocols. The collaborating center has a chance to check if there is a suitable candidate among the collaborating centers for a particular high PRA recipient, enhancing donor pool utilization and access for highly sensitized patients.

Results: The program facilitated 8 successful paired donations in 2 years, including 2 triplets and 6 dual exchanges. Female donors constituted 54.7% of participants. All age differences between matched donor couples don't exceed 10 years. 4 of the recipients involved were highly sensitized (22%) with positive PRA and high HLA MFI levels (>10000). Triplets included at least one highly sensitized recipient. Blood group compatibility was achieved in all cases. The mean follow-up of the cases is 10 months and all recipients had good graft function.

Conclusions: The "Match My Kidney" program illustrates the potential of algorithm-driven paired donation systems to address donor-recipient incompatibility and expand transplant opportunities, especially for highly sensitized patients. Its simplicity and collaborative use among the paired donor lists of different centers make it a valuable tool for increasing the donor pool.



EP_195 THE USE OF A MODIFIED GREAT SAPHENOUS VEIN FOR THE RECONSTRUCTION OF HEPATIC VEINS IN RIGHT LOBE LDLT

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Background: Reconstruction of hepatic veins is the most difficult stage of LDLT. Impaired venous outflow from the transplant is one of the main causes of liver failure in the postoperative period.The aim of the study was to evaluate the results of complex reconstruction of hepatic veins during transplantation of the right lobe (RL) of the liver in our clinic.

Methods: The modified great saphenous vein (GSV) is prepared by obtaining it from operated patients diagnosed with varicose veins of the lower extremities in the vascular surgery department. Subsequently, one GSV is longitudinally incised, and then two veins are combined to form one large vein with a diameter of over 10 mm. From December 2011 to November 2024, 306 LT in adults and children were conducted in Syzganov National Scientific Center of Surgery. The following types of grafts were used: RL – 208 (68%), left lobe – 24 (7.8%), posterior lateral sector – 1 (0.3%), dual graft – 1 (0.3%), left lateral sector – 43 (14.1%), whole liver – 29 (9.5%). Reconstruction of hepatic veins of segment 5 and 8 during transplantation of the RL of the liver was performed in 84 (27.4%) cases. Of these, reconstruction of hepatic veins of the 5 and 8 segments of the liver using the recipient's portal vein in 60 (71.5%) cases, vascular prosthesis in 11 (13.5%) cases, with a modified GSV in 10 (12%) cases and vessels of a deceased donor in 3 (3%) cases. To assess the functioning of the reconstructed veins, patients underwent a control CT scan after 7 days, 14 days, 1 month, 3 months.

Results: The overall survival rate of patients after LT from a living donor was: 5 years – 74.3%; 10 years – 71.7%. The patency of neo-MHV using the recipient's portal vein at 1 week was 90%, at 2 weeks 86.7%. In the group with reconstruction using a vascular prosthesis, patency at 1 week was 81.9%, at 2 weeks 72.8%. In the group with reconstruction using a modified GSV, the patency at 1 week was 100%, at 2 weeks 90%. In patients who underwent reconstruction of the hepatic veins of segments 5 and 8 of the liver, there were no complications related to the hepatic veins.

Conclusions: Reconstruction of hepatic veins of the 5 and 8 segments of the liver using a modified GSV gives good results, as well as reduces the time of thermal and cold ischemia and the anhepatic phase, which subsequently has a positive effect on rehabilitation in the postoperative period.

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EP_196 GRAFT INFLOW MODULATION IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Liver transplantation from a living donor (LTLD) is a globally recognized alternative to standard liver transplantation. Small-for-size syndrome (SFSS) is a group of signs and symptoms that occur when, after living donor liver transplantation (LDLT) or partial orthotopic liver transplantation, the insufficient liver mass is unable to meet the metabolic needs of the patient. The aim of the study is to evaluate the outcomes of graft inflow modulation in LDLT at our clinic.

Methods: From December 2011 to November 2024, 306 liver transplants in adults and children were performed at the Syzganov's National Scientific Center of Surgery. The lowest GRWR was 0.5. We divided all patients with GRWR ranging from 0.5 to 0.8 into 2 groups: the first group was without modulation, and the second group was with graft inflow modulation (GIM). 29 (10.4%) patients were observed in the first group, 18 (6.5%) in the second group. In the second group, where graft flow was modulated: splenectomy in 5 (1.8%) cases, SAL in 6 (2.1%) cases, ligation of the LRV in 2 (0.7%) cases, ligation of the splenorenal shunt in 1 (0.3%) case, ligation of coronary vein in 3 (1.0%) cases and temporary portocaval shunt in 1 (0.3%) case.

Results: The MELD score in the first group averaged 17.1, in the second 18.7. Cold ischemia in the first group was 31.3 min, in the second 33.1 min. In both groups, postoperative complications were observed in 16 (34.0%) patients. In the first group: arterial thrombosis in 4 (13.8%) patients, hyperperfusion in 1 (3.4%) patient, portal anastomosis thrombosis in 2 (6.8%) patients, stroke in 1 (3.4%) patient, rejection in (3.4%) case and small intestine perforation in 1 (3.4%). Hospital mortality was observed in 5 (17.2%) patients. In the second group: biliary complications were observed in 3 (15.7%) cases, pulmonary edema in 1 (5.0%) case, embezzlement syndrome in 1 (5.0%) case and portal anastomosis thrombosis in 1 (5.0%) case, which required re-operation, hospital mortality in 1 (5.0%). SFSS developed in 5 (17.2%) patients in the first group, and in 2 (11.2%) patients in the second group.

Conclusions: GIM reduces the likelihood of SFSS and is an important tool in partial graft transplantation. Intraoperative hepatic hemodynamic changes can assist surgeons in choosing the appropriate strategy for GIM.

EP_197 COMPUTATIONAL FLUID DYNAMICS FOR VASCULAR ASSESSMENT IN LIVER TRANSPLANTATION: A PILOT STUDY

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Background: In liver transplantation surgery, postoperative impaired blood supply due to vascular mismatch, undiagnosed arterial abnormalities or mismatched arterial and venous blood flow can lead to severe postoperative complications and organ loss. Computational fluid dynamics (CFD) has previously been successful in revealing distinct features of haemodynamic abnormalities. The aim of our study is to describe the feasibility of a computational fluid dynamics model to predict blood flow behaviour in the hepatic artery and portal vein in liver transplantation.

Methods: This is a pilot study involving patients undergoing deceased donor orthotopic liver transplantation at a single centre. All patients had significant portal hypertension. Preoperative computed tomography images and intraoperative vascular flows were used to develop the computational model. Iterative simulations were performed to adjust model resistances to simulate the resistance of the cirrhotic liver and its effect on liver inflow. The interaction between arterial and portal flow was also used to adjust the computational model.

Results: The chosen methodology was shown to be reproducible. A computational model was developed to study vascular flow in liver transplant recipients. The interaction between hepatic arterial and portal blood flow due to the buffer effect could be reproduced, the model showed a decrease in arterial flow after an increase in portal flow.

Conclusions: The computational fluid dynamics model seems to predict the interaction between arterial and venous blood flow during liver transplantation in cirrhotic patients with portal hypertension. Several clinical applications could be derived from this development. Further studies are needed to validate this method.

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EP_198 OVERCOMING TRANSPLANTATION CHALLENGES IN MNGIE SYNDROME:A REDUCED-SIZE LIVER GRAFT CASE AND COMPLEX POSTOPERATIVE CARE

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Background: Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE) is a rare autosomal recessive disorder caused by TYMP gene mutations, leading to thymidine phosphorylase (TP) deficiency. The liver, a key source of TP, has positioned liver transplantation as a safer alternative to hematopoietic stem cell transplantation. MNGIE typically presents with gastrointestinal dysmotility, severe weight loss, ophthalmoplegia, leukoencephalopathy, and peripheral neuropathy. Here, we present a 22-year-old male with MNGIE treated successfully at our center.

Methods: A 22-year-old Caucasian male diagnosed with MNGIE in 2010 presented with severe cachexia, a low BMI, small torso and a small abdominal cavity. The patient underwent pre-habilitation with total parenteral nutrition (TPN) and physiotherapy for three weeks to optimize his nutritional and physical condition before transplantation. To address size mismatch, a reduced-size liver graft was used.

Results: The cadaveric liver graft was prepared on the backtable as a reduced-size graft with preservation of the right and middle hepatic vein. The left portal vein and hepatic artery were ligated at the hilum. Postoperatively, the patient developed gastric dysmotility, managed with nasogastric tube placement and prokinetics, leading to gradual improvement. Importantly, the patient's pre-existing neurological symptoms did not progress, aligning with outcomes in similar cases. The graft functioned optimally, and recovery was uneventful. The patient was discharged in stable condition on postoperative day 34.

Conclusions: This case demonstrates the feasibility of liver transplantation with a reduced-size graft in MNGIE syndrome. The absence of neurological progression and resolution of metabolic complications support its potential as a therapeutic option. Advanced surgical techniques and a multidisciplinary approach were critical to managing the complexities of this rare disorder, ultimately improving the patient's quality of life.

Patients Characteristics	
Age	22
BMI (kg/m^2)	12,8
Underlying Disease	MNGIE
Prior Surgeries	None
Graft weight/Reduced-size liver graft	1323gr/1080gr

EP_199 HEART TRANSPLANTATION FOR MITOCHONDRIAL CARDIOMYOPATHY AND ASSOCIATED METABOLIC SYNDROMES

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Background: Mitochondrial diseases encompass a wide range of heterogenous metabolic syndromes. These metabolic syndromes can lead to cardiomyopathy, in which case they are collectively referred to as "cardiomyopathies and mitochondrial syndromes". This systematic review delves into the practical implications of heart transplantation for individuals with mitochondrial disease. It discusses the experiences of performing heart transplantation in two specific mitochondrial syndromes: maternally inherited diabetes and deafness, and homoplasmic m.4300 mutation syndrome. These cases mark the first instances of heart transplantation for these syndromes.

Methods: We conducted a systematic literature review using Medline with the search terms "heart," "transplantation," and "mitochondrial diseases." From 186 papers, 16 met our inclusion criteria, with the majority being case reports. We reviewed the relevant literature and share our institutional experience.

Results: The existing literature on heart transplantation in mitochondrial diseases is deficient. It includes only a few specific syndromes. Successful heart transplants have only been documented for mitochondrial encephalopathy, lactic acidosis, stroke-like episodes, Kearns-Sayre syndrome, Friedreich's ataxia, and respiratory chain defects. Many of these cases were involving paediatric patients. In our experience, it is crucial to manage and prevent systemic metabolic syndromes, such as stroke-like episodes, during the perioperative period. Furthermore, using mechanical circulatory support as a bridge to transplantation is also feasible. Our experience has been one of compatible survival outcome to that of our general transplanted population. Preoperative fasting was abandoned in these patients. Patients tolerating immunosuppressive medications and maintaining stable cardiac functions in the short to medium term.

Conclusions: Heart transplantation is feasible and, when indicated, can prevent major adverse cardiac events in adults with mitochondrial disease. Successful outcomes however rely heavily on the effective management of metabolic complications. In our experience, a multidisciplinary approach, including input from specialists in neuromuscular degenerative diseases, proved crucial.

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Current challenges in transplantation procedures

EP_200 BALANCING EDUCATION AND EMOTION: A STUDY ON SURGICAL RESIDENTS IN ITALIAN LIVER TRANSPLANT CENTERS

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Background: Transplantation practice requires dedicated training, integrated within the general surgery residency program, often starting with multi-organ procurement. At the same time, rotations in liver transplant (LT) centers provide exposure to training relevant for abdominal surgery, particularly laparotomic procedures. However, international literature reports high levels of emotional involvement and anxiety associated with these rotations. The aim of our study is to describe the training practices and their educational and emotional impact on residents in an Italian context.

Methods: We conducted a prospective, bicentric study based on Likert scale questionnaires (1="not at all" to 5="fully"), semi-structured interviews, and the State-Trait Anxiety Inventory (STAI) scales. Residents working in LT centers during the study period were enrolled, and their STAI scores and interview results were compared with those of attending physicians. Results are expressed as median [min-max].

Results: A total of 10 residents (3rd [1st-5th] year) and 12 attending physicians were included. After 8 [5-13] months of rotation at LT centers, residents performed 6 [1-30] "warm phases" and 0 [0-21] "cold phases" of multi-organ procurement as primary operator, achieving a self-assessed autonomy level of 3 [1-5] in this procedure. Interviews revealed themes related to "educational needs" (both theoretical and emotional) and "ethical issues related to the concept of death," despite the training being rated at level 4 [3-5] in both practical and theoretical aspects. Conversely, attending physicians highlighted themes of "emotional involvement" and "satisfaction within the necessity of achieving results.". The STAI tests identified state anxiety in 1 (10%) resident versus 4 (33%) attending physicians (p=0.112) and trait anxiety in 3 (30%) residents versus 7 (58%) attending physicians, although neither reached statistical significance (p=0.098). The translational impact of the training was rated 5 [3-5] by the residents.

Conclusions: Extended rotations (>12 months) in LT centers have a positive impact on transplant and general surgical training for residents without adversely affecting their emotional well-being

EP_201 A PROPOSED CLASSIFICATION OF LATERAL ABDOMINAL WALL INCISIONAL HERNIA AFTER KIDNEY TRANSPLANTATION

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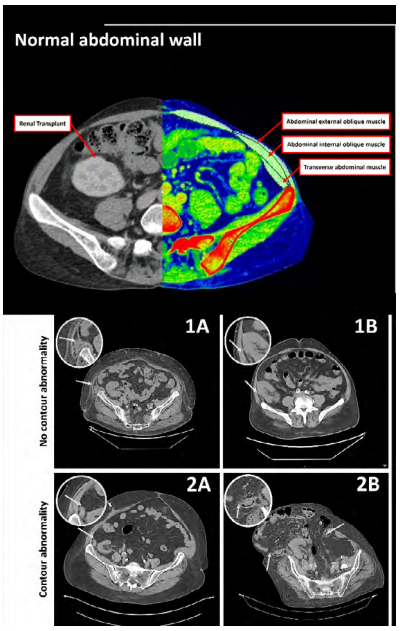
Background: The reported incidence of incisional hernia (IH) after kidney transplantation is 1-7%, but limited awareness, combined with diagnostic challenges, most likely makes it an underdiagnosed complication. Computed tomography (CT) imaging of the abdominal wall is an excellent tool to detect IHs, but there is significant interobserver variability in diagnostic accuracy of IHs after kidney transplantation. This study aims to improve diagnostic precision.

Methods: Hospital records of all adults undergoing kidney-alone transplantation between 2010-2017 at two Swedish sites were reviewed. Abdominal CT scans were obtained and the medical records screened for reported symptoms of IH. The CT images underwent multidisciplinary evaluation by a radiologist, a transplant surgeon, and a hernia surgeon specialist. Clinical data were blinded and decisions about the abdominal wall integrity made by consensus. Defects without contour abnormality were labelled class 1 and defects with contour abnormality, i.e. protrusion, as class 2. Muscular discontinuity was graded; grade A representing an incomplete hernia, and grade B, a complete hernia regardless of any visible interruption of the external aponeurosis. This provided 4 subgroups of IHs: type 1A, 1B, 2A and 2B (Fig). The classification was subsequently evaluated by four external radiologists.

Results: Abdominal CT scans were available in 361 out of 673 study participants (50%) at a median of 43 months posttransplant (IQR 55 months). An IH was detected in 243 radiologically examined subjects (68%), of whom 70 subjects were diagnosed with a type 1A IH, 89 with a type 1B IH, 11 with a type 2A IH and 73 with a type 2B IH. Hernia-like symptoms were reported in 87 subjects (36%). The percentage of symptomatic subjects increased with IH severity; 11% with type 1A, 13% with type 1B, 36% with type 2A and 86% with type 2B, ($p < .01$). The detection rate of IH by four external radiologists increased from 54% to 76% before and after self-study of the proposed classification ($p = .03$).

Conclusions: There is a significant likelihood that the incidence of IH following kidney transplantation is underreported. The proposed classification enhances the detection of IH, thereby facilitating more accurate diagnosis, appropriate clinical management, and the development of preventive strategies.



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Current challenges in transplantation procedures

EP_202 SINGLE-GRAFT KIDNEY TRANSPLANT WITH KARPINSKI SCORE 5 ORGANS FROM DONOR OLDER THAN 70 YEARS: OUR EXPERIENCE

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Background: Pre-transplant biopsies on grafts from a donor are evaluated by the Karpinski score. Pairs scoring 4 and 5 require double kidney transplant (DKT). However, there is a tendency in performing KT on two recipients for pairs scoring 4 and 5. Our study analyzes outcomes of score 4 vs 5 single-graft KT, investigating possible correlations with characteristics of donors and recipients.

Methods: Retrospective study of Karpinski score 4 and 5 single-graft KT at our institution (January 2014-December 2022). Exclusion criteria: donors after cardiac death, graft explant within 5 days, previous solid organ transplant, follow-up for past malignancy.

Results: 100 patients included (63 men). Donors divided into two groups by their score (67=4; 33=5) had no significant differences (e.g. age, arterial hypertension). Recipients divided by the score of their graft had no significant differences (e.g. characteristics, delayed graft function, mortality). Five-year survival for recipients of score 4 (96.5%± 2.5) vs score 5 grafts (93.8%±4.2) had no significant difference (p=0.987). Five-year graft survival for Karpinski 4 (87.9%±4.4) versus 5 grafts (86.6%±6.4) had no significant difference (p=0.857). Five-year survival of grafts from donor >70 years was significantly worse (p=0.010). Score 5 grafts from donors >70 had a significant (p=0.014) worse 5-year graft survival (50.0%+/-18.6) than score 5 grafts from donors aged 31-60 (100%) and 61-70 (100%).

Conclusions: Patient survivals had no significant differences, confirming the viability of score 5 grafts in single KT. However, score 5 grafts from donors >70 had significantly worse 5-year graft survivals. Considering the absence of relevant differences in donor and recipient populations, our data indicate that KT with a single score 5 graft has acceptable results, but donors >70 years appears to be a significant negative factor for long-term outcome, suggesting that DKT with such grafts would be the optimal approach.

EP_203 EMERGENCY KIDNEY TRANSPLANT WITH VENOUS DRAINAGE ON THE INFERIOR MESENTERIC VEIN: CASE REPORT AND LITERATURE REVIEW

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Background: Vascular access failure is a common complication in hemodialysis (HD) patients which sometimes can lead to emergency kidney transplantation as the only life-saving alternative.

Methods: We describe the case of a 36 yr old obese man (BMI 44 kg/m2) with severe congenital uropathy, previous left nephrectomy and recurrent pyelonephritis, complicated by sepsis, cardiorespiratory arrest, hypoxic damage and psychomotor retardation. He received a deceased donor kidney transplant in 2001, after 13 yrs he rejected the graft and went back to HD. Over the years, he experienced repeated vascular access failures due to infection or thrombosis. In 2024 the patient was admitted with complete thrombosis of the superior and inferior vena cava (IVC), iliac, femoral, subclavian and jugular veins, rendering HD impossible. He was placed on the national emergency list and was successfully transplanted within 3 days. A systematic literature review was conducted using PubMed, Scopus and Web of Science, including articles published until December 2024.

Results: The inferior mesenteric vein (IMV) was used for venous drainage while the arterial anastomosis was made to the left common iliac artery, with immediate reperfusion and urine production. Ten months post-transplant, the patient remains in good health, with normal renal and hepatic function and no signs of portal hypertension. The review identified 409 articles, 37 analyzed as full text, 12 were selected for review. The studies were of good quality and reported the effective use of the IMV (6 cases) portal or IVC for venous anastomosis in complex vascular conditions.

Conclusions: IMV can be used as an alternative vessel for venous drainage in emergency, life-saving situations. Alternative, personalized approaches should always be considered in addressing the challenges of renal transplantation in such complex cases.

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Current challenges in transplantation procedures

EP_205 RISK FACTORS FOR PRIMARY HEPATIC GRAFT DYSFUNCTION AT A TRANSPLANT REFERENCE CENTER OVER THE LAST FIVE YEARS

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Background: Primary graft dysfunction (PGD) is one of the leading causes of liver transplant failure, directly impacting in recipient survival. Factors related to the donor, recipient, and surgical procedure, such as ischemia time and clinical conditions of those involved, play a crucial role in this outcome. Although the incidence of PGD has decreased with advances in modern medicine and transplantation, factors such as organ scarcity, the use of donors with expanded criteria, and recipient comorbidities have contributed to its persistence. Understanding the mechanisms underlying primary graft dysfunction is essential for improving liver transplant success rates.

Methods: Observational, analytical, and retrospective study with a total of 572 patients. Among these 286 recipients and 286 organ donors for liver transplants performed between 2019 and 2023 on this service. Data were obtained from records of the National Transplant System (SNT), and also through information from medical records. Regarding donors and receptors, the following were evaluated: length of stay in the ICU, cause of death, comorbidities, use of vasoactive drugs, age, liver function, race, time of organ ischemia during harvesting until implantation, and presence of cardiorespiratory arrest, MELD, presence of intraoperative portal thrombosis, etiology of cirrhosis. Pacients who were submitted to multi-organ transplants, such as liver-kidney or liver-pancreas-kidney, pediatric donors or recipients, under 18 years of age and who did not die due to causes related to primary dysfunction, such as infection, mechanical or surgical complications, were not applied to the study.

Results: The current study is under development, according to the deadline of the evaluated institution, scheduled to be completed by January 31, 2025. The partial result that was observed is the death of 36 patients out of a total of 286 patients transplanted in the period, representing 12.5% of the sample.

Conclusions: The results of this study will highlight the relevance of early identification and proper management of primary graft dysfunction as a critical complication in liver transplantation. These findings may underscore the need for more rigorous clinical protocols and individualized monitoring strategies to improve patient outcomes.

EP_206 UROLOGICAL COMPLICATIONS IN KIDNEY TRANSPLANTATION: IMOACT ON GRAFT FUNCTION AND INFECTIONS

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Background: Urological complications remain a challenge, affecting graft function and patient morbidity. This study evaluates their incidence, risk factors, and impact on graft function and infections

Methods: Retrospective case-control study conducted on patients undergoing renal transplantation at Bologna Hospital from 2016 to 2023.

Results: Among the 890 kidney transplants performed, 111 patients (12.47%) experienced urological complications. The most frequent issues were obstructive uropathy (OU) in 65 patients (7.3%) and vesicoureteral reflux (VUR) in 46 patients (5.17%). The development of OU was significantly associated with factors such as advanced donor age (p = 0.004) and the presence of multiple renal arteries (p = 0.002). VUR was more frequently observed in cases where the donor had a BMI greater than 30 (p = 0.036), in double kidney transplants (p = 0.006), and in grafts with multiple arteries (p = 0.005). Primary endpoint weredeath, graft survival and graft function worsening. Among these, a 30% decline in eGFRoccurred in 18.9% of affected patients within the first year (vs 8.1%control, OR 2.59, CI 1.05–6.38, p = 0.038). At two years,13.8% experienced this decline (vs. 2% control, OR 9.40, CI 1.09–80.99, p = 0.041). Secondary endpoint was urinary tract infections, more frequent in the complication group (58vs10, OR 5.22, CI 2.85–9.56, p < 0.001). Risk of severe infections (urosepsis, pyelonephritis) was also higher, (OR 6.00; CI 2.53–13.69, p < 0.001) and (OR 7.07; CI 2.35–21.22, p < 0.001), respectively.

Conclusions: The incidence of urological complicationswas 12.47%. After a two-year follow-up from the development of urological complications, we observed a significant risk of a 30% decline in eGFR. Infectious complications were also significantly higher in the urological complication group.

	Univariate			Multivariate		
Characteristics	**OR**	**CI**	**P value**	**OR**	**CI**	**P value**
Death	2.36	0.42-13.21	0.328	1.70	0.26-11.12	0.577
Graft loss t12	2.02	0.18-22.58	0.569	1.30	0.61-27.73	0.865
Graft loss t24	9.21	1.11-76.41	0.045	6.33	0.65-60.88	0.109
eGFR 30% t12	2.64	1.15-6.06	0.021	2.59	1.05-6.38	0.038
eGFR 30% t24	8.33	1.81-38.32	0.008	9.40	1.09-80.99	0.041
UTI	5.22	2.85-9.56	<0.001	2.88	1.35-6.13	0.006
Pyelonephritis	7.07	2.35-21.22	<0.001	6.38	2.00-30.20	0.002
Urosepsis	6.00	2.63-13.69	<0.001	9.77	3.52-27	<0.001

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EP_207 PREDICTION OF COMPLEX TOTAL HEPATECTOMIES IN LIVER TRANSPLANTATION - THE COMPLEXITY SCORE

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Background: Liver transplantation (LT) with caval sparing represents a complex procedure. Defining a difficult LT remains subjective, primarily based on the surgeon's perception. Previous studies identified various factors of surgical difficulty, but they did not differentiate between the two stages of LT: total hepatectomy (TH) and graft implantation. This study aimed to identify recipient-related factors associated with a difficult TH.

Methods: This is a retrospective study on all consecutive LTs performed in a single center from 2017 to 2021. Complex TH was defined by the presence of at least one criterion among: TH duration >3 hours, red blood cell transfusion ≥3 units, and use of vasopressive drugs ≥1 microgram/kg/min over 5 minutes. Independent factors associated with complex TH were identified to establish a predictive model of TH difficulty.

Results: Out of 394 patients analyzed, 148 (37.6%) underwent complex TH. Four independent factors were identified: previous abdominal infection, esophageal varices, segment 1 hypertrophy, and indication for LT (Figure 1). These factors were integrated into a predictive score, demonstrating good calibration and discrimination (AUC=0.662), and low optimism upon cross-validation (0.03), thus suggesting good reproducibility. Recipients undergoing complex TH had higher rates of early allograft dysfunction (39% vs 25%, p=0.004) and early relaparotomies (39% vs 28%, p=0.03), an increased 90-day comprehensive complication index (CCI) (56 vs 45, p<0.001), and decreased 1-year patient survival (84% vs 90%, p=0.06) (Table 1).

Conclusions: The presented score serves as a practical and simple tool to predict complex TH in order to enhance surgical safety, optimize donor-recipient matching, and facilitate young surgeon training.

COMPLEXITY score		
Item	**Details**	**Points**
Previous abdominal infection	No	0
	Yes	1
Oesophageal varices	< grade II	0
	≥ grade II	1
Segment 1 Hypertrophy (C/RL ratio > 1)	No	0
	Yes	2
Indication for LT	Malignancy/Acute liver failure or acute hepatitis	0
	Decompensated cirrhosis	2
	Redo-liver transplantation /Polycystic liver disease	3
	Other	1

Abbreviations : C/RL, caudate-right lobe ratio; LT, liver transplantation

Figure 1

	Overall n=386	Non complex TH n= 241	Complex TH n= 145	P value
Overall morbidity				
CCI score				
3 months	47 (30-73)	45 (30-65)	56 (36-81)	**< 0.001**
12 months	60 (40-89)	56 (36-81)	70 (45-87)	**0.006**
EAD	116 (30%)	60 (25%)	56 (39%)	**0.004**
MEAF score	5.27 (4.29-6.41)	5.07 (4.14-6.26)	5.63 (4.57-6.59)	**0.005**
Missing data	*4*	*2*	*2*	
Primary non function	5 (1.3%)	4 (1.7%)	1 (0.7%)	0.70
1 year arterial complication	79 (20%)	42 (17%)	37 (26%)	0.06
1 year biliary complication	81 (21%)	55 (23%)	26 (18%)	0.30
Postoperative data				
Retransplantation	12 (3.1%)	6 (2.5%)	6 (4.1%)	0.40
Post LT ICU stay (days)	6 (4-12)	5 (4-9)	7 (4-15)	**0.002**
Missing data	*12*	*6*	*6*	
Post LT hospital stay (days)	21 (15-34)	19 (14-29)	24 (16-42)	**0.001**
Missing data	*16*	*11*	*5*	
Post operative dialysis	102 (26%)	55 (23%)	47 (32%)	**0.04**
Post operative encephalopathy (> 3 days within POD 7)	35 (9.1%)	19 (7.9%)	16 (11%)	0.30
Relaparotomy < 3 months	124 (32%)	68 (28%)	56 (39%)	**0.03**
AST peak	937 (600-1933)	862 (563-1587)	1186 (656-3247)	**0.004**

Note: Data are expressed as n (%) or median (IQR).

Abbreviations : TH, total hepatectomy; CCI, comprehensive complication index; EAD, early allograft dysfonction; MEAF, Model for Early Allograft Function; LT, liver transplantation; ICU, intensive care unit; POD, post operative day; AST, aspartate aminotransferase; IQR, interquartile range

Table 1

EP_208 SEMI-ELECTIVE LUNG TRANSPLANTATION: A PROSPECTIVE CLINICAL STUDY ON HYPOTERMIC CONTROLLED STORAGE

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Background: Donor lung preservation at 10°C is emerging as an innovative and promising technique that can improve transplant logistics by extending cold ischemia time, while achieving outcomes comparable to traditional ice-cooler storage. This cohort study details our experience with 10°C graft preservation and "semi-elective" transplantation.

Methods: We conducted a prospective cohort study on consecutive bilateral lung transplants using graft preservation at 10°C, from April 2023 through December 2024.Lungs (from both DBD and DCD donors) were retrieved using standard procedures and transported in an ice-filled cooler. Upon arrival, the lungs were placed in a temperature-controlled incubator set to 10°C, where cold static preservation was maintained until implantation. Transplantation was consistently scheduled for the morning.The main outcomes considered were the occurrence of grade 3 primary graft dysfunction at 72 hours (PGD), the duration of postoperative invasive ventilation (IV), and the length of stay in the intensive care unit(ICU-LOS).Appropriate regression analyses were used based ondata characteristics.

Results: This study included 52 recipients. Among the donors, 75% experienced encephalic death, and 53.8% had a P/F ratio greater than 450 at the time of referral. A total of 15 grafts underwent ex vivo lung perfusion.Ten degree storage was extended up to 23 hours and 38 minutes. The table lists some of the main parameters.None of the donor, recipient, or operative variables were found to correlate with PGD. Similar results were observed for IV and ICU-LOS, except for donor age, which showed significant correlations (p = 0.037 and p = 0.004, respectively).

Conclusions: Our prospective cohort study provides a snapshot of how graft preservation at 10°C can be practiced in 'real-life' settings.In our cohort of patients, graft preservation at 10° did not impact short-term outcomes. The "semi-elective" scheduling of lung transplantation appears feasible and safe.

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EP_209 TRANSPLANT PHARMACISTS ROLE IN PREOPERATIVE ASSESSMENT OF LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS AND DONORS

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Background: At Oxford Transplant Centre, a pharmacist review is an established role within the preoperative assessment clinic for Living Donor (LD) kidney transplant recipients and donors. The emergence of Electronic Patient Record (EPR) systems has enabled advance prescribing via a future state 'PowerPlan', streamlining the patient pathway with donor and recipient admissions direct to Theatre Direct Admissions unit on the day of surgery.

Methods: A pharmacist-led, structured preoperative medication review for LD transplant recipients involves evaluating all current medications, determining which should continue, be adjusted, or discontinued prior to surgery. Continuing medicines, peri- and post-transplant medications, including immunosuppression, antimicrobial prophylaxis and thromboprophylaxis, are prescribed in advance via the 'PowerPlan' (Figure 1), and activated at time of surgery. The pharmacist provides education on post-transplant medication regimens during consultations. Live donors also have a comprehensive medication review and explanation of their intended discharge medications.

Results: On average 65 live donor-recipient pairs are reviewed annually. Recipients receive on average 1.5 hours of pharmacist consultation, while donors typically receive 30 minutes. Pharmacist interventions are associated with timely identification and resolution of medication-related issues prior to planned surgery. An overview of the structured assessment process and examples of interventions is provided in Table 1. In some cases, intervention may result in surgery postponement, such as when a donor is found to be taking combined oral contraceptive pill.

Conclusions: The pharmacist's involvement in this clinic greatly enhances the multidisciplinary team (MDT) review, with overwhelmingly positive feedback from both staff and patients. Through comprehensive medication reviews, informed decision-making, and patient education, the pharmacist ensures a safer surgical pathway for both recipients and donors, mitigates medication-related risks, and facilitates advance prescribing of pre-, peri- and post-transplant medicines. Additionally, by streamlining admission on day of surgery, this approach delivers substantial cost saving for the NHS and broader healthcare system.

Figure 1: Future state Transplant-Kidney (DBD/DCD/LD) PowerPlan

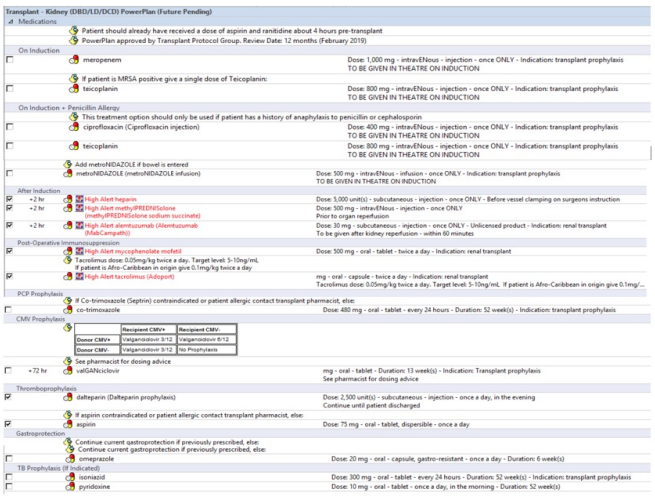

Table 1: Structured LD transplant recipient pharmacist review

- Date of Transplant (Tx)
- Tx type: LRD, LURD, Paired Exchange, Altruistic, ABOi, HLAi
- Immunosuppression protocol: Standard, Young Adult, Trial, Off-protocol (justification)
- Indication for transplant
- Donor details/HLA MM
- Medication review
  - Medications to continue post-Tx
  - Medication to stop post-Tx
  - Medication advice on morning of Tx
  - Allergies
- Dialysis History
- Pt anthropometrics
  - Weight / height
  - Adjusted Body Weight for tacrolimus dosing BMI>30
- Thrombosis History: identifying need for extended VTE prophylaxis post-Tx
- Smoking History: identifying need and prescribing of NRT
- COVID-19 vaccine status
- Previous Parathyroidectomy: Alfacalcidol replacement
- Donor/Recipient serology, corresponding antimicrobial prophylaxis/additional blood tests requests
  - CMV
  - EBV
  - HBV
  - Latent TB risk assessment
- Medicines management discussion and actions
  - Post-Clinic bloods review
  - Epoetin/bicarbonate dose adjustment
  - Prescribe preoperative potassium binder
  - Prescribe tacrolimus pre-loading (when necessary)
  - Azathioprine adjustment based on TPMT status
  - Warfarin bridging
- Medicines education in preparation for Transplant
  - Indications of all drugs
  - Common side effects
  - Vaccination advice
  - Pregnancy / contraception advice

EP_210 THE EFFECT OF POSTOPERATIVE GLYCAEMIC CONTROL IN PANCREAS TRANSPLANT RECIPIENTS: A FEASIBILITY PROTOCOL

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Background: Postoperative hyperglycaemia has been associated with an increased risk of non-technical graft loss up to 3-fold in the first 3 years after pancreas transplant. Whether this relationship is causal or represents early graft dysfunction has not yet been determined. As such, prevention of glucotoxicity and providing β-cell rest during a turbulent physiological phase are possible mechanisms for improving β-cell outcomes. We hypothesise that postoperative tight glycaemic control following pancreas transplant will lead to improved graft survival, with possible secondary outcomes of improved graft function. We present the protocol of our feasibility assessment for a study exploring this hypothesis.

Methods: The protocol details a single-arm feasibility study evaluating the use of a computer-based algorithm to achieve normoglycaemia following pancreas transplant. After providing informed consent, enrolled patients will undergo controlled normoglycemia (4.4-6.1mmol/L) using a computer-based algorithm to inform insulin infusion rates and blood glucose monitoring requirements for the first 5-postoperative days. The intervention will take place in the intensive care unit and all other care will be provided according to local standard clinical procedures. Additional follow-up evaluations include a 90-day mixed-meal tolerance test of serum C-peptide and insulin, and HbA1c. Additional survey feedback from participants and clinical staff will assess tolerability of the intervention.

Results: Indicators of trial feasibility are the primary outcomes of this study. Utilising existing literature, a traffic light system to indicate appropriateness to proceed to full RCT, with or without protocol amendments, has been developed across four domains: safety, intervention adherence, recruitment and retention and completeness of data (Table 1.). Using recruitment as the primary outcome, with a target of >92% retention, a sample size of 20 will enable us to identify this with a 95% binomial confidence interval of 70.9-99.3%.

Conclusions: We present a feasibility protocol evaluating the use of a computer-based algorithm to achieve normoglycaemia to inform a definitive RCT assessing the effects of postoperative tight glycaemic control following pancreas transplant.

	Safety	Adherence	Recruitment	Completeness
Measurement	Episodes of severe hypoglycaemic events per total patients (%)	Percentage of blood glucose readings ≤15 mins later than the recommended time (%)	Percentage of eligible patients who complete the study intervention period (%)	Median percentage of completed critical secondary outcome measures (%)
Red	>20.4%	<80%	<67%	<50%
Amber	17.4 – 20.4%	80 - 90%	67 - 92%	50 - 95%
Green	<17.4%	>90%	>92%	95%

Table1. The proposed limits of the traffic light systems for each of the four domains.

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Current challenges in transplantation procedures

EP_211 BEST PRACTICES ALONG THE KIDNEY TRANSPLANTATION CLINICAL JOURNEY

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Background: Kidney transplantation (KTx) clinical practice varies greatly across providers. However, little is known about what constitutes best practice (BP).

Methods: Four critical domains were identified: Chronic Kidney Disease (CKD), Kidney Donation and Transplantation, Transplant Recipients, and Management of Donation and Transplantation Service. A survey tool was designed and validated to collect data on clinical practice and patient experience across domains. Survey respondents (253) included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: Key elements for best practices along the KTx clinical journey were identified: (1) development of protocols to standardise the variable monitoring of CKD, to minimize urban-rural differences in clinical practice due to limited resources and follow-up care; (2) enhanced primary care training and targeted resource allocation to diagnose and monitor early-stage CKD; (3) donor coordination and promotion of living donation, addressing gaps in patient awareness and access to care; (4) development of communication protocols on living donation; (5) implementation of targeted patient and donor educational campaigns on living donation; (6) enhanced post-transplant follow-up care by nephrologists; (7) integration of quality-of-life assessments and psychological donor support post-transplantation; (8) increased availability of transplant coordinators to promote equitable resource allocation and the adoption of innovative practices; (9) streamlined governance structures along clinical journey; and (10) equitable funding models with consistent reimbursement policies across patient groups.

Conclusions: This study recommends a set of practices including standardized care pathways and protocols, improvement of primary care and patient education, and advancements in quality-of-life metrics and governance.

EP_212 RENAL FUNCTION BEFORE LIVER TRANSPLANT AS A PREDICTOR OF MORTALITY: A THREE-YEAR RETROSPECTIVE ANALYSIS

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Background: Liver transplantation is considered the most complex procedure in contemporary surgery, as no other simultaneously interferes with so many body functions. In addition to liver failure, renal disease (acute or chronic) often coexists - a situation that makes the management of patients even more complex, as renal dysfunction (before and after) liver transplantation is an important factor complicating prognosis, being correlated with increased morbidity, mortality, and the final cost of treatment.

Methods: The objective of this study was to evaluate the short- and long-term survival rates of patients with variable renal dysfunction and to compare them with normal renal function. To this end, a retrospective analysis was carried out, whose final sample was composed of 148 medical records of patients who underwent liver transplantation in 2016 and 2017 in a transplant service in the metropolitan region of Curitiba.

Results: The result shows that the risk of death in recipients with Glomerular Filtration Rate (GFR) < 30 before transplantation is about twice as high as the risk of death of a recipient with GFR ≥ 30 (p=0.028).

Conclusion: It is concluded that the surveillance of renal function before and after transplantation should be strongly encouraged as a way to prevent mortality, in the short and long term, of patients undergoing liver transplantation.

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EP_213 LIVING DONOR TRANSPLANT PRACTICES IN ASTS FELLOWSHIP TRAINING IN THE UNITED STATES

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Background: Living donor transplantation should be a cornerstone for transplant surgeons, but achieving technical independence, especially in living donor liver transplantation (LDLT), remains a challenge. This study evaluates the experiences and barriers during the American Society of Transplant Surgeons (ASTS) Fellowship and proposes solutions to improve autonomy in living donor transplantation.

Methods: A 93-item questionnaire was distributed to former ASTS fellows, gathering training experiences and autonomy in living donor kidney (LDKT) and LDLT after the 2-year fellowship. 94 participants, covering 74.2% of targeted U.S. institutions. Statistical analysis identified trends, challenges, and predictors of independence.

Results: The survey revealed significant differences in independence between LDKT and LDLT. While 70.73% of fellows felt confident in LDKT, only 17.08% felt similarly for LDLT (p<0.001). A majority (90.24%) believed the ASTS structure enabled independence in LDKT, but only 9.76% thought the same for LDLT (p<0.001). Robust training in LDKT was reported, with 85.36% of fellows prepared to interpret preoperative donor imaging and 75.61% in selecting donors (p=0.041). Furthermore, 63.41% of fellows achieved independence in donor nephrectomy compared to 14.64% in donor hepatectomy (p<0.001). Fellows performed an average of 29.3 ± 4.1 living donor nephrectomies as primary surgeons but only 6.1 ± 2.9 hepatectomies during the fellowship (p<0.0001). Low LDLT case volumes, lack of structured curricula, and limited opportunities to act as primary surgeons were key barriers. 68.3% felt prepared to lead a living donor program in LDKT, compared to 21.95% in LDLT (p<0.0001). To note, compared to the European system, a structured program as ASTS fellowship allows for independence in LDKT, providing the basis for further growth in LDLT skills.

Conclusions: The ASTS fellowship provides an excellent foundation for LDKT. Independency in LDLT remains difficult to achieve under the current structure. Solutions include formalized curricula, mandated primary surgeon roles in LDLT procedures, and double-console robotic systems for guided learning. Addressing these gaps is essential to prepare future transplant surgeons for the increasing demands of living donor transplantation programs.

Variables	Living Donor Kidney Transplant (LDKT)	Living Donor Liver Transplant (LDLT)	
Dedicated multidisciplinary meeting	Yes 70.3%	Yes 58%	p>0.05
Ability to read and interpret pre operative donor imaging	Fully-mostly prepared: 85.36%	Fully-mostly prepared: 56.10% (41% RMN)	P=0.01
Independently select living donor	Fully-mostly prepared: 75.61%	Fully-mostly prepared: 34.15%	p=0.041
Living donors performed as primary surgeon	29,3 ± 4,1	6,1 ± 2,9	p<0.0001
Level of independency in donor nephrectomy VS donor hepatectomy	Independent-mostly independent: 63.41%	Independent-mostly independent: 14.64%	p<0.001
Approach	Laparoscopic 75.61%	Open 85.3%	
Independence Back table	Independent-mostly independent: 92.6%	Independent-mostly independent: 36.59%	p=0.002
Independency on recipient from living donation	Independent-mostly independent: 90%	Independent-mostly independent: 29.27%	p<0.001
Confidence to be independent in living donor transplantation	Very-completely confident: 70.73%	Very-completely confident: 17.08%	p < 0.001
ASTS education quality (congress, seminar, webinar, website)	Intermediate-good: 65.86%	Intermediate-good: 54.16%	p=0.67
Is becoming independent a realistic goal after ASTS fellowship, as the fellowship is currently structured	Yes: 90.24%	Yes: 9.76%	p < 0.001
After potential changes is being independent still a realistic goal	Yes: 90.49%	Yes: 14.64% P=0.09	p < 0.001
Ready to start living program	Fully-mostly prepared: 68.30%	Fully-mostly prepared: 21.95%	p<0.0001

Challenges and Proposed Solutions for LDLT Training During ASTS Fellowship	
Training Essentials	HPB training is essential
	Establishment of a formalized surgical training
	Training in other countries with more volume
Training Limitations	Limit LDLT training only in high-volume centers
	Limit LDLT training only in centers with HPB program

EP_214 DIFFERENT IMPACT OF THE COMPLEXITY CRITERIA FOR SURGICALLY COMPLEX KIDNEY TRANSPLANTATION

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Background: Complexity in transplantation is becoming more established in daily practice. In establishing the new national criteria, the Ministry has focused exclusively on surgically complex renal transplantation. Our objective is to assess the impact of surgical complexity with national complexity criteria.

Methods: Retrospective study. The criteria for surgically complex transplants established by the national body: vascular and urological complexity, equal to or greater than 3 transplants and BMI equal to or greater than 35. The impact on the main outcomes and the greatest impact on the results by the complexity criteria were analyzed. Study approved by the Ethics Committee

Results: 122 patients (54.6±14.2 years (18-90), 37% women) of 619 transplant recipients (2021-2023) met national criteria (43vascular complexity, 30urological, 45 3 transplants, 21 BMI>35); 17 patients with several criteria. In 18.31±10.19 (0-38.9) months of follow-up, no differences in donor age (p=0.852) or recipient (p=0.801), type of transplant (p=0.320) or mortality (p=0.070); but there was an impact on graft loss (p=0.048) and rejection (p=0.004). related to mortality, only vascular complexity (p = 0.008) of the national complexity criteria was associated, being the same the most determining factor in the multivariate analysis (p = 0.006; Exp (B) 4.174); also donor type (p = 0.005), DCD (p = 0.033), recipient age (p = 0.000) and donor (p = 0.002). In graft loss, only vascular complexity (p = 0.0023) as a national complexity criterion, and being again in the multivariate the most associated factor (p = 0.026; Exp (B) 2.642); also with donor type (p = 0.035; Exp (B) 2.881) and donor age (p = 0.017; Exp (B) 1.037). Interestingly, urological complexity was the factor most associated with acute rejection excluding borderline in the multivariate (p=0.000; Exp(B) 7.469) with donor type (p=0.024; Exp(B) 5.642); transplants>3 only in the univariate (p=0.048). BMI>35 was not associated with any of the main outcomes.

Conclusions: Not all criteria established by the national committee have the same impact on the main outcomes of the transplant, with vascular complexity being the most determining complexity and BMI>35 not having an impact, so it should be reviewed as a criterion to establish surgical complexity in a transplant.

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EP_215 VENTRICULAR INFLUENCE ON PRIMARY GRAFT DYSFUNCTION AFTER HEART TRANSPLANTATION

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Background: By employing the standardized criteria defined by ISHLT, we investigated the outcomes associated with left ventricular primary graft dysfunction (PGD-LV) and right ventricular primary graft dysfunction (PGD-RV) in this single-center study.

Methods: A retrospective analysis was conducted on adult heart transplant (HTx) recipients at our center between 1984 and 2021. A total of 830 patients underwent a HTx in our center between 1984 and 2021. After exclusions for age <18 years or missing data, the main analysis included 667 (80.4%) adult patients. Medical records were examined for pre-, intra- and post-operative data with focus on the 24 hours after HTx and long-term survival using the ISHLT definition for PGD-LV and PGD-RV.

Results: Out of the 667 patients that we analyzed, 70 (10.5%) fulfilled the criteria for PGD, whereof 41 (6.1%) had PGD-LV and 29 (4.3%) had PGD-RV. Among those with PGD-LV, 5 cases (12%) exhibited moderate PGD-LV, while 36 cases (88%) demonstrated severe PGD-LV. We had no cases of mild PGD-LV. The PGD-LV and PGD-RV cohorts were largely comparable, with smoking history being the sole significant differentiating factor (p=0.035). No significant differences were observed in donor-related or intraoperative factors between the groups. Outcome analysis revealed higher in-hospital mortality in the PGD-LV group compared to the PGD-RV group (58.5% vs 27.6%). Similarly, all-cause mortality or retransplantation (re-Tx) rates at 30 days (56.1% vs 27.6%) and 1 year (61% vs 34.5%) were elevated in the PGD-LV cohort as well as at long-term (Fig 1). Conversely, the PGD-RV group experienced longer overall hospital stays (42.4 vs 26.5 days, p=0.0085) and ward stays (22.8 vs 12.6 days, p=0.017).

Conclusions: In this single center study, we have demonstrated that PGD-LV appears to be more common than PGD-RV in HTx recipients. Additionally, the severity and outcomes associated with PGD-LV were notably more critical, with higher in-hospital mortality and increased rates of death or re-Tx at 30 days and 1 year compared to PGD-RV.

EP_216 A DRUG FREE APPROACH TO MANAGE HEADACHE IN KIDNEY TRANSPLANTATION: A CASE REPORT

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Background: Kidney transplantation (KT) improves patient survival and quality of life compared with hemodialysis. Neurological complications in KT has a prevalence between 15 -30 %, can arise due to various factors, including the underlying kidney disease, the transplant procedure itself, immunosuppressive medications, and other medical conditions. Headache, in particular, is a not specific condition with a prevalence between 3.2 and 35.2% and impact negatively on the quality of life of kidney recipients. Non-steroidal anti-inflammatory drugs, the most common class of drugs utilized in this condition causes nephrotoxicity. Acupuncture is an established form of complementary medicine recommended by World Health Organization (WHO) for its potential benefits in various medical conditions. In particular, in the setting of transplantation, the use of acupuncture is a valuable opportunity to support patient in the post operative care to avoid new drug prescription and limit related toxicity.

Methods/Results: We present the case of a 49 year old male transplanted for IgA nephropathy in 2022 with a history of chronic multifactorial headache before KT and chronic abuse of NSAIDs. Due to the worsening and severity of headache episodes (one per week) after KT he performed a new neurological assessment and a brain MRI that ruled out organic or infective diseases. As for protocol different and consecutive drugs have been prescribed without any benefit for the patient: propranolol, lamotrigine, amitriptyline and rizatriptan. According to the evidence treatment with acupuncture was proposed to our patient, after obtaining an informed consent. Patient was treated with 12 sessions within 2 months with a progressive clinical improvement and decrease of episodes to very mild symptoms occurring 1-2 times per month that did not require drug treatments. No side effects were recorded and elevated satisfaction was shown by the patient.

Conclusions: Acupuncture should be integrated into a holistic drug-free approach in kidney transplant care, alongside standard medical treatments and lifestyle adjustments, to manage side effects and improve quality of life.

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EP_217 GENDER MISMATCH OUTCOMES IN HEART TRANSPLANTATION: INSIGHTS FROM A LATIN AMERICAN COHORT

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Background: While heart transplantation (HTx) has shown significant success, the role of gender mismatch (donor-recipient gender differences) remains understudied. This study evaluates the impact of gender mismatch on outcomes in HTx patients.

Methods: A retrospective cohort study analyzed 542 HTx performed between 2013 and 2024 at Brazil's largest transplant center. Gender mismatch and its association with pre-, intra-, and postoperative variables were investigated. Data included demographics (age, blood type, and Predicted Heart Mass Index [PHMI]) and postoperative echocardiographic measures, such as left ventricular ejection fraction (LVEF) and systolic pulmonary artery pressure (sPAP). Outcomes included rejection, infections, and survival (30-day and long-term up to 11 years). Statistical analysis was conducted using STATA 16.1, with $p < 0.05$ considered significant.

Results: Of 542 transplants, gender combinations were male donor to female recipient (122; 63.2%), male donor to male recipient (309; 88.5%), female donor to male recipient (40; 11.5%), and female donor to female recipient (71; 36.8%). Gender mismatch occurred in 162 cases (29.89%). Among mismatched patients, 74.1% had PHMI ≥1.2 (p = 0.000), and 41.98% had PHMI ≥1.5 (p = 0.001). Postoperative echocardiography revealed a significant LVEF improvement in mismatched patients from 54.25% (postoperative day 1) to 57.69% (postoperative day 5) (p = 0.0004), whereas non-mismatched patients showed no significant change (p = 0.1444). Long-term survival rates were similar: 66.05% (107 of 162) for mismatched recipients and 62.37% for non-mismatched recipients. Overall, 344 patients (63.47%) survived over the 11-year follow-up period.

Conclusions: Gender mismatch in HTx was associated with higher PHMI and some increased risks of postoperative complications, such as rejection and infections. However, it did not adversely affect long-term survival. Most mismatched patients demonstrated significant LVEF improvement and comparable survival outcomes to non-mismatched recipients, with 107 of 344 long-term survivors showing a favorable prognosis.

Table 1. Sample's characteristics and outcomes of HTx patients with and without gender mismatch. Sao Paulo, Brazil, 2024.

	Gender Mismatch			
	Yes (n=162)		No (n=380)	
	n	%	n	%
Age < or = 59 years	123	75.93	314	82.63
Age > or = 60 years	39	24.07	66	17.37
ABO donor system				
A	50	30.86	147	38.68
AB	2	1.23	2	0.53
B	23	14.2	38	10
O	87	53.7	192	50.53
Recipient ABO system				
A	57	35.19	157	41.32
AB	9	5.56	17	4.47
B	27	16.67	44	11.58
O	69	42.59	162	42.63
Etiology				
Chagas	67	41.36	109	28.68
Idiopathic	41	25.31	123	32.37
Ischemic	8	4.94	69	18.16
PHMI > or = 1.2	120	74.07	130	34.21
PHMI > or = 1.5	68	41.98	15	3.95
Ischemic time > 240 minutes	41	25.31	85	22.37
Inotropes use	107	66.05	263	69.21
IABP	101	62.35	213	56.05
ECMO	7	4.32	20	5.26
Outcomes				
Cellular rejection	4	7.69	7	1.84
Infections	10	19.23	32	8.42
Primary Graft Dysfunction	2	3.85	7	1.84
ABO incompatibility	2	1.23	0	0
30-day mortality	25	15.43	53	13.95

EP_218 PUBLICATION DYNAMICS OF SOLID ORGAN XENOTRANSPLANTATION STUDIES: A SYSTEMATIC REVIEW

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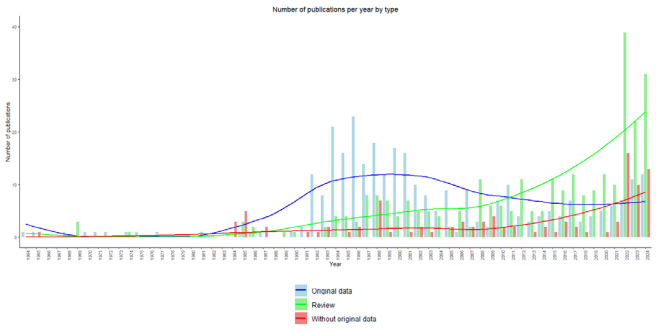
Background: Xenotransplantation has emerged as a promising solution to address organ shortage with numerous publications. However, there are no studies capturing the dynamics of xenotransplantation publication activity. We thus aimed to provide a systematic assessment of xenotransplantation research.

Methods: A systematic literature search in PubMed was conducted from 1960 to October 2, 2024 including publications in English, with no limitations on study design. Studies on solid organs involving humans or perfusion with human blood and its derivate were included. Eight experts assessed the publications and for each included publication collected following data: publication type, country, journal, organ, donor species, main topics.

Results: Among 2944 publications identified, 706 met the inclusion criteria. Publication activity displayed two peaks: first in the 1990s, driven by genetic engineering advancements, followed by a period of latency. Second peak emerged following first pig-to-human deceased recipient transplantation (Figure). There were 291 (41.2%) original articles, 290 (41.1%) reviews, 101 (14.2%) without original data publications, 11 (1.6%) case reports, 9 (1.3%) research letters and 4 (0.6%) systematic reviews. The top 5 publishing countries were USA (48.2%), Germany (10.2%), UK (5.4%), Sweden (4.8%) and China (4.2%). Xenotransplantation journal accounts for 19.7% of all publication activity, while the top five transplantation journals (Transplant Proceed, Transplantation, JHLT, AJT and Transpl Int) account for 25.8% (11.2, 9.6, 1.8, 1,7 and 1.7% each). General audience journals represent 5.4%, with Lancet publishing the most (2.3%). The most studied organ was the heart (24.2%), followed by islet (23.4%), kidney (22.7%), liver (17.4%), and lung (12.3%). 356 topics were identified and will be grouped into categories.

Conclusions: his study is one of the first systematic assessment of publication activity in xenotransplantation underscoring its growing global interest and evolving focus areas. Low proportion of original data publications suggests the crucial need for original studies to advance the field forward. Limited activity of general audience journals highlights the importance of engaging a broader audience as xenotransplantation nears clinical trials.

Figure



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Current challenges in transplantation procedures

EP_219 PORTAL INFLOW MODULATION BEFORE LIVER TRANSPLANTATION IN PATIENTS WITH INCREASED RISK OF INTRAOPERATIVE BLOOD LOSS

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Background: Liver transplantation may be associated with an increased intraoperative blood loss (IBL). Severe portosystemic collaterals due to portal hypertension are potential origin of increased IBL. Preoperative, significant decrease of portal hypertension may potentially play a role in limiting IBL. We present a study protocol for a prospective, randomized study with an aim to compare effectiveness of two preoperative methods for portal hypertension modulation in accordance to the risk of IBL durgin liver transplantation.

Methods: Patients with clinically significant portal hypertension scheduled for an elective liver transplantation will be evaluated for participation in the study. Patients with an increased risk of massive IBL will be included and defined based on selected risk factors: retransplantation, previous upper abdominal surgery, planned portal vein thrombectomy, history of variceal bleeding or spontaneous bacterial peritonitis. Two interventions will be compared prior to liver transplantation: A. nonselevtive beta-blockers treatment B. nonselective beta-blockers treatment + transjugular porto-systemic shunt implantation. Primary outcome is the number of intraoperative blood units transfused during liver transplantation. The sample size is calculated to include 104 patients, 52 in each arm (p=0.05; 1-?=0.9). Secondary outcomes are IBL [ml], operative time, postoperative complications in accordance with Clavien-Dindo classification and Comprehensive Complication Index, intraoperative direction and velocity of portal blood flow, duration of hospitalization, episodes of variceal bleeding prior to liver transplantation, overall 90-day postoperative survival.

Conclusions: We hypothesize that significant decrease in portal hypertension resulted from transjugular porto-systemic shunt may significantly decrease IBL during liver transplantation in patients the most exposed for severe IBL. Moreover, we expect to observe increased postoperative short-term results due to decreased IBL.

EP_220 DOES GRWR REALLY MATTERS WHEN GRAFT WEIGHT IS MORE THAN 650 GMS IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Living donor liver transplantation (LDLT) is a vital solution for patients with end-stage liver disease, especially in countries where deceased donor organs are scarce. A key consideration in LDLT is the graft-recipient weight ratio (GRWR), with a recommended threshold of >0.8% to reduce complications like small-for-size syndrome (SFSS). However, transplants with a GRWR <0.8% are occasionally performed, particularly when the graft weight (GW) is >650 grams. This study analyzes the outcomes of LDLT cases with a GRWR <0.8% and a GW >650 grams, focusing on mortality and post-transplant complications.

Methods: A retrospective analysis was conducted on 4253 LDLT procedures performed between September 2006 and May 2024.Of these, 239 patients (5.6%) received transplants with a GRWR <0.8% and a GW >650 grams.

Results: The recipients had a median age of 47.8 years, with a predominance of males (87%). Major post-operative complications included short for size syndrome (**SFSS) 15.4%,** biliary complications 20.5% (n-49, Bile leak-7.53%, Biliary stricture-15.9%), and vascular complications 5.9% including HAT (n- 4) PVT (n-4), MHV blockage (n-9) patients. Despite the low GRWR, most of recipients showed satisfactory graft function, with 91.4% surviving beyond one year post-transplant.The 1 year mortality rate was 9.6%

Conclusions: The study reveals that while a GRWR <0.8% does not increase risks, careful donor selection and surgical expertise can yield acceptable outcomes, especially when the graft weight is > 650 grams. This approach may expand the donor pool and offer life-saving transplants for recipients who otherwise face limited options. However, optimizing pre-operative planning, intraoperative techniques, and post-operative care remains critical for further improving outcomes in this group.

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Current challenges in transplantation procedures

EP_221 BEST PRACTICES IN THE MANAGEMENT OF DONATION AND TRANSPLANTATION SERVICES

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Background: Effective management of donation and transplantation services is essential to ensure equitable access and optimize resource utilization to provide high-quality care for both patients and donors. This study explored current practice and how it aligns with best-practice recommendations.

Methods: A survey tool was designed and validated to collect data on the management of donation and transplantation services. Survey respondents included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: Among 253 survey participants, financial support was rated on a 10-point Likert scale for dialysis (average: 5.9/10), pre-transplant (average: 6.1/10), and post-transplant (average: 6.2/10) patients. A high demand for increased workforce capacity, particularly for transplant coordinators, was identified in focus groups. Reimbursement policies were reported as orthogonal to clinical decision-making for kidney transplantation. Financial incentives and penalties are predominantly related to patient reported outcome metrics (PROMS) rather than mortality rates. Performance and quality indicators for kidney donation and transplantation were viewed as somewhat adequate by 51% of participants, while protocols for monitoring risk adjustment variables were rated as 'very' to 'moderately' effective (87%). However, only 13% of institutions routinely collected PROMS. While electronic medical records (EMRs) were primarily used to track patient health data, some institutions still relied on paper-based systems.

Conclusions: Standardised protocols for collecting and monitoring performance and quality of care data, e.g. PROMS, financial incentives, and the widespread use of EMRs to enhance continuity of care were identified as essential elements of the efficient management of donation and transplantation services.

EP_222 EFFECTS OF PROGESTERONE TREATMENT REDUCING CENTRAL NERVOUS SYSTEM INJURY INDUCED BY ISCHEMIA AND REPERFUSION PROCESS

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Background: The process of ischemia and reperfusion of the organ during transplant surgery is a relevant an activator of injury related cascades. IR induced systemic inflammation can lead to neurological and cognitive complications; related to the activation of microglia. Progesterone is considered neuroprotective, modulating neuroinflammation and neurogenesis. Here we investigate the effects of progesterone (P4) treatment on the brain parenchyma after visceral ischemia and reperfusion (VIR).

Methods: Male Wistar rats were divided in 3 groups (n= 6/group): Sham, surgically manipulated; VIR, animals subjected to ischemia and reperfusion; and P4, animals treated with progesterone (2 mg/Kg, i.v.) at the beginning of reperfusion. VIR was induced by insertion of a 2-Fogarty® catheter in the descending aorta (aortic occlusion for 30 min, followed by a reperfusion period of 2h). Immunohistochemistry of anti-Iba-1 also know AIF-1 (Allograft inflammatory factor 1) and Fluoro-Jade C staining were performed to assess microglia activation and neurodegeneration in the brain parenchyma (prefrontal cortex, hippocampus, as well as the thalamus and hypothalamus).

Results: The number of active resident microglia cells was higher in the prefrontal cortex of both hemispheres in the VIR group compared to Sham ($p<0.0001$). There was a reduction of active cells count in the P4 group when compared to the VIR group ($p<0.0001$). Similar results were observed for thalamus and hypothalamus. In parallel, the Fluoro-Jade C staining was also higher in the prefrontal cortex of of both hemispheres in VIR group compared to Sham ($p<0.05$), with P4 treatment leading to a reduction of the staining mainly on the right side ($p<0.05$). The same was observed for thalamus and hypothalamus with higher numbers in VIR group and reduction in P4, also mainly on the right side ($p<0.05$).

Conclusions: Our results showed that the systemic inflammation triggered by visceral ischemia and reperfusion was responsible for activating microglia and cause neurodegeneration. However, treatment with P4 proved to be an important therapeutic agent to protect CNS, by effectively controlling microglia activation and reducing the neuronal degeneration.

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EP_224 EVALUATION OF LUNG GRAFTS PRE AND POST TRANSPLANTATION: LONG-LASTING INFLAMMATORY RESPONSE

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Background: Lung ischemia reperfusion injury leads to important alterations that can culminate in primary graft dysfunction after lung transplantation. The understanding of the time course of the pathway activations for the physiological response can contribute to the development of new therapeutic measures. In this study the lung inflammatory response and the expression of apoptotic markers were evaluated during the transplantion process.

Methods: Brain death donor lung biopsies from 10 transplants performed were collected at the end of cold preservation period (cold ischemia –CI) and 2-hours after reperfusion (reperfusion- R). Additionally, samples were maintained in culture medium for 24 hours and tissue and medium were stored (CI-24 and R-24). Gene and protein expressions of IL-6 and apoptotic markers (caspase-3 and BCL-2) were analysed. Lung tissue sections were analysed for edema and hemorrhage and immunohistochemical analysis of MPO.

Results: Regarding histological analysis, no difference was observed in pulmonary edema, but there was a significant increase in hemorrhage after reperfusion in relation to cold ischemia period. Caspase-3 and BCL-2 gene and protein expression did not differ in CI or R samples, but after 24 h their levels decreased in both (CI-24 and R-24). Regarding IL-6, gene expression increased in R samples in comparison to CI, but the IL-6 protein content was similar on CI and R samples. After culture, the release of IL-6 to the medium was high in both samples (CI-24 and R-24). MPO expression was increased in CI-24 in relation to CI and to PR-24.

Conclusions: Our research identified that between cold preservation period and 2 hours after reperfusion, no significant changes were observed in the inflammatory process and in apoptotic markers in lung tissue. However, after 24 hours in tissue culture, the analysis of the original samples showed that a long-lasting release of inflammatory mediators and a decrease in cell apoptosis can potentially occur in the lung tissue. These results open a possible application of this procedure to better identify the potential evolution of the transplanted graft.

EP_225 ADVANCING GREEN PRACTICES: CYANOACRYLATE ADHESIVES IN TRANSPLANT WOUND MANAGEMENT VS STANDARD DRESSINGS

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Introduction: Cyanoacrylate adhesives (glues) have gained traction for their rapid polymerization, forming strong, bactericidal bonds ideal for transplantation. They expedite healing, reduce scarring, and naturally degrade, eliminating removal needs. By minimizing dressing changes, discomfort, and medical waste, these adhesives align with greener surgical practices. This study aims to evaluate the clinical, economical, and environmental impact of glue in transplant wound closure.

Methods: Retrospective analysis was performed of kidney transplant over 12 months between 2020 and 2021. Data collected included patient demographics, type of skin closure and wound dressing along with surgical site occurrence (SSO) and skin dehiscence rate. Cost comparison and nursing survey were also conducted to compare the two techniques. The carbon footprint was calculated as the sum of greenhouse gas emissions (GHG) attributed to a certain process, is expressed in “carbon dioxide equivalents” (CO2e) based on the latest NHS England data using the formula:

=(No. of dressing equipment×cost×emission factor)+(No. of dressing equipment×weight×emission factors for incineration)

Results: The skin clips group had more patients than the glue group (n = 168 vs. n = 64), with similar demographics. SSI rates were not statistically significant (1.2% vs 3.1% staples vs. glue, p = 0.31). Collection rates were higher in the clips group (31.1% vs. 25%, p = 0.36). Dehiscence was absent in the glue group but occurred in 7.1% of the clips group (p = 0.028). Subjectively, nurses preferred glue due to reduced time spent on wound care (15 minutes for clips vs. 2 minutes for glue), better cosmesis, and no need for dressings in a clinic environment. Glue’s cost was half that of clips (£5.61 vs. £10.42) over 14 days. The carbon footprint of glue was almost negligible compared to clips (7.45 kgCO2e vs. 145.27 kgCO2e per patient).

Conclusion: Glue, in conjuction with monocryl subcuticular closure, showed favourable outcomes in kidney transplant incisions. With a carbon footprint almost a hundredth of that of clips and dressings, glue is a sustainable. Using clips and dressings results in about 150 kg CO2e, equivalent to a plane flying for one hour at 850 km/h, compared to 7.45 kg CO2e for glue, marking a key step in greener healthcare

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EP_226 DECISIONAL ALGORITHM AND MINI-INVASIVE TECHNIQUE ALLOW OPTIMAL OUTCOMES IN POLYCYSTIC KIDNEY DISEASE

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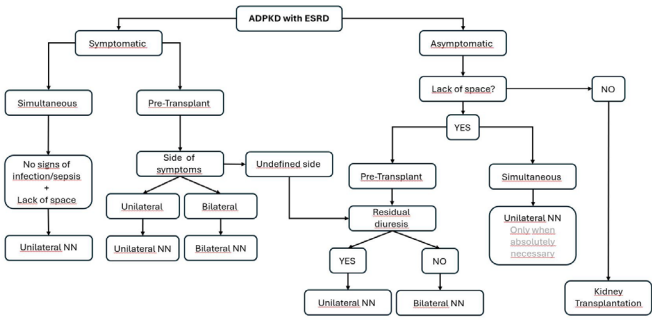
Background: Autosomal Dominant Polycystic Kidney Disease (ADPKD) frequently requires native nephrectomy (NN) before kidney transplantation (KT). NN may be performed before or simultaneously with KT. The ideal timing of NN in relation to KT remains a matter of debate, with no universal consensus. Several issues must be addressed in the decision-making process, including the importance of symptoms, residual diuresis, the availability of a living donor (LD) and longer operative times and higher complication rates for the combined procedure. Based on our experience, we sought to establish an algorithm to guide the decision-making process for assessing the indications and timing of NN in ADPKD patients awaiting KT.

Methods: We analyzed prospectively collected data on ADPKD patients who underwent laparoscopic NN, either unilateral or bilateral, at our department between 2018 and 2025. Demographic and clinical characteristics, as well as preoperative, intraoperative, and postoperative parameters, were recorded. The study population was divided into 2 groups based on the type of NN: unilateral (UNN) and bilateral (BNN).

Results: During the study period, 166 patients underwent NN (M:F=90:76): 140 UNN (73 right, 67 left), and 26 BNN. Among the study population, 17 patients required blood transfusions (14 in the UNN group, 3 in the BNN group). Overall, according to the Clavien-Dindo classification, we observed class III-IV post-operative complications in 9 patients (5.4%). No open conversions occurred and the 90-day postoperative mortality rate was 0.6% (one death after discharge due to sepsis).

Conclusions: Laparoscopic NN has proven to be technically feasible and safe for ADPKD patients. Based on our experience and results, we consider it a viable option to perform UNN laparoscopically before KT in symptomatic patients or asymptomatic patients with insufficient space for a transplant. BNN is reasonable in patients without preserved diuresis or those with a scheduled LD KT. The simultaneous procedure should be reserved for few selected cases: lake of space detected at the time of KT or the onset of symptoms at the time of KT, by balancing the related risks and benefits for both the graft and the patient. The minimally invasive technique and the algorithm depicted in Fig. 1 allow for favorable KT outcomes and patient safety.



EP_227 CAN PREOPERATIVE MEASUREMENT OPTIMIZE PEDIATRIC KIDNEY TRANSPLANTS?

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Background: Since its introduction in the late 1950s, pediatric kidney transplantation (PKTx) has become a routine procedure, demonstrating excellent graft and patient survival rates. To address organ shortages, adult-sized kidneys are often transplanted into pediatric patients with comparable functional and survival outcomes. However, such transplants pose challenges due to size mismatch, potentially causing abdominal compartment syndrome and vascular complications, such as kinking or stenosis. This study aimed to determine optimal organ sizes for adult-to-pediatric kidney transplantation.

Methods: A total of 107 patients undergoing living-donor nephrectomy (2016–2020) were included. After organ explantation and preparation, morphologic parameters (height, width, weight) were recorded. Correlations between organ characteristics and glomerular filtration rate (GFR) one-year post-transplant were analyzed. Magnetic resonance imaging (MRI) of pediatric patients (<6 years old, to account for greater size mismatch due to smaller abdominal cavities) listed for PKTx was reviewed to measure abdominal radii and assess suitability for adult-sized organs.

Results: Kidney width showed similar distribution between males and females (median 5.6 cm vs. 5.7 cm, p=0.51), unlike height (10.8 cm vs. 11.5 cm, p<0.01) and weight (median 5.6 cm vs. 5.7 cm, p<0.01). GFR at one year was significantly correlated with kidney width (Pearson correlation=0.495, p<0.01), but not with height (0.182, p=0.24) or weight (0.056, p=0.72). Pediatric abdominal radii ranged from 5–11 cm. Only 50% and 84% of adult-sized kidneys could be transplanted into recipients with radii of 5–6 cm and 6–7 cm, respectively, while 100% could be transplanted for radii >8 cm.

Conclusions: Kidney width is a critical predictor of post-transplant function and serves as a key feasibility indicator for surgical implantation. Preoperative imaging to measure pediatric abdominal radii can guide donor organ selection, minimizing technical complications and improving outcomes in PKTx.

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EP_229 INCISIONAL HERNIAS AFTER LIVER TRANSPLANTATION: A COHORT-BASED RISK FACTOR ANALYSIS WITH FOCUS ON IMMUNOSUPPRESSION

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Background: Incisional hernias (IH) are a burden in visceral surgery with an occurrence of 12.8 % in general and up to 43 % after liver transplantation (LTx). Some relevant risk factors for the development of IH are already known like diabetes, adiposity, age or intake of specific immunosuppressants. The aim of this study was to target perioperative variables and their impact on IH occurrence and further recurrence after surgical hernia repair in a cohort of 121 liver transplanted patients with focus on immunosuppression to shed light on possible levers for prevention.

Methods: Herein, we perform a cohort-based risk factor analysis for the occurrence and reoccurrence of IH following LTx and surgical hernia repair. All adult patients who underwent surgical hernia repair due to IH following LTx at University Hospital Regensburg between 2006 and 2022 were screened to meet inclusion criteria of a minimum 12-month follow up and compared to an equal sized control cohort. Clinical data and blood serum levels for immunosuppression were retrospectively collected and analyzed.

Results: We recorded an IH occurrence post LTx of 17.9 %. Patients treated with mTOR inhibitors had a 4.6-times higher risk to develop IH ($p = 0.014$). Comparing Calcineurin inhibitors we firstly target Tacrolimus superior to Cyclosporine treatment with a significant protective effect in our cohort (OR 0.049, $p < 0.001$, binomial logistic regression analysis). Measured serum levels and used products of immunosuppressant groups were further uninformative. Recurrence rate of IH after surgical hernia repair was 38.7 %, notably immunosuppressive therapy regiment did not influence recurrence. Mesh implantation was preventive for IH recurrence with an OR of 0.167 ($p = 0.047$). No significant difference between technics of mesh implantation or mesh material was observed.

Conclusions: We recommend careful evaluation of mTOR inhibitors during immunosuppressive therapy induction after LTx, Further, we observed beneficial effects of Tacrolimus compared to Cyclosporine administration in the context of incisional hernia development in our cohort. Mesh implantation was significantly risk minoring for IH recurrence. Interestingly, immunosuppressants had no influence on IH recurrence, presumably to perioperative adjustments avoiding mTOR inhibitor intake.

EP_230 IMPACT OF URETERAL STENT PLACEMENT ON EARLY AND MID-TERM GRAFT OUTCOMES IN LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Routine ureteral stent placement is a common practice in kidney transplantation to prevent ureteral complications. However, its impact on post-operative outcomes remains controversial. This study aimed to evaluate the effect of ureteral stent placement on early and mid-term graft function in living donor kidney transplantation.

Methods: A retrospective, single center analysis was conducted on 245 patients who underwent living donor kidney transplantation between June 2022 and December 2024. Patients were divided into two groups based on whether a ureteral stent was placed: Stent group (n=63) and non stent group (n=182). Demographic characteristics, urologic complications, 5th-day creatinine levels, final creatinine levels, 5th-day GFR, final GFR, graft dissection time, and incidence of slow graft function (SGF) were compared.

Results: The stent group included 32 females and 31 males, with a mean age of 40 ± 18.96 years, mean BMI of 26.2 ± 4.1, and a mean follow-up period of 10.91 ± 8.39 months. The non stent group included 53 females and 129 males, with a mean age of 42.08 ± 13.37 years, mean BMI of 25.86 ± 5.2, and a mean follow-up period of 9.85 ± 8.72 months. No significant differences were observed between the groups in terms of 5th-day creatinine levels, final creatinine levels, 5th-day GFR, final GFR or SGF rates ($p>0.05$). However, graft dissection time in donor was significantly higher in the stent group compared to the non stent group ($p=0.0003$). The urologic complications requiring intervention occurred in 3 patients and all were in stent group.

Conclusions: Ureteral stent placement does not appear to impact early graft function outcomes. The significantly longer dissection time in the stent group highlights a potential trade-off between surgical complexity and ureteral protection, suggesting that patient selection criteria for ureteral stent placement may need further refinement.

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EP_231 OPTIMIZING DONOR SELECTION IN LIVING KIDNEY TRASPLANTATION USING 3D MODELS AND THE LIVING KIDNEY DONOR PROFILE INDEX

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Background: Living donor kidney transplantation is one of the most effective treatment options for patients with end-stage renal disease. However, the functionality of the transplanted kidney can vary significantly depending on various factors, including donor and transplant characteristics.

Methods: At our center, we employ 3D surgical modeling technology originally developed for hepato-biliary-pancreatic surgery. This allows us to reconstruct the kidneys of potential living donors in three dimensions. These 3D models aid in surgical planning and provide a volumetric assessment of renal parenchyma, crucial for optimizing donor selection. Along with anatomical and functional data, this information helps determine the appropriate laterality for the transplant. The aim of this study is to evaluate the relationship between the ratio between the kidney volume (donated organ) and the recipient's weight and the estimated Glomerular Filtration Rate values correlating these factors with post-transplant renal function, assessed by scintigraphy, immediately after the transplant and during the following six months. Donors are also stratified using the Living Kidney Donor Profile Index.

Results: Our preliminary analysis indicates that kidney volume, relative to the recipient's weight, is directly correlated with the post-transplant renal function. Donors with higher kidney volume relative to the recipient's body weight appear to contribute to improved short-term and long-term transplant outcomes. Additionally, the use of 3D volumetric data, when combined with the Living Kidney Donor Profile Index, allows for a more personalized and accurate donor selection process, potentially increasing the likelihood of successful graft function. These findings suggest that volumetric measurements can complement traditional anatomical and functional assessments in transplant planning.

Conclusions: Incorporating 3D kidney volumetry into pre-transplant evaluation enhances the precision of donor selection, potentially improving both early transplant function and long-term outcomes. The findings support the hypothesis that kidney volume is an important determinant of transplant success. Further studies are needed to validate these results and refine the approach to donor matching.

EP_232 US BEDSIDE DURING THE DONOR SURGERY TO IMPROVE LIVER ALLOCATION IN TRANSPLANTATION

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Background: In Italy, like everywhere in the world, before the beginning of the procurement, is not always available the liver biopsy report, or is not always available CT imaging on site or transferable by internet, for the best selection of the recipient.

Methods: Often the donor surgeon can modify the choices on allocation after the macroscopic evaluation before and after the cold perfusion during the procurement, based on the available imaging and based on the histological report performed during the surgery; obviously if is available an expert pathologist on this field. This can in some cases, increase the CIT (cold ischemia time) or the hemodynamic instability of the donor, if the biopsy is sent for evaluation in another hospital affiliated. Consequently, it would be better to have the correct evaluation already at the beginning of the procurement, in order to allocate as best as possible, the liver organ.

Results: The aim of the study is to compare in 50 subsequent donors performed by our centre, the CT scan of the donor and liver biopsy, with a hepatosplenic ultrasound made at the back table, (the proposed ultrasound study evaluating the histogram in the grey scale of a specific area of parenchyma) in the way to correlate them with the follow up of patient transplanted until dismission from the hospital. (blood exams of organ function, CIT, length of hospital stays, ALT peak and complications)

Conclusions: Therefore, considering that level 2 imaging exams are not always available at the procurement hospital sites, and that the expert pathologist is not always available 24/7, the possibility of having a portable ultrasound scanner with a specific grey scale program, can enforce the visual evaluation of the donor surgeon providing an objective result that can improve the allocation and reduce ischemia times.

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EP_233 A QUALITATIVE STUDY ON THE IMPORTANCE OF PSYCHOLOGICAL SUPPORT DURING THE HEPATIC PRE-TRANSPLANT PHASE

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Background: A study conducted by FNETH in 2021 on health-related quality of life (HRQoL) among individuals who had undergone transplantation and had been taking immunosuppressants for more than 10 years highlighted the importance of psychological support in this process.

Methods: A qualitative study was conducted to understand the importance of psychological support during the waiting list phase for a liver transplant. Participants were selected based on a prior survey and divided into two groups: those who received psychological support and those who did not. Focus groups, life histories, and psychometric questionnaires (Beck Depression Inventory (BDI), Short Form Health Survey (SF-36), and State-Trait Anxiety Inventory (STAI)) were used to collect data.

Results: The study revealed that participants commonly experienced symptoms such as apathy, sadness, fatigue, and psychological distress. Additional issues included anxiety, fear, irritability, anhedonia, loneliness, stress, and guilt. Men reported higher levels of anxiety, stress, sadness, apathy, fatigue, fear, anhedonia, guilt, and loneliness, while women scored higher in distress and anger. Participants who received psychological support reported better quality of life, more effective coping strategies, and improved management of negative thoughts. Both groups reported common symptoms, including apathy, sadness, fatigue, anxiety, fear, as well as social, familial, and occupational challenges.

Conclusions: Psychological support is essential in the liver transplant process, as it helps patients cope with the emotional and psychological challenges of waiting for an organ. Although all participants acknowledged the importance of psychological support, only 75% received it. Greater efforts are needed to improve the availability and accessibility of psychological support for patients on the liver transplant waiting list.

EP_234 IMPROVED MITOCHONDRIAL FUNCTION FOLLOWING PAEDIATRIC LIVER TRANSPLANTATION IN MNGIE SYNDROME - SINGLE CENTRE EXPERIENCE

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Background: Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE) is a rare disorder caused by thymidine phosphorylase (TP) deficiency, leading to toxic thymidine buildup and progressive symptoms, including dysmotility and neuropathy. Hematopoietic stem cell transplant restores TP activity but poses high risks. This study presents three pediatric MNGIE patients who underwent liver transplantation (LT).

Methods: Three patients (ages 12, 15, and 16) underwent LT. Pre-transplant symptoms included poor weight gain and elevated lactate (2.5–6.9 mmol/L). Patient characteristics are detailed in the table.

Results: Post-LT, metabolic parameters normalized with stable thymidine levels. Neurological improvements included better power, sensation, and reflexes. Despite persistent gastrointestinal dysmotility requiring parenteral nutrition (PN), patients reported better oral intake and reduced PN dependence over time. Complications included one case of biliary stricture managed with PTC and dilatation and another of acute rejection and PTLD treated with Basiliximab.

Conclusions: LT effectively slows MNGIE progression by restoring TP levels, improving metabolism, and alleviating some symptoms. However, gastrointestinal challenges persist, and long-term follow-up is crucial to evaluate the neurogastrointestinal impact.

Patient	Sex	Age at transplant	Weight Pre-transplant (z score)	Weight 6 Months Post-Tx	Weight 12 Months Post-Tx	Weight 24 Months Post-Tx	Secondary Dx	Type of Graft
1	Male	12 years 4 months	16.4Kg (-4.47)	16.4Kg (-4.47)	16.4Kg (-4.47)	16.4Kg (-4.47)	Gastroparesis, leukoencephalopathy, severe polyneuropathy, foot drop	Isolated Liver Graft
2	Male	15 years 7 months	30.6Kg (-1.63)	30.6Kg (-1.63)	30.6Kg (-1.63)	30.6Kg (-1.63)	Mild biliary narrowing, leukoencephalopathy, resolved foot drop, new hand	Isolated Liver Graft
3	Female	16 years 9 months	24.1Kg (-5.7)	24.1Kg (-7.05)	24.1Kg (-8)	24.1Kg (-6.8)	No other secondary problems	LLC DAD

Table.

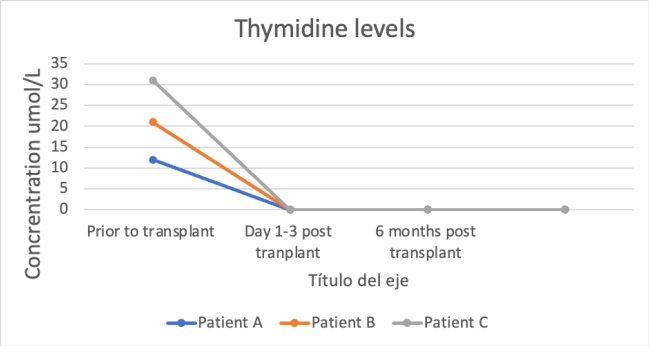

Figure: Normalization of thymidine levels post-transplantation

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Current challenges in transplantation procedures

EP_235 DONOR'S BLOOD CELL RETRIEVAL FOR SUSTAINABLE RECIPIENT'S INTRAOPERATIVE TRANSFUSIONS: PRELIMINARY RESULTS OF BLEED STUDY

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Background: Liver transplantation (LT) is a complex and high-risk surgery often associated with significant blood loss. Despite the progressive trend toward a restrictive transfusion strategy, in most LTs packed red blood cell (PRBC) transfusion is unavoidable. Donor blood is discarded during the liver harvest. However, its utilization for the LT transfusion support has been pioneered by some authors (Shaylor R, et al. Transplantation 2021; 105:1556). The BLEED study (Clinical.Trial.gov NCT05835882) is a pilot study with the main objective to confirm the feasibility of recovering blood from liver donors during the organ harvest and processing it into RBC concentrates to be used for the intraoperative transfusions of LT recipients.

Methods: Adult patients receiving a LT from in-hospital deceased donors, with identical donor ABO group, and giving signed informed consent to the study participation are enrolled. Negative donor-recipient RBC crossmatch results are documented before the harvesting procedure. Livers are perfused with UW solution. After heparin administration, donor blood is retrieved and processed using the continuous autotransfusion system CATSmart (Fresenius Kabi) to remove plasma, leukocytes and UW residuals, and suspended in saline solution with a target hematocrit of 50-70%. Donors and recipients' demographics and clinical data were collected.

Results:

	DONOR						RECIPIENT						
Pt	Age	Death Cause	ABO group	Htc (%)	PRBC harvest (ml)	PRBC Htc (%)	Age	Indication	MELD	Pre-LT Htc (%)	Donor PRBC (ml)	Auto trasfusion (ml)	Allo PRBC units (n)
1*	68	ICH	B pos	42.2	820	57.0	64	Alcohol-HCC	12	38.9	820	320	0
2	54	ICH	0 pos	49.9	1400	68.0	56	MASLD-HCC	7	37.1	0	350	0
3	52	ICH	B pos	46.1	842	67	66	MASLD-HCC	14	27.4	0	130	0
4	61	ICH	0 pos	42.8	900	nr	63	MASLD-HCC	12	39	0	0	0
5	84	Trauma	A pos	39.7	400	nr	69	Alcohol	11	33.9	0	0	0
6*	74	ICH	A pos	45.1	900	nr	56	MASLD-HCC	14	35.3	900	1000	0

* No transfusion related adverse events were recorded, including hemolysis, TRALI and AKI.

Conclusions: Processing deceased donor blood into PRBCs for the transfusion support of LTs is a feasible and safe procedure. These preliminary data suggest that it may limit blood product consuming in recipients and reduce the risk associated with multiple blood donor exposure.

EP_236 IMPLEMENTATION OF A ADULT LDLT PROGRAM IN A HIGH-VOLUME LIVER TRANSPLANTATION CENTER: A CASE SERIES

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Background: Living donor liver transplantation (LDLT) was developed to address the organ shortage faced by patients with end-stage liver disease. This technique is a proven, non-inferior alternative to deceased donor liver transplantation (LT). However, it is technically demanding and requires substantial clinical expertise.

Methods: We conducted a retrospective review of patients who underwent LDLT as part of a novel program at a high-volume liver transplantation center.

Results: Between October 2024 and January 2025, three patients underwent LDLT. The indications for LT included multiple hepatic epithelioid hemangioendothelioma lesions, cirrhosis due to Wilson's disease, and primary sclerosing cholangitis. All patients received right lobe liver grafts, which were harvested from living first-degree relatives. One case involved complications necessitating endovascular intervention and reoperation. No additional complications were observed, and both recipients and donors were successfully discharged.

Conclusions: The LDLT program was successfully implemented, yielding promising initial outcomes. Introducing an LDLT program is feasible and safe in high-volume centers with expertise in LT and hepatobiliary surgery.

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EP_237 THE SATA MULTICENTER LIVER TRANSPLANT ANESTHESIA OUTCOMES DATABASE

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Background: Most research in Liver Transplant Anesthesia is retrospective and based on single-center data, limiting its generalizability. Registries like the Scientific Registry of Transplant Recipients (SRTR) in the USA lack granular intraoperative data. The Society for the Advancement of Transplant Anesthesia (SATA) addresses this gap with the Multicenter Liver Transplant Anesthesia Outcomes Database (SATA Liver Database). It is designed to standardize data collection, facilitate collaborations, and provide a platform for research and quality improvement in liver transplantation at no cost. It can be implemented locally using the Research Electronic Data Capture (REDCap) system or a simple spreadsheet. We want to provide an update on the SATA Liver Database and encourage interested international centers to adopt the platform for their practice.

Methods: We provide the following resources: - A data dictionary with standardized variable definitions on fluid management, blood product usage, monitoring, acute kidney injury, extubation, and ICU length of stay. - A REDCap template for easy deployment. Data is collected locally and remains under the control of the individual center. - Centers in the United States can share de-identified data with the University of California, San Francisco, and data will be linked to SRTR outcomes data. - Bylaws governing data sharing, use, and authorship for publications.

Results: As of January 2025, 33 institutions with a yearly volume of 3,900 liver transplants (39% of all liver transplants in the United States) are participating. Twenty-two centers are collecting data. Twenty centers have completed data use agreements with UCSF. We are preparing the first merged dataset, with completion anticipated in early 2025. This will enable multicenter research projects and demonstrate the database's potential to transform collaborative research and quality improvement in liver transplantation.

Conclusions: The SATA liver database enables the collection of standardized perioperative data for liver transplant anesthesia, facilitates multicenter research in liver transplant anesthesia, and has the potential to improve perioperative care and patient outcomes significantly. More information: www.liverdatabase.com; Submitted for the SATA Liver Database Investigators.

EP_239 TOWARD REAL-TIME AI ASSISTANCE IN HARDN: LEVERAGING CNN FOR SURGICAL STANDARDIZATION

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Background: Hand-Assisted Retroperitoneoscopic Donor Nephrectomy (HARDN) is a minimally invasive surgical technique that requires high precision and technical expertise. Variability in outcomes and procedural challenges underline the necessity of advanced decision-support tools. Artificial Intelligence (AI), particularly Convolutional Neural Networks (CNN) and computer vision, offers promising solutions for optimizing surgical workflows. This study aims to develop and validate an AI-driven surgical guide for HARDN, leveraging CNN to analyze and process video recordings of surgeries.

Methods: This ongoing study involves a retrospective analysis of 500 recorded HARDN procedures. High-resolution surgical videos are being pre-processed and annotated to train CNN models capable of recognizing critical procedural steps, anatomical landmarks, and potential risk areas. The model development is focused on achieving real-time performance metrics, such as accuracy, precision, and recall. The data processing and training phases are currently underway, with initial analyses validating the feasibility of the approach. Simulated environments are being prepared to test the real-time application of the developed AI system.

Results: Preliminary findings indicate that the CNN models can identify key procedural steps and anatomical structures with promising accuracy. Early testing in the training phase suggests a recognition rate exceeding 90% for critical steps, though further refinement and validation are ongoing. The dataset continues to be processed to enhance model robustness, and subsequent simulations will determine its utility as a surgical guidance tool.

Conclusions: Although this study is in progress, early results support the feasibility of integrating AI-driven systems into HARDN workflows. This approach has the potential to standardize surgical procedures, enhance decision-making, and improve patient outcomes. Future steps include finalizing data processing, validating the model in live settings, and exploring its application to other surgical techniques.

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EP_240 GRAFT LOSSES AND PATIENT SURVIVAL AFTER KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background: Reduction of graft losses and improvement of patient survival are the main problems in transplantation. Evaluation of impacting factors may help to identify those factors that could be modified to improve transplantation outcomes. The aim of this study was to evaluate factors impacting graft and patient survival in our transplant center.

Methods: This study included 882 consecutive kidney transplantations from deceased donors performed from 01.01.2004 till 31.12.2017 in one transplantation center. We analyzed impact of donor (demographic factors, diagnosis, hospitalization data, laboratory values, expanded criteria for donation), recipient (demographic factors, diagnoses, dialysis mode, sensibilization, re-transplantations), transplantation factors (cold ischemia time, graft anatomy and pre-transplant vascular reconstruction, re-transplantation) and presence of posttransplant complications (delayed graft function, surgical complications, acute rejections) on graft and patient 5-year survival.

Results: Early kidney graft thrombosis and primary non-function were observed in 12 cases (1,36%) and were associated with peritoneal dialysis mode in recipients, higher hemoglobin/ hematocrit levels in donors and re-transplantations. In later period graft losses (21.9%) were associated with donor hemodynamical instability in pre-explant period, recipient age, sensibilization, development of delayed graft function, surgical complications and acute rejections in posttransplant period. Patient survival showed association with donor age, presence of expanded criteria recipient age and weight, development of delayed graft function and urological complications.

Conclusions: Graft losses have multifactorial reasons, including delayed graft function, development of surgical complications and acute rejections. Improvement in donor management, organ storage, intraoperative and early postoperative management may reduce negative impact of some affecting factors.

EP_241 VALIDATION AND ADAPTATION OF THE EUROTRANSPLANT DATA-BASED CLINICAL KTOP AND CLINICOPATHOLOGICAL 2-STEP SCORE TO US DATA

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Background: Scores that predict outcome after kidney transplantation are numerous, but only recently have two Eurotransplant (ET) data-based models, KTOP and 2-Step Score, been developed. External validation is an important step in assessing quality and reliability before their use. The availability of extensive validation data, such as the UNOS dataset, should be seen as an opportunity to further adapt the scores. A particular focus will be on organs from medically complex donors in terms of their clinical parameters, as they have the highest discard rates, possibly unreasonably. Ultimately, we want to use the new scores to reduce the number of kidneys discarded due to transplantability and quality assessment.

Methods: The UNOS dataset analysed includes donors and recipients aged > 18 years with single kidney transplants performed since 2015. The dataset is split into a training and validation set stratified by pseudomized centre ID and year of transplantation. Approximately 5000 observations are randomly selected from each training and validation set. For KTOP and 2-Step Score, the risk of one-year death-censored graft loss is predicted, the risk of delayed graft function is assessed by the 2-Step Score. Discrimination, calibration and overall performance according to Brier Score are assessed on the validation set. Subgroups of interest are based on Kidney Donor Risk Index (KDRI), donor setting (DBD vs. DCD), perfusion pump availability vs. cold storage, and the intermediate risk group according to the 2-Step Score. Adaptation of the 2-Step Score to the UNOS data is performed on the training set and validated on the validation set for comparison.

Results: As the UNOS data are still being processed, the validation and score adaptation results are expected by the end of April 2025. Of particular interest in the adaptation step is the update with histological parameters, which have been systematically collected in UNOS since 2024.

Conclusions: We expect both ET-based scores to perform well, comparably to scores based on UNOS data. The inclusion of histological findings should significantly improve the accuracy of prediction compared to scores based on clinical parameters only, both overall and in the intermediate risk subgroups according to the 2-Step Score and the high-risk subgroups according to the KDRI.

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EP_242 FUNDAMENTAL STRATEGIES AND TECHNICAL PERSPECTIVES IN BILIARY RECONSTRUCTION FOR LIVING DONOR LIVER TRANSPLANTATION

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Background: Biliary reconstruction is a critical procedure in living donor liver transplantation (LDLT), influencing postoperative recovery and quality of life. Preventing biliary complications, such as stricture and leakage, requires meticulous surgical techniques. This study aims to discuss the surgical approaches and techniques used to improve patient outcomes.

Methods: This retrospective study includes 500 biliary reconstructions performed by a single surgeon. Biliary anastomosis should be started by selecting the recipient's bile duct with adequate blood supply and diameter at least 1.5 times larger than the donor's. The anastomosis method was performed using 6-0 PDS interrupted sutures, and an external stent was placed in nearly all cases. The inner surfaces of the bile ducts were closely aligned, and the outer surfaces were positioned with thicker contact, ensuring the recipient's bile duct covered the donor's, minimizing the risk of leak and stricture. Preoperative data were collected for analysis, including bile duct number, size, and donor surgical methods.

Results: Biliary complications were observed in 8.4% of cases, with strictures in 8.4% and leaks in 0.26%. Notably, strictures that required treatment with endoscopic or percutaneous drainage were more prevalent in recipients with donors who had smaller or multiple bile ducts and in laparoscopic donor hepatectomy, demonstrating statistically significant results.

Conclusions: In LDLT, selecting an appropriate anastomosis site and meticulous surgical techniques are essential in reducing biliary complications. These factors are critical in lowering postoperative complication rates and improving long-term outcomes, highlighting the importance of precision in surgical practice.

EP_243 SYSTEMATIC REVIEW AND META ANALYSIS OF AORTO-HEPATIC CONDUITS IN LIVER TRANSPLANTATION

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Background: Aorto-hepatic conduits (AHCs) are used for liver allograft revascularisation when the native hepatic artery is unusable. Studies suggest that outcomes with AHCs are inferior compared to native hepatic artery inflow.

Methods: This systematic review and meta-analysis assess the outcomes based on different inflow sites for AHCs. The review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) standards (PROSPERO ID: CRD42024545810).

Results: Fourteen studies included 32,486 deceased donor liver transplants, of which 1,136 (3.5%) required AHCs. The most common indications were poor arterial flow, intimal dissections, and hepatic artery thrombosis (HAT). Among the AHCs, 18.2% were supra-coeliac (SC), 65% were infra-renal (IR), and 2.2% used iliac artery conduits. Pooled analysis showed comparable demographics across groups. The median follow-up ranged from 18 to 52 months. No significant differences were found between SC and IR conduits in early (OR 0.94; P = 0.86) or late occlusions (OR 0.46; P = 0.15), early allograft dysfunction (OR 0.82; P = 0.51), biliary complications (OR 1.10; P = 0.68), renal replacement therapy (OR 1.12; P = 0.62), or major surgical complications (OR 1.06; P = 0.79). Median graft occlusion occurred at 142 days (range: 13–3,313). One-year graft survival rates were 77%–81.1% (SC) and 66%–79.1% (IR), with five-year rates at 53.9%–67% (SC) and 50%–56% (IR).

Conclusions: There were no significant differences in early or late outcomes between SC and IR AHCs, though IR conduits showed a trend toward higher late occlusion rates.

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EP_246 OUTCOMES OF SIMULTANEOUS PANCREAS & KIDNEY TRANSPLANTATION, A TERTIARY CARE CENTER EXPERIENCE, INDIA

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Background: Pancreatic transplantation is a complex surgical procedure which has the highest rate of complications among all the solid organ transplants, with wide range of postoperative complications that can significantly impact graft function and patient outcomes. The risk of complications is specifically high in the early stages especially in emerging center which can be easily controlled with adequate gain of experience in SPK management leading to successful results with promising long term outcomes. The aim of our study is to report the emerging experience from a tertiary care center where the highest number of SPK transplants take place in the country.

Methods: This is a retrospective study analysing the data of all patients who underwent SPK transplantation at our center – Department of Renal Transplant Surgery, PGIMER, Chandigarh, India during 2014 to 2024.Total 55 patients were divided into 3 cohorts based on the year of transplant; Group A(2014-2017), Group B(2018 to 2020), Group C(2021 to 2024) and the graft outcomes are presented.

Results: • Group A with 11 patients; had 7 relaparotomy, 3 graft pancreatectomy, 6 DGF & 2 mortality. • Group B with 13 patients; had 5 relaparotomy, 2 graft pancreatectomy, 2 DGF and no mortality. • Group C with 31 patients; had 5 relaparotomy,1 graft pancreatectomy, 1 DGF & 1 mortality. The complications significantly reduced in later stages over 10years. Relaparotomy rates reduced from 63% to 16% ; graft pancreatectomy reduced from 27% to 3% & delayed graft function reduced from 54% to 3%. Insulin independence increased from 72% to 96% of cases.

Conclusions: This study presents the outcomes of SPK transplantation from an emerging transplant center, highlighting that initial outcomes were suboptimal, with a high rate of complications which significantly decreased over time with gain in experience of donor management, patient selection, and effective postoperative care, including the early diagnosis and treatment of complications.

	Group A (2014-17)	Group B (2018-20)	Group C (2021-24)
Number	11	13	31
Mean Sr. creat (mg%)	1.15 ± 0.35	0.85 ± 0.25	1.07 ±0.5
Delayed graft function	6/11	2/13	1/31
Hospital stay (days)	44.2 ± 23.8	30.1 ± 24.9	21.9±11.3
Re exploration	7/11	5/13	5/31
Graft pancreatectomy	3/11	2/13	1/31
Insulin independence	8/11	11/13	30/31
30 Day mortality	2 /11	0/13	1/31

EP_247 OPTIMIZING ADJUSTED ARTERIAL AND PORTAL FLOW PREDICTORS FOR PRIMARY GRAFT DYSFUNCTION IN LIVER TRANSPLANTATION

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Background: Primary graft dysfunction (PGD) significantly impacts outcomes after liver transplantation. Accurate intraoperative predictors, such as arterial and portal flows adjusted for graft weight, can improve early detection and management. This study evaluates a combined predictive model using adjusted flows to enhance risk stratification.

Methods: A retrospective analysis was conducted on 462 liver transplant recipients. PGD occurrence, defined by clinical and biochemical markers, was the primary endpoint. Predictors included adjusted arterial flow (8.3 ± 3.1 ml/min*100g) and adjusted portal flow (69.8 ± 19.4 ml/min*100g), analyzed using logistic regression. Receiver operating characteristic (ROC) analysis assessed model performance, with the Youden Index identifying the optimal threshold. Statistical significance was set at $p \leq 0.05$.

Results: PGD occurred in 22.5% of cases. Patients with PGD had significantly lower adjusted arterial flow ($p < 0.001$) and adjusted portal flow ($p = 0.009$) compared to those without dysfunction. The combined model demonstrated moderate predictive ability (AUC = 0.68), with an optimal threshold of 0.176 (sensitivity = 56.25%, specificity = 86.18%). Individually, adjusted arterial flow performed better (AUC = 0.72) than adjusted portal flow (AUC = 0.61). However, the combined model provided a balanced approach, improving specificity while maintaining acceptable sensitivity.

Conclusion: Adjusted arterial and portal flow measurements are significant predictors of PGD. The combined model demonstrates moderate predictive accuracy and high specificity, supporting its utility in targeted interventions. Prospective studies are needed to validate these findings and refine predictive thresholds.

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EP_248 COMBINED LIVER-KIDNEY TRANSPLANTATION IN POLYCYSTIC DISEASE: A SINGLE CENTER'S ROLE IN CHRONIC DONOR SHORTAGES

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Background: Combined liver-kidney transplantation (CLKT) is a critical therapeutic intervention for patients with end-stage liver disease (ESLD) and chronic kidney disease (CKD), particularly in polycystic liver and kidney disease (PLKD). The increasing number of combined liver-kidney transplants has resulted in a large cohort of patients who need to be studied in detail to identify factors (both donor- and recipient-related) that are associated with better outcomes. This manuscript details our center's unique position as a leader in transplantation in Sicily, a region characterized by a high rate of donation refusals (36.3% in 2024) and a severe organ shortage.

Methods: Between 2008 and 2024, we performed 17 CLKTs, predominantly utilizing extended-criteria donors (ECDs). Advanced techniques such as hypothermic machine perfusion (HMP) and delayed kidney transplantation have enabled exceptional outcomes despite challenging donor conditions.

Results: All patients underwent simultaneous liver-kidney transplantation (SLKT). The mean cold ischaemia time (CIT) for the kidney graft was 750 minutes (range: 481-1020 minutes). Pre-operative dialysis was performed to avoid the need for continuous veno-venous haemofiltration (CVVH), and post-operative haemodialysis was performed as required. Immunosuppression included tacrolimus, mycophenolate mofetil, and steroids for all recipients. All patients 17/17 (100%) are still alive and in good clinical condition, only 1/17 (5.8%) has kidney graft loss and is listed for retransplantation.

Conclusions: Our findings highlight the pivotal role of our institution in addressing regional challenges through innovative approaches, extensive clinical expertise, and strategic policy adaptation. These results underscore the potential to replicate such successes in similar high-opposition regions.

Donation, preservation & regeneration

EP_249 ACCURACY BETWEEN ESTIMATED GRAFT VOLUME AND ACTUAL GRAFT WEIGHT IN LIVER TRANSPLANTATION

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Background: In the living donor liver transplant (LDLT) one of the preoperative evaluation stage is the calculation of graft-recipient-weight ratio (GRWR) and remnant liver volume. According to the our criteria, the remant volume should be at least 40% and the GRWR should be at least 1%. We aimed to determine the accuracy of pre-operative computed tomography (CT) graft measurements with actual graft weights in LDLTs in our centers.

Methods: Since 1988, 767 liver transplants have been performed by our team. Of these 767 liver transplants, 547 were LDLTs. Preoperative CT images and intraoperative graft weights were analyzed retrospectively.

Results: Three hundred six (56%) of 547 donors were female and 241 (44%) were male. The mean age of donors was 44 ± 8.5 years. The mean weights of donors was 76 ± 12.5 kg. Of the donor hepatectomies, 47% (n=258) were left hepatectomy, 31% (n=173) right hepatectomy and 22% (n=116) left lateral hepatectomy. The mean total liver volume of donors measured by CT was 1555.41 ± 235 cm3. The mean graft volüme was 519.41 ± 250 cm3 and the mean graft weight was 507.37 ± 242 cm^3 When we measured the graft weights during surgery, we found that its ratio to the volume measurements made radiologically was 1.03. Remant liver volume in donors was 64.28 ± 15.7% of the total volume.

Conclusions: To prevent, small-for-size or large-for-size for the recipient and liver failure for the donor, preoperative radiological assessment of the donor's liver is very important.

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EP_250 ARE EXISTING CLASSIFICATIONS SUFFICIENT FOR DETECTING HEPATIC ARTERY VARIATIONS?

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Background: Liver transplantation (LT) from a living donor is a more complex and difficult method than deceased LT. Because during the separation of the graft from the donor, the liver part that will remain in the donor and the vascularity of the graft must be preserved. For surgical planning, in addition to calculating volumetric data with multi detector tomography before the operation, the anatomy of the hepatic artery, portal vein and hepatic vein must be determined. The most commonly used classification methods for hepatic artery variations are the Michels and Hiatt classifications. However, in our daily practice, we sometimes encounter many patients who cannot be grouped or who are accompanied by other variations in addition to the defined group.

Methods: In this study, we examined the hepatic artery computed tomography angiography tests taken before the operations of 297 live liver donors performed at our hospital between January 2012 and August 2024 and grouped the hepatic artery variations according to the Michels and Hiatt classifications. We also identified and classified the cases that could not be classified using either classification method.

Results: Many variations that did not comply with the Michels and Hiatt classifications were observed in our patient group. Especially the variations in the medial and lateral segmental branches of the left hepatic artery, the variations in the origin of the right hepatic artery, and the separation of the arteries in the form of trifucation are among the important variations that stand out.

Conclusions: Based on our data, Michels and Hiatt classification systems are inadequate in determining hepatic artery variations in many patients. We think that a more comprehensive classification system that includes segmental arteries should be developed.

EP_251 ARE RENAL CYSTS A BARRIER TO DONATION AND KIDNEY TRANSPLANTATION?

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Background: In order to expand the donor pool in kidney transplantation (KT), it has been reported that there is no contraindication kidneys with simple cysts below 3cm transplanting them. On the other hand, there are also studies suggesting that simple cysts increase in size and number over time, disrupt the renal structure and cause an increase in creatinine values. We aimed to evaluate the long-term outcomes of transplanted kidney grafts with cysts.

Methods: Among KT performed by our team between February 2012 and August 2023, those whose grafts contained simple cysts were retrospectively analyzed. Demographic characteristics, cyst size, perioperative complications, postoperative creatinine levels and cyst size during the follow-up period were recorded.

Results: Between February 2012 and August 2024, 65 KT were included in the study. The mean age of the recipients was 50.3 years and 38 were women. The mean cyst size was 14 mm. Of the grafts, 8 (12.3%) had cysts <5 mm, 17 (26.1%) had cysts between 5-10 mm, and 40 (61.5%) had cysts >10 mm. No intraoperative complications were observed in any of the donors or recipients. Urinary tract infection developed in 8 patients within 1 week postoperatively, but recovered completely with iv. antibiotic treatment. In the control ultrasonography performed at the 6th postoperative month, 43 of 65 patients showed a decrease in the size of the cyst in the graft kidney, while 15 patients had enlarged cysts. Except for 1 patient, the enlarged cysts did not require additional intervention except for follow-up. Only 1 patient's cyst was >5cm and excision was performed. Postoperative day 1, week 1, month 1 and year 1 values were 2.48 mg/dl, 1.42 mg/dl, 1.23 mg/dl and 1.42 mg/dl, respectively.

Conclusions: Kidney grafts with simple cysts do not constitute an obstacle for KT provided that the transplantation is performed by experienced centers and they are followed up regularly.

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EP_252 LONG TERM RESULTS OF KIDNEY TRANSPLANT WITH DONOR GIFTED NEPHROLITHIASIS

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Background: In the literature, there are studies indicating that a stone in the graft kidney may cause urinary tract infection in the recipient and may cause ureteral obstruction leading to graft loss. We investigated the long-term outcomes of donor gifted nephrolithiasis performed in our center on recipients.

Methods: Between February 2012 and August 2024, we retrospectively analyzed the kidney transplants (KT) performed in our center for those who had stones in the graft. Radiological evaluation of all donors was performed with high sensitive multisection computed tomography in the preoperative period. Preoperative parathormone (PTH) and calcium (Ca) levels of donors, preoperative PTH and Ca levels of recipients, size and number of stones in the graft kidney, perioperative complications, postoperative serum creatine levels and postoperative ultrasonographic findings were recorded and analyzed.

Results: Donor gifted nephrolithiasis was detected in 19 patients. All of these grafts were obtained from living donors. All donors were asymptomatic and had no history of stone-related disease. The mean preoperative PTH was 46 ng/L, the mean Ca was 9.4 mg/dl. Thirteen (78%) of the recipients were female and the mean age was 43 (25-67) years. Recipients mean preoperative PTH was 625 ng/L and the mean Ca was 9.3 mg/dl. All grafts had one stone and the mean stone size was 4.1 mm (1-10 mm). No intraoperative stone-related complications were observed in any patient. Urinary tract infection developed in 3 patients in the early period and was treated with antibiotic therapy. Creatinine values of the recipients were 3.02 mg/dl on postoperative day 1 and 1.11 mg/dl on postoperative year 1. Ultrasonography performed 6 months after KT showed no stones in 18 recipients. In 1 patient, the stone persisted in the same size.

Conclusions: Transplantation of kidney grafts with single and asymptomatic stones is not a barrier for KT.

EP_253 LIVER STEATOSIS ASSESMENT FOR TRANSPLANTATION: VITAMIN A FLUORESCENCE AND NEAR-INFRARED SPECTROSCOPY

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Background: Liver steatosis, marked by excess fat in hepatocytes, is central to conditions like Non-Alcoholic fatty liver disease and Non-Alcoholic Steatohepatitis. Accurate quantification is essential, especially in the context of liver transplant, but current methods, such as biopsies, are very variable and local. Optical methods such as Near-infrared diffuse reflectance spectroscopy (NIR DRS) which uses fat absorption properties and fluorescence spectroscopy of Vitamin A, naturally present in fat droplets, offer a non-invasive alternative for fat quantification. This study integrates both methods to enhance steatosis quantification.

Methods: We used NIR SG1 (InnoSpectra) spectrometer to measure NIR DRS spectra and a homebuilt experimental setup to make fluorescence measurements. Preclinical data were acquired on mice fed with Methionine/Choline Deficient (MCD) diet during 0 to 6 weeks to induce steatosis. An example of data acquisition with both devices are presented in Figure 1. Results obtained with optical methods were compared to gold standard Hematoxylin/Eosin histology.

Results: NIR DRS accurately quantified fat volume fractions in the murine steatosis model, with strong correlation to histopathological analysis. This method is able to quantify efficiently fat content in every group of mice, with steatosis fraction going from 0 to 80 % (control to MCD 6 weeks diet). Fluorescence spectroscopy identified significant correlation between hepatic vitamin A concentrations and steatosis fraction obtained by histological analysis (R^2>0.7). This confirms the presence of Vitamin A in fat droplets and validates its biomarker potential for steatosis assessment.

Conclusions: This study highlights the potential of combining NIR DRS with fluorescence vitamin A analysis for non-invasive, precise liver steatosis assessment. Future validation in clinical settings could broaden its application to severe liver conditions, offering a robust alternative to biopsies. Next application of those measurements would be to evaluate not only steatosis degree but also discriminate micro and macro steatosis using information obtained by both methods.

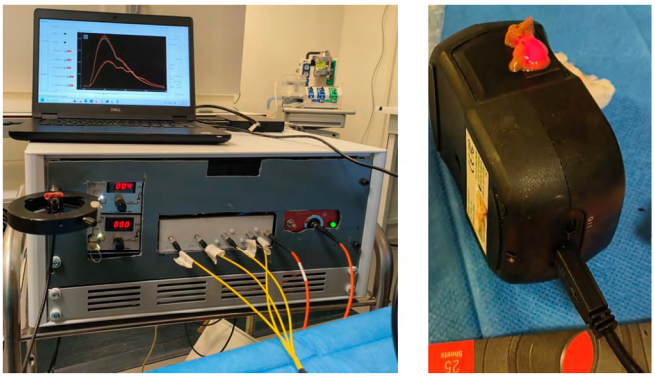

Figure 1 Data acquisition on mice livers with fluorescence setup (left) an NIR SG1 spectrometer (right)

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EP_254 OPTIMIZING POSTOPERATIVE PAIN MANAGEMENT IN HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY: A MULTIMODAL APPROACH

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Background: Effective postoperative pain management is crucial for the recovery of living kidney donors and the reduction of complications. This study evaluates the outcomes of multimodal pain management versus conventional strategies in living kidney donors undergoing hand-assisted laparoscopic donor nephrectomy (HALS).

Methods: This single-center, retrospective cohort study analyzed 200 kidney donors who underwent HALS between February 2023 and March 2024. A multimodal pain management protocol, incorporating a pain management initiative, was introduced in August 2023, replacing conventional PRN opioid analgesics with scheduled acetaminophen and PRN non-opioid analgesics. Donors were categorized into pre-protocol (n=100) and post-protocol (n=100) groups. Pain scores (Numeric Rating Scale, NRS), use of patient-controlled analgesia (PCA), PRN analgesic consumption, opioid-related side effects, and renal function were analyzed.

Results: Multimodal pain management significantly reduced pain scores compared to conventional methods (POSTOP: 5.68 vs. 5.26; **POD#1: 4.44 vs. 3.96, p<0.05**; POD#2: 3.63 vs. 3.43; POD#3: 3.01 vs. 2.92; POD#4: 2.45 vs. 2.44; POD#5: 1.45 vs. 1.68). Despite a slight increase in PCA fentanyl usage (1228.9±562.7 mcg vs. 1256.19±700.8 mcg), fewer patients required PRN analgesics (68 vs. 51). Opioid use significantly decreased, with pethidine reducing from 1,125 mg to 50 mg and tramadol from 11,750 mg to 150 mg for postoperative pain management. The number of patients who used anti-emetics also decreased (45 vs. 42). There was no difference in kidney function between the two groups.

Conclusions: Multimodal pain management, combining scheduled acetaminophen with PRN non-opioid analgesics, effectively reduces postoperative pain and opioid consumption in living kidney donors undergoing HALS. This approach provides a safe and efficient framework for optimizing pain control.

EP_255 THE DEVELOPMENT PROGRESS OF "THE SHANXI MODEL": THE FIRST INDEPENDENT PROVINCIAL OPO IN CHINA

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Background: In the past decade, the reform of organ donation and transplantation (OD & OT) in China has achieved success. Currently, there exist 109 organ procurement organizations (OPO) and 4 models in total, while the provincial OPO model is considered as the final goal in achieving self-sufficiency in OT. Shanxi OPO was founded as the first independent provincial OPO in China. This study compares differences before and after the establishment of Shanxi OPO in regard to the quantity, quality and efficiency of OD & OT within Shanxi Province, as well as current progress of the OPO. With this study, our intention is to share our experience and try to explore a feasible procurement management mode in China.

Methods: In terms of organizational structure, equipment management and core quality indicators, we analyze relevant data from 2015 to 2023 and compare the outcomes before and after the establishment of the provincial OPO.

Results: In the past few years, a professional team with 10 functional departments has been built. In 2020, a scientific committee was established to guide scientific research. In 2022, a Pathology Lab was founded to carry out pathological examinations to evaluate the quality of organs timelier. Moreover, we issue the annual Scientific Report to provide the analysis and summary of relevant quality indicators. Over the years, the number of OD has increased from 35 cases (PMP: 0.99) in 2015 to 105 cases (PMP: 3.02) in 2023, with an increase rate of 200%. The number of organs procured from per donor and the organ utilization rate remains stable. Furthermore, we are more engaged in scientific work through initiating expert consensus on family approaching and ethical review; undertaking national research projects; organizing regular multi-disciplinary professional trainings.

Conclusions: The operation structure has been developing towards professionalism and the efficiency and quality of our work have been improved in the past few years. The “Shanxi Model”--independent provincial OPO may provide a solution for the standardization of organ procurement in China. Notwithstanding, OPO mode suitable for national conditions and feasible for new circumstances requires further exploration.

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EP_256 RACIAL AND SOCIAL DISPARITIES AMONGST DECEASED ORGAN DONORS IN SOUTH AFRICA. A NATIONWIDE STUDY

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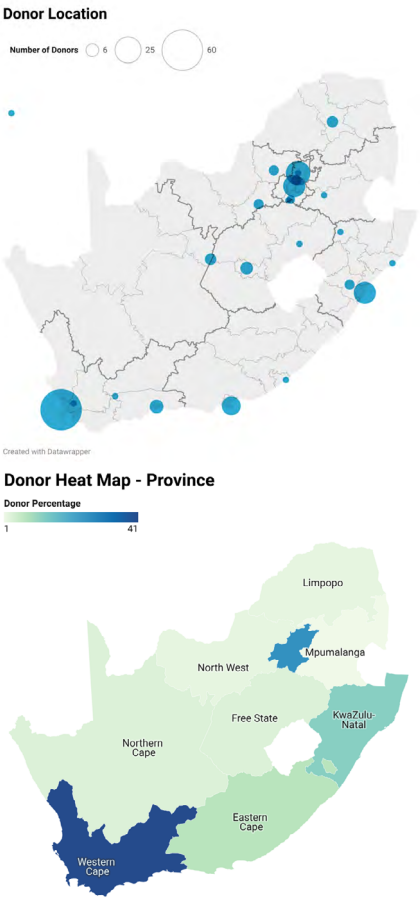
Background: End stage liver disease is lethal. There only curative option is a liver transplant. South Africa has one of the lowest rates of deceased organ donors in the world. This study aims to identify the demographic profile of deceased liver donors in South Africa, as well as their geographical distribution, with the intention of interrogating the data in order identify interventions which will assist in increasing the donor pool

Methods: This was a retrospective review of all consented donors referred for potential liver donation to the Wits Donald Gordon Medical Centre between January 2018 and April 2024

Results: There were 176 referrals over the 5 year period. Fifty two percent were male donors. The mean age was 39.4 (SD 18.2). Caucasians were the most likely to be organ donors, representing 55.6% of all donors and were followed by donors of mixed race (26.8%). The major causes of death were trauma (41%) and intracranial haemorrhage (37.6%). The Western Cape and Gauteng accounted for 67% of all donors. The Western Cape which accounts for 12% of the total population of South Africa, accounted for 41% of donors. Fifty two percent of donors were referred from private hospitals with the other 48% from government hospitals.

Conclusions: This is the first study looking at organ donors nationally in South Africa. It was found that organ donors were more likely to be white or of mixed race, which is also reflected in the higher donor rates from provinces with larger white or mixed-race populations. Government hospitals have fewer organ donors per percentage population than private hospitals. These findings should serve as a basis to tailor interventions to increase donor numbers.



EP_257 INITIAL OUTCOMES OF KIDNEY TRANSPLANTATION USING HYPOTHERMIC MACHINE PERFUSION IN KOREA

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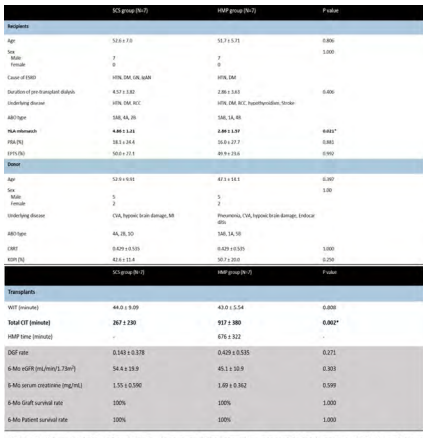
[1]Jeju National University Medical Center; Abdominal Transplant Surgery; Surgery, [2]Samsung Medical Center; Department of Surgery

Background: Multiple studies have reported that hypothermic machine perfusion (HMP) shows better results in the preservation of the marginal donor than traditional static cold storage (SCS) methods. This study was performed to evaluate the effect of HMP by comparing short-term outcomes of patients who underwent deceased donor kidney transplantation using HMP and SCS.

Methods: There are fourteen patients with DDKT from March 1 2022 to February 29, 2024 who were enrolled in this retrospective study. The renal grafts of seven patients were preserved by SCS methods, and seven grafts of patients were preserved by the HMP method. The characteristics of donors, recipients, and transplant process were compared between SCS and HMP groups, respectively. Delayed graft function (DGF) rate, post-operative 6-month graft and patient survival, and estimated glomerular filtration rate (eGFR) were compared in these two groups.

Results: The HLA mismatch of recipients was higher in the SCS group (4.86 ± 1.21) compared to the HMP group (2.86 ± 1.57) (p=0.021). There were no significant differences between the two groups in the donors' characteristics. The cold ischemia time (CIT) was significantly longer in the HMP group than in the SCS group (917 vs 267 minutes, p=0.002). The DGF rate, 6-month graft survival, and patient survival were not statistically different. Additionally, short-term eGFR and serum creatinine levels did not show meaningful differences in these two groups. In the HMP group, the last renal resistance of all 4 patients at the end of HMP use were less than 0.4 mmHg/mL/min, and the last flow rate were higher than 60 mL/min in all seven patients.

Conclusions: HMP can be applied to the deceased donor kidney grafts with prolonged CIT with favorable short-term results and the HMP parameters including the renal resistance and flow rate are probably able to be used for the prediction of post-transplantation graft outcomes.



	SCS group (N=7)	HMP group (N=7)	P value
Recipients			
Age	52.0 ± 7.0	51.7 ± 5.71	0.806
Sex Male Female	7 0	7 0	1.000
Cause of ESRD	HTN, DM, GN, IgAN	HTN, DM	
Duration of pre-transplant dialysis	4.57 ± 3.82	2.86 ± 3.63	0.406
Underlying disease	HTN, DM, RCC	HTN, DM, RCC, hyperthyroidism, Stroke	
ABO type	SAB, 4A, 2B	SAB, 1A, 4B	
HLA mismatch	4.86 ± 1.21	2.86 ± 1.57	0.021*
PRA (%)	18.1 ± 24.4	16.6 ± 27.7	0.981
FPTS (%)	50.0 ± 27.1	49.9 ± 29.6	0.992
Donor			
Age	52.0 ± 9.91	47.1 ± 14.1	0.267
Sex Male Female	5 2	5 2	1.00
Underlying disease	CVA, hypoxic brain damage, MI	Pneumonia, CVA, hypoxic brain damage, Endocrine	
ABO type	4A, 2B, 1O	SAB, 1A, SB	
CRRT	0.429 ± 0.535	0.429 ± 0.535	1.000
KDPI (%)	82.6 ± 11.4	50.7 ± 29.0	0.250
	SCS group (N=7)	HMP group (N=7)	P value
Transplants			
WIT (minute)	44.0 ± 9.09	43.0 ± 5.54	0.808
Total CIT (minute)	**267 ± 230**	**917 ± 380**	**0.002***
HMP time (minute)	-	676 ± 322	-
DGF rate	0.143 ± 0.378	0.429 ± 0.535	0.271
6-Mo eGFR (mL/min/1.73m²)	54.4 ± 19.9	45.1 ± 10.9	0.303
6-Mo serum creatinine (mg/mL)	1.55 ± 0.590	1.69 ± 0.362	0.599
6-Mo Graft survival rate	100%	100%	1.000
6-Mo Patient survival rate	100%	100%	1.000

Table 1. Characteristics of recipients, donors, and the transplant process in both groups. (ESRD, end stage renal disease; HLA, human leukocyte antigen; PRA, panel reactive antibody; EPTS, estimated post-transplant survival; CRRT, continuous renal replacement therapy; K-KDPI, Korean Kidney Donor Profile Index; WIT, warm ischemia time; CIT, cold ischemia time). Short-term outcomes were evaluated, including post-operative 6-month DGF rate, eGFR, serum creatinine levels, graft, and patient survival rate. (DFG, delayed graft function; eGFR, estimated glomerular filtration rate).

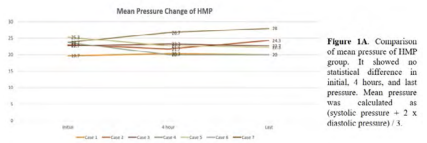


Figure 1A. Comparison of mean pressure of HMP group. It showed no statistical difference in initial, 4 hours, and last pressure. Mean pressure was calculated as (systolic pressure + 2 x diastolic pressure) / 3.

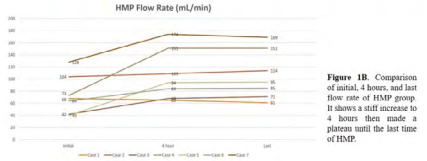


Figure 1B. Comparison of initial, 4 hours, and last flow rate of HMP group. It shows a stiff increase to 4 hours then made a plateau until the last time of HMP.

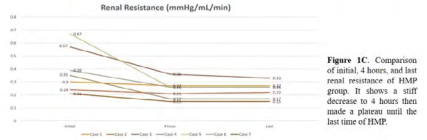


Figure 1C. Comparison of initial, 4 hours, and last renal resistance of HMP group. It shows a stiff decrease to 4 hours then made a plateau until the last time of HMP.

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EP_258 SCIENTIFIC WORK OF AN INDEPENDENT PROVINCIAL OOO IN CHINA, EMPOWER THE DEVELOPMENT OF ORGAN DONATION

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[1]Shanxi Provincial Organ Procurement And Allocation Center, [2]Shanxi Provincial Organ Procurement and Allocation Center, [3]Shanxi Provincial Organ Procurement And Allocation Center; Scientific Committee

Background: Currently, in China, provincial OPO model is considered as the final goal in achieving self-sufficiency in OT. Shanxi OPO was founded as the first independent provincial OPO in China, the "Shanxi Model" provides a solution for the standardization of organ procurement in China. To push the scientific development of our OPO, furthermore, to promote the professionalism of OD, a Scientific Committee was founded. Over 20 experts from multidisciplinary background are brought together to provide guidance on the direction of scientific research, as well as offer advice on the professional construction of our OPO.

Methods: Consultations were made with professionals to carry out scientific research programs and formulate expert consensus. Through combining research results with clinical experience, we try to figure out how to promote the professionalism of OD.

Results: The building of the OD discipline requires the training of application-oriented professionals. Thus, a reference standard for the construction of coordinator training base, together with a comprehensive training program were developed. Except for regular trainings for coordinators, we organize OD trainings for healthcare professionals to foster supporting network for OD. Family approaching is considered a critical and professional matter. Thus, we initiated an expert consensus on effective family approaching. Fundamentally, the knowledge basis of OD is a medical-centered subject with sociological, humanistic, psychological, and ethical attributes. Thus, together with ethicists, we study how to establish the trust system for OD; together with humanists, we explore how to incorporate OD practice into hospice care service; together with intensivists, we research on the role of critical care professionals in OD, and etc.

Conclusions: The scientific work of our OPO has achieved progress under the support of multidisciplinary experts. Achievement has also been seen through the improvement of professional competence of our team, the increasing recognition and participation of relevant HCP in our donation work, and finally through the professional development of our OPO. Therefore, promoting the OD discipline development and OPO professional construction is positive to further promote the sustainable development of OD & OT.

EP_259 RESEARCH PROGRESS IN COGNITION, ATTITUDE AND WILLINGNESS FOR ORGAN DONATION AMONG ICU STAFF IN CHINA

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Background: In recent years, organ donation and transplantation (OD & OT) have entered a stage of steady development in China. Nevertheless, the contradiction between supply and demand of organs are still the bottlenecks to achieve "self-sufficiency in OT" advocated by WHO. High-efficiency and high-quality development of OD cannot be achieved without the support of intensive care medicine, which are highly associated with ICU staff's cognition, attitudes and participation of OD. Thus, ICU staff play a key role in the OD process.

Methods: In this paper, we reviewed, screened, compared, and analyzed literatures on related topics, on the basis of which, ICU staff's cognition, attitude and willingness for OD were reviewed, relevant influencing factors were discussed, and then targeted suggestions on how to resolve difficulties were offered.

Results: In terms of longitudinal analysis, the level of ICU staff's knowledge of OD is generally increasing year by year. Besides, their knowledge of clinical medicine is proficient, while knowledge of the principles, standards and procedures of OD is relatively weak. Knowledge is the basis of attitude, in terms of ICU staff's attitude towards OD, the results showed that the higher the level of knowledge about OD, the more positive the attitude. Awareness, knowledge, recognition, willingness and action is of a progressive relationship. As the issue becomes more personalized, the attitudes of ICU staff become less optimistic. Additionally, we also studied the relationship between Chinese culture and the attitudes of ICU staff toward OD. Actually, Chinese culture is not the hinder, instead, many history stories and the Confucianism indicate support for OD. Besides, current life education in China advocates OD as an effective way to develop a new concept of death, body and value of life. In the end, we tried to give recommendations for improving the situation from the point of popularization of OD among ICU personnel and enhancement of OD training for them.

Conclusions: In recent years, due to the steady development of OD & OT, and the deepening of publicity on OD & OT, ICU staff's awareness of OD has been increasing and their attitudes have been changing positively, but their willingness to donate and participate in OD work still needs to be improved.

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EP_260 IMPACT OF DONOR FACTOR ON ORGAN UTILISATION AND PANCREAS TRANSPLANT OUTCOMES: A SYSTEMATIC REVIEW

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Background: Donor selection in pancreas transplantation (PT) is subjective with variation amongst centres and clinicians. This systematic review aimed to evaluate donor factors on outcomes to assist clinician donor selection.

Methods: A systematic search of Embase, MEDLINE and Cochrane Library was conducted to identify studies reporting donor factors and outcomes following PT up to May 2024 (Prospero: CRD42024559594).

Results: 36 retrospective cohort studies were reviewed (1993-2021; 115, 731 PT recipients; median sample size of 516; IQR 159-2650). Examined donor factors included Pancreatic Donor Risk Index (PDRI) (7 studies), DBD/DCD (7), age (5), Pre-Procurement Pancreas Suitability Score (P-PASS) (4), body mass index (BMI)(3), cardiopulmonary resuscitation (CPR) (3), race matching, ABO compatibility, insulin and noradrenaline use, asphyxiation, amylase and hypertension (single studies). Heterogeneity existed amongst categorised variables and outcome metrics. Elevated BMI was associated with poorer graft (GS) and patient survival ($p<0.05$ in 1 of 3 studies). Donor insulin use and hypertension were associated with increased risk of PT graft failure. P-PASS score >17 was associated with reduce GS in 1 of 4 studies and with elevated PDRI score in 3 of 7 studies. Donor noradrenaline use was associated with a 26% lower risk of graft loss. Younger donors were associated with improved GS in 50% of studies (n=2). No difference in outcomes was seen between donation category (DBD/DCD), CPR status or asphyxiation status.

Conclusions: Quality and heterogeneity of studies limit the generalisability of current evidence. Future studies should focus on establishing a standard for donor factor definitions to establish a standardized selection process.

EP_261 TURKISH ADAPTATION STUDY OF LIVE DONOR ASSESSMENT TOOL VERSION 2 - LDATV2

Yaprak Sarıgöl Ordin[1], Gülay Aksu Kul[2], Serap Arıcı[3], Zeynep Deveci[4], Özgül Karayurt[5], Mürvet Çağrı Ganol[3], Murat Kılıç[6], Adam Uslu[7], Hakan Delibaş[8], Dianne LaPointe Rudow[9]

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Background: The Live Donor Assessment Tool (LDAT) is a semi-structured psychosocial assessment tool utilized to standardize the living donor psychosocial evaluation. LDAT Version 2 (LDATV2) includes 34 items by adding 5 items to the old version developed by the same research group. To determine its utility in Turkish population, this study aims to evaluate the validity and reliability of LDATv2 in Turkish living donor candidates.

Methods: 60 liver and 40 kidney living donors were evaluated. Item analyses, internal consistency coefficients, and parallel forms reliability were used to measure the reliability of LDATV2. The validity of LDATV2 was assessed by content validity and comparing LDATV2 scores to clinical decision and psychosocial effectiveness in 3rd month after surgery.

Results: The total score of LDATV2 was 75.55±12.35 for liver donors candidates and 85.72±3.1 for kidney donor candidates. The mean score of potential donor candidates was 80.88±8.03 and 39.00+17.32 for those who were not suitable as donors. 19 items were removed from the scale because their item score correlation was very low. Scale item total score correlations were found to between 0.26 and 0.79. The cronbach alpha was found 0.90. The Spearman Brown correlation coefficient was 0.85. With a cut-off score of 61.5, LDATV2 was found to have high sensitivity and specificity.

Conclusions: The Turkish version of the LDATV2 was found to be reliable and valid tool. It can be used to standadized psychosocial assessment of living donors adn develop clinical interventions targeted to improve psychosocial outcomes.

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EP_262 TWO ERAS OF KIDNEY TRANSPLANTATION: COMPARING OUTCOMES ACROSS A 26-YEAR JOURNEY

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Background: Kidney transplantation has evolved over time, with recipient and donor populations undergoing significant changes. There has been an increase in older, more comorbid recipients, while organ shortage has led to increased use of “marginal organs”. This study aims to describe changes in kidney transplant (KT) populations and compare outcomes over a 26-year period at a single center in Portugal.

Methods: We included all deceased donor KTs performed at our unit between July 1997 and July 2023. Transplants performed before January 1, 2010 (Group A, n=180) were compared to those performed on or after this date (Group B, n=211).

Results: Recipient’s average age was higher in Group B (55.0±11.0 vs. 48.2±12.8 years, p<0.001), as was donor’s age (56.0±14.0 vs. 45.8±16.2 years, p<0.001). Cold ischemia time was longer in Group B (18.6±5.3 vs. 15.9±5.1 hours, p<0.001), as was serum creatinine one year post-transplant (1.68±0.66 vs. 1.49±0.76 mg/dL, p<0.001). There were no significant differences between groups regarding pre-transplant diabetes prevalence, HLA mismatches, or second transplant rates. Recipient survival was lower in Group B (p<0.05), with 1-, 5-, and 10-year survival rates of 96.3%, 91.2%, and 84.2% in Group A, compared to 95.4%, 86.1%, and 64.3% in Group B. Graft survival, uncensored for death, was similar between groups. However, death-censored graft survival was significantly better in Group B (p<0.01), with 1-, 5-, and 10-year survival rates of 99.0%, 93.1%, and 90.5% compared to 95.7%, 88.9%, and 79.7% in Group A.

Conclusions: Despite an increasing number of higher-risk KTs in recent years, overall KT outcomes have not worsened, likely reflecting improvements in pre- and postoperative management. The higher recipient mortality in Group B may reflect the increasing number of older, more comorbid patients on KT waiting lists.

EP_263 MEASURED GFR IMPROVES LIVING DONOR SELECTION COMPARED TO CKD-EPI2021 EGFR

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Background: Living kidney donation (KD) evaluation particularly focuses on glomerular filtration rate (GFR). Assessing GFR in living kidney donors can be done by estimation (eGFR) or measurement (mGFR). This study aims to evaluate the impact of different eGFR equations, focusing on CKD-EPI 2021 for donor eligibility and reclassification of donors excluded by eGFR criteria to mGFR assessments.

Methods: Retrospective, single-center observational study of 2,512 kidney donors evaluated between 2011 and 2023. We performed analyses and comparisons of 6 eGFR formulae and 2 mGFR methods in terms of performance, eligibility criteria according to KDIGO guidelines / age-adjusted criteria, eligibility reclassification, and subgroup analyses.

Results: The CKD-EPI 2021 equation resulted in a higher percentage of patients being eligible for kidney donation (81.4%) and achieved the highest P10 (32-34%) and P30 (87-88%) across all mGFR methods. When an eGFR formula classified a patient as ineligible, this was revised to eligible in about 90% of cases upon reassessment with mGFR, with a higher reclassification rate observed when IoCl was used instead of CrCl, Figure 1). In Black potential donors, mGFR increased the number of potential eligible donors to 96.6% using IoCl from 75.9% using CKD-EPI 2021 formula. Reclassification of ineligible to eligible was higher in females, with a similar trend in males. Reclassification from eligible to ineligible was lower in the older age group (3.1%, age >60 years old compared to 8%) and conversely a lower reclassification from ineligible to eligible in the younger age group (75%, <40 years old compared to 84%).

Conclusions: The CKD-EPI 2021 equation performs best for screening potential KD. If a KD is deemed ineligible by CKD-EPI 2021, there is a high likelihood they will be reclassified as eligible when assessed with mGFR. Age, sex and race may be affected. This study strongly advocates for using mGFR in donor evaluations to ensure a more accurate assessment of GFR criteria and screening using eGFR CKD EPI 2021 may exclude potential donors before measurement.

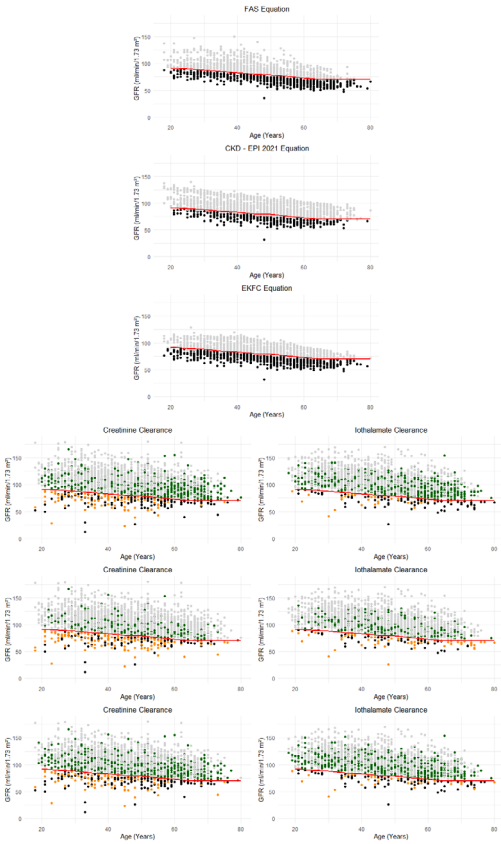

Figure 1

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EP_264 VASCULAR ANATOMIC VARIATIONS IN LIVING DONOR KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background: The increased risk of removal and implantation of kidneys with higher number of vascular structures or anatomical variations is widely known in the literature. Within the framework of the Transplantation Program of Semmelweis University live donor nephrectomies have been performed with hand-assisted technique since March 2008.

Methods: Between the 18th of March 2008 and the 31st of December 2023, a total number of 466 hand-assisted laparoscopic donor nephrectomies were performed at our institution. In our present study we investigated the association of multiple donor vascular structures and anatomical variations with the difficulty of nephrectomy and implantation, the incidence of postoperative complications and graft survival rates at 1 and 5 years in comparison with donor kidneys of normal anatomy. We illustrate the potential surgical solutions of major vascular variations with case presentations.

Results: Multiple arteries in harvested kidneys were observed in 32% of cases, an average of 7 cases a year (4-12), venous variations were present in 17%, a yearly average of 4 cases (2-7). These incidence rates fall in line with the international data. Inferior vena cava on the left side of the aorta, circumaortic or retroaortic venous variations were found sporadically. Neither death, nor the need for dialysis occurred in our donors. The most severe complication was the loss of the transplanted kidney graft, seen in two cases with multiple arteries. Donor reoperation for bleeding was rarely required. Minor complications (i.e. seromas, incisional hernias, hematomas) developed in low numbers. No infections were observed. Anatomical variations rarely resulted in surgical complications.

Conclusions: Transplantation of donor kidneys with multiple vascular structures or anatomical variations might increase the risk of surgery, therefore the preoperative planning requires particular attention involving 3-dimensional imaging modalities in clinical practice. According to our findings, hand-assisted live donor nephrectomy is considered a safe procedure in the presence of anatomical variations as well

EP_265 KEY DONOR FACTORS INFLUENCING KIDNEY TRANSPLANT OUTCOMES: A MONOCENTRIC STUDY FROM THE TORV VERGATA TRANSPLANT CENTRE

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Background: The scarcity of suitable kidney donors remains a critical challenge in transplantation medicine. Factors such as donor age, sex, and body mass index (BMI) are thought to influence transplant outcomes. This study aims to evaluate how these donor characteristics affect kidney transplant outcomes at the Tor Vergata Transplant Center, with a focus on delayed graft function (DGF), estimated glomerular filtration rate (eGFR), patient survival, and graft survival.

Methods: This monocentric retrospective study included 247 single-organ kidney transplants performed between January 2015 and December 2019. Donor characteristics such as age, sex, and BMI were assessed for their impact on transplant outcomes, with a follow-up period of 24 months. Data were collected from the GEDON system and patient records, and statistical analysis was performed to identify correlations between donor factors and post-transplant outcomes.

Results: The analysis found a significant correlation between higher donor BMI and an increased incidence of DGF, with a 25-40% increase in DGF cases among obese donors (BMI > 30 kg/m²), compared to those with normal weight (BMI < 25 kg/m²). Male donors were also associated with a higher risk of DGF ($p = 0.02$). No significant relationship was found between donor characteristics and long-term graft survival or patient survival ($p > 0.05$). Donor BMI also showed a trend towards lower eGFR, with obese donors presenting a decrease in eGFR from 58.3 ± 5.1 mL/min/1.73m² in normal-weight donors to 50.7 ± 7.3 mL/min/1.73m² at the one-year follow-up. However, no significant difference was observed across BMI categories in long-term eGFR ($p = 0.31$).

Conclusions: Donor BMI and sex significantly influence early transplant outcomes, particularly in relation to DGF, but do not appear to affect long-term kidney function or patient survival. These findings suggest that while high-BMI and male donors pose a higher risk for DGF, they do not substantially impact the long-term success of the transplant. Optimizing donor-recipient matching, particularly for extended-criteria donors, is critical to improving early outcomes. Further research is necessary to refine donor selection criteria, particularly in the context of obesity, to enhance transplant outcomes for high-risk patients.

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EP_266 THE ROLE OF ELDERLY DONORS IN KIDNEY TRANSPLANTATION: A 10-YEAR REVIEW

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Background: As the number of older and more comorbid patients on kidney transplant (KT) waiting lists is increasing, organ shortage is leading to a rising incidence of KT from elderly donors. We will review our unit's data from deceased donor KT in the last 10 years and compare outcomes between KT from elderly and younger donors.

Methods: We included all deceased donor KT taking place in our unit between July 2013 and July 2023. We considered group A for KT from donors aged 70 or older and group B for donors younger than 70 years of age.

Results: Donors from group A had a higher prevalence of hypertension (72.4% vs 40.3%; p=0.002) and a higher Kidney Donor Profile Index score (0.95±0.04 vs 0.62±0.23 on average; p<0.001) comparing to group B. There was no statistical difference between groups regarding diabetes prevalence in the donor and terminal serum creatinine (sCr) level. On average, kidneys from group A were transplanted into older recipients (61.2±6.6 vs 53.4±11.0 years old; p<0.001) with longer cold ischemia times (20.3±6.6 vs 18.6±5.0 hours; p=0.025), but HLA mismatches, induction immunosuppression choice and delayed graft function incidence weren't statistically different between groups. Group A was associated with higher sCr levels (2.05±0.81 vs 1.65±0.60 mg/dL; p=0.01) and lower estimated glomerular filtration rates (38.0±14.0 vs 51.0±20.2 mL/min/1.73 m2; p=0.003) one year after KT. However, no difference was found between groups regarding the incidence of acute rejection in the first year after KT, hospitalizations in the first year after KT and, more importantly, patient survival and death-censored graft survival.

Conclusions: Although kidney graft function was worse in recipients from elderly donors, there is a likely benefit in patient morbidity and survival compared to remaining on dialysis. Elderly donors appear to be a reliable source of grafts, especially when considering older candidates to KT.

EP_267 THE AUTOETNOGRAPHY OF A LIVER DONOR

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Background: Organ transplantation is a life-saving procedure, yet significant gender disparities persist globally. Women experience longer waiting times, limited autonomy in decision-making, and systemic biases in organ allocation and post-transplant care. This autoethnographic study examines the lived experience of being a liver donor through the lens of "gender as structure" theory, focusing on the institutional and social inequalities embedded in organ transplantation systems. Based on five years of doctoral research and my personal experience as a liver donor, this work explores the ethical, social, and emotional dimensions of living organ donation in Turkey, a country with one of the highest rates of living organ transplants. Despite the critical role of living donors, donor-specific organizational and support mechanisms remain scarce, leaving many to navigate this life-altering process with limited assistance.

Methods: The study employs autoethnography, drawing on my personal narrative as a donor alongside in-depth interviews conducted with female organ donors over six years. These narratives are analyzed within the framework of "gender as structure" to uncover systemic inequalities and gendered dynamics within the transplantation ecosystem.

Results: The findings reveal how gendered assumptions and institutional biases shape the experiences of female organ donors, from decision-making to post-operative care. The lack of donor-centered support systems exacerbates the physical and emotional burdens donors face, particularly for women, who are often expected to prioritize caregiving roles. My dual role as both an academic and a donor underscores the disparities in access to resources and platforms for addressing these issues.

Conclusions: This study highlights the critical need for comprehensive, donor-centered support systems and institutional accountability to address the systemic inequities in organ transplantation. By bridging personal narratives and structural analysis, it advocates for a transformation in how living donors are recognized and supported within healthcare systems.

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EP_268 GENDERED RISKS IN LIVING LIVER DONATION: EXAMINING DEMANTIA AND LONG TERM PSYCHOSOCIAL OUTCOMES FOR WOMEN DONORS

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Background: The benefits of living liver donation for recipients are well-documented, and the physical risks associated with the donation process are relatively low. However, the psychosocial and long-term health risks for donors, particularly for women—who make up the majority of living donors worldwide—remain underexplored. Emerging research suggests potential links between liver function and cognitive health, indicating associations with conditions such as dementia.

Methods: This study emphasizes the need to address these risks by advocating for interdisciplinary research that combines medical and social science perspectives. Specifically, it proposes investigating the experiences of women who have served as liver donors over the past 20 years. By examining their cognitive and psychosocial health outcomes, this research aims to uncover the underlying mechanisms and systemic gaps contributing to these risks.

Results: Female donors are more likely to report that the donation experience is stressful, especially when they face perioperative complications. In healthcare settings, women's symptoms are often dismissed or attributed to psychological factors due to gender biases. This poses a significant risk for female liver donors who may experience memory loss or other cognitive issues after donation. The absence of systematic long-term follow-up exacerbates this issue, particularly since women constitute the majority of living organ donors globally. When post-donation symptoms are overlooked or misinterpreted as psychological rather than physiological, the potential—though low—risk of developing dementia or other cognitive impairments remains inadequately addressed. This situation creates a critical gap in ensuring the safety and well-being of female donors, highlighting a major concern within the field of liver transplantation.

Conclusions: The findings will provide vital insights for developing gender-sensitive follow-up protocols and improving donor care, ultimately leading to a more equitable and comprehensive approach to living organ donation.

EP_269 COMPARABLE LONG-TERM OUTCOMES FROM EXTENDED VS STANDARD CRITERIA LIVING KIDNEY TRANSPLANTATION

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Background: Living donor kidney transplantation (LDKT) is the gold standard for treating end-stage kidney disease (ESKD). While previous studies have explored the impact of donor and recipient demographics on post-transplant outcomes, the long-term effects of using extended criteria donor (ECD) kidneys in LDKT remain less defined. This retrospective cohort study evaluates 5-year outcomes associated with ECD kidneys compared to standard criteria donors (SCD) in LDKT.

Methods: Data from adult LDKTs performed between April 2017 and January 2020 were retrospectively analysed. Five-year recipient survival and graft outcomes were compared between ECD and SCD groups.

Results: A total of 112 donor-recipient pairs were included, with 62 recipients receiving SCD kidneys. 50.9% of pairs were genetically related, and 47.3% were pre-emptive LDKT. Graft survival was lower in the ECD group (90.1% vs. 95.2%, p = 0.048). Rejection was negatively correlated with graft survival (r = -0.189, p = 0.024) and function (r = -0.318, p < 0.001) in the overall cohort. However, subgroup analysis did not identify rejection as the primary factor contributing to graft survival differences. Detailed patient characteristics and outcomes are presented in Table 1.

Conclusions: Extended criteria donors represent a viable option for expanding access to LDKT, offering comparable long-term recipient survival and graft function. Recipients should be counselled on the marginally statistically significant lower graft survival of ECD kidneys, which remains clinically acceptable in the context of increasing transplant opportunities.

	Overall (112)	SCD (62)	ECD (50)	p-value
Recipient Age	48.3±13.5	48.8±12.3	47.7±14.9	0.648
Recipient Diabetes Mellitus (DM)	17%	9.7%	10%	0.078
Recipient atheromatic disease (AD)	10.7%	11.3%	10%	0.826
Recipient (Body Mass Index) BMI	27.1 (4)	27.4 (4.5)	26.8 (4.58)	0.392
Donor Age	48.4±12.4	44±11	53.8±12	<0.001
Donor DM	8%	0%	18%	<0.001
Donor AD What is this?	1%	0%	2%	0.263
Donor HTN	1%	0%	2%	0.263
Donor BMI	28.3 (5.25)	26 (4)	31 (5)	<0.001
Pre-formed donor DSA	2.7%	0.9%	1.8%	0.437
Delayed Graft Function	0.9%	1.6%	0%	0.368
Rejection	17%	20%	14.3%	0.434
Recipient survival	95.5%	96.8%	94%	0.48
Graft survival	90.1%	95.2%	84%	0.048
Graft function	54.5 (27.5)	58 (23)	49 (28)	0.123

Table 1. Patient characteristics and 5-year outcomes.

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EP_270 EXTENDED CRITERIA DECEASED DONATION - WHAT DO WE GAIN?

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Background: Kidney transplantation (KT) from extended criteria (EC) deceased donors has expanded the donor pool and made transplant accessible to the increasing number of complex patients suffering from end-stage kidney disease. We aim to compare two extreme categories in kidney transplantation: EC deceased donor/recipient pairs versus standard criteria living donor (LD) counterparts to showcase the impact of EC KT.

Methods: We retrospectively analysed data of pairs of EC deceased donor/recipient pairs of KT in the year 2022 and matched them for vascular anatomy and mismatch category to standard criteria LD KT counterpart pairs from 2017 to 2022. We compared patient and graft survival as well as graft function one- and two-years post-transplant and used Jamovi 2.3.28 for statistical analysis.

Results: There were 134 EC deceased donor/recipient pairs of KT performed in 2022, 54 of which were matched to standard criteria living donor pairs. The mean CIT was statistically significant longer in the deceased donor pairs (542±109 min vs 231±74 min). Patient characteristics and outcomes are presented in Table 1.

Conclusions: Despite the anticipated lower patient and graft survival and function from the deceased EC pairs, deceased EC KT outcomes are clinically comparable to standard LD KT outcomes and far superior to those of dialysis. These data can be used in informing patients when making decisions regarding accepting kidneys from EC donors.

	Living (54)	Deceased (54)	p-value
Recipient Age	41.5±10	57.2±10.6	<0.001
Recipient Diabetes Mellitus (DM)	0%	46.3%	<0.001
Recipient Atheromatic disease (AD)	0%	27.8%	<0.001
Recipient Body Mass Index (BMI)	25.5±2	28.8±6	<0.001
Donor Age	42.9±10.3	60.2±13.3	<0.001
Donor DM	0%	16.7%	0.001
Donor HTN	0%	46.3%	<0.001
Donor AD (What is this?)	0%	5.5%	0.073
Donor BMI	25.2±2.77	26.9±4.9	0.17
Pre-emptive	46.3%	7.4%	<0.001
CIT	231±74.4	542±109	<0.001
1-year Recipient survival	100%	90.7%	0.022
2-year Recipient survival	100%	89%	0.012
1-year Graft survival	100%	94%	0.150
2-year Graft survival	100%	92.3%	0.042
1-year Graft function	63.5±15.3	47±20	<0.001
2-year Graft function	53±8.3	45±18	0.007

Table 1. Patient characteristics and outcomes

EP_271 A QUALITATIVE INVESTIGATION OF THE EMOTIONAL AND PRACTICAL NEEDS OF ORGAN DONOR FAMILIES

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Background: Before deciding on organ donation, family members must come to terms with the fact that their loved one is brain dead, which allows for donation through the donation after brain death pathway. The study aimed to investigate the factors that contribute to the healing process of loved ones of deceased organ donors in coping with grief and loss.

Method: The present study was conducted out using a qualitative approach and conventional content analysis following Graneheim and Lundman's approach. Twelve close families of organ donors participated by purposeful and snowball sampling method. Data were gathered by using semi-structured interviews and critical discourse analysis.

Results: Participants were 8 females and 4 males; the mean age of families was 55.23 ± 2.24. Data analysis led to the emergence of two themes (supporting system, coping strategy), 6 Subthemes (psychological issues, social issues, communication with others, social support, meaning-making, coping with their grief), 17categories (Grief processing, emotional resilience, understanding mixed emotion, social support networks, stigma, social Interaction, communal narratives, narrative therapy approaches, open communication, coping strategies, professional support, support groups, honor their memory, practice self-care, seek spiritual support, create rituals, be patient with grief, limit stressors), 65 subcategories and one thousand two hundred and thirty-seven (1,237) initial codes.

Conclusions: To enhance the organ donation process, the study suggests the need for improving education and cultural sensitivity regarding brain death, counseling resources for families, and creating support networks. Furthermore, establishing clearer communication about organ allocation can foster trust between families and medical institutions.

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EP_272 IMPROVING DONOR TRANSPORT OUTCOMES: INSIGHTS FROM IRANIAN PRACTICES

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Background: Organ transplantation is a complex process that involves various medical, legal, and social factors. The organ demand continues to outweigh the supply, leading to global challenges in expanding transplant programs. Ischemic time is crucial for the viability of organs, and efforts are being made to reduce transport time to improve transplant success rates. One important factor in successful organ transplantation is minimizing the ischemic time. This is important to ensure the viability and quality of the organ for transplantation.

Methods: Today, a new method is being implemented in Iran, in which instead of transferring organs and reducing organ quality due to ischemic time, the donors themselves are transferred to transplant centers with the help of a trained team after brain death is confirmed and with the consent of the family. It is worth mentioning that, during the transfer process, an anesthesiologist or nurse specialized in caring for the donor performs the relevant transplant procedures.

Results: The successful transportation of donors to OPUs/OPOs for organ procurement requires meticulous planning, trained personnel, and adherence to safety protocols. Quality assurance measures, including audits and safety protocols, are in place to ensure the timely and safe delivery of donated organs. Ultimately, improving transportation processes for organ donation can enhance transplant success.

Conclusions: Successful transportation of donors to OPUs is crucial for reducing ischemic time and improving the success rate and quality of organ transplants. Careful planning, communication, and collaboration among healthcare professionals are necessary for the timely and safe delivery of donated organs.

EP_273 COMPARISON OF OUTCOMES IN DECEASED DONOR LIVER TRANSPLANTATION USING IDEAL AND MARGINAL DONOR GRAFT

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Background: The utilization of marginal liver graft has been increased along with expanding donor pools because of shortage of deceased donors. However, the effectiveness and safety of marginal graft remain controversial. We analyzed the outcomes of deceased donor liver transplantation (DDLT) using marginal graft in a single center.

Methods: Ninety-seven patients who received DDLT from Nov 2009 to Dec 2023 were included in this study. Clinical data of donors and recipients were retrospectively analyzed and compared between standard and marginal graft group according to the criteria of marginal liver graft. Univariate and multivariate analysis was performed for identification of risk factors of perioperative mortality and overall survival.

Results: According to our criteria of marginal liver graft, 35 patients were included in marginal graft group and 62 patients were included in standard graft group. There were no significant differences between groups in clinical characteristics of recipients and surgical outcomes such as operation time, hospital stay period, incidence of perioperative complication, in-hospital mortality. There was no primary nonfunction after liver transplantation in both groups. Serologic laboratory test at postoperative 1and 2 weeks were comparable in both groups. With a median follow-up 36 months, the 1-,3-, and 5-year survival were 85%, 77%, 72% in standard group and 84%, 77%, and 71% in marginal group (p=0.819). On multivariate analysis, MELD≥38 (HR 5.461, 95% CI 1.447 – 20.613, p=0.012) and operation time > 420 min (HR 3.322, 95% CI 1.010 – 10.922, p=0.048) were identified as independent risk factors for perioperative mortality and preoperative ICU stay > 7days (HR 4.332, 95% CI 1.651 – 9.616, p<0.001) and operation time > 420 min (HR 2.337, 95% CI 1.058 – 5.161, p=0.036) were independent risk factors of overall mortality.

Conclusions: Utilization of marginal liver graft seems not to increase postoperative morbidity and mortality and may be an important strategy to expand the donor pool. Operation time and recipient factors such as high MELD score and preoperative ICU stay were an independent risk factors for perioperative and overall mortality.

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EP_274 3D AUTO-SEGMENTATION FOR HEPATIC VENOUS TERRITORIES OF LIVING LIVER DONOR: AN AUTOMATED AI APPROACH

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Background: This study focuses on an AI model for automatic segmentation of liver territories in living liver donors based on hepatic venous territories

Methods: Utilizing SwinUNETR v2 and trained on 95 CT cases, the model was evaluated with the Dice Similarity Coefficient (DSC).

Results: The approach yielded promising DSC scores across various regions, with an average of 81.0%. Regarding portal vein territories divided by four, the average DSC score was 87±2.6. Regarding hepatic venous territories divided by three, the average DSC score was 85.5±4.3. The DSC scores for V5 and V8 were 75.7±6.3 and 67.2±8.6, respectively.

Conclusions: The autosegmentation AI model showed promising results. Increasing the dataset size is expected to enhance performance, making this method potentially valuable for surgical planning and liver transplantation.

EP_275 ASSOCIATION OF INTRAOPERATIVE BLOOD PRESSURE IN RENAL ALLOGRAFT FUNCTION: A META-ANALYSIS

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Background: Effective intraoperative blood pressure (BP) management during Kidney Transplantation (KT) is critical to optimize patient and graft survival. Delayed graft function (DGF), often associated with suboptimal BP control, compromises outcomes by increasing the risk of graft failure and reducing long-term survival rates. Studies have shown effective blood pressure (BP) management during anesthesia protects the graft, but the optimal intraoperative BP thresholds for KT remain unclear.

Methods: This systematic review and meta-analysis followed the PRISMA-P protocols focusing on studies involving adult and pediatric living donor kidney recipients. Relevant research was identified using the search technique through searches in Cochrane Library, PubMed, Google Scholar, HERDIN, and Science-Direct. Relevant studies were found using “blood pressure”, “graft survival”, and “graft function”. Heterogeneity was assessed using the I^2 statistics.

Results: Seven studies with low risk for bias were included. The pooled risk ratio showed that intraoperative hypotension (SBP<110mmHg, MAP <70mmHg) significantly increased the risk of graft failure (RR=1.91, 95% CI=1.26 to 2.88, p=0.002) while hypertension (SBP>140mmHg, MAP>93mmHg) lessens it (RR=0.62, 95% CI=0.47 to 0.82, p=0.0008). However, no significant difference in risk was observed for DGF between hypotension (RR=1.17, 95% CI=0.74 to 1.86, p=0.51) and hypertension (RR= 1.62, 95% CI: 0.37-6.98, p=0.52). Maintaining BP within defined thresholds minimized the risk of graft failure as the findings suggest. All studies included showed homogenous results.

Conclusions: The study highlights the critical importance of intraoperative BP management in improving graft survival in KT recipients. Hypotension increases the risk of graft failure significantly, while moderate hypertension (SBP>140mmHg, MAP>93mmHg) is associated with reduced risk. Individualized BP targets and continuous monitoring during KT are essential for optimizing outcomes. Focusing on identifying the safe upper limit of intraoperative BP levels and evaluating the effects of co-morbidities on BP management strategies are suggested for future studies.

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EP_276 NOREPINEPHRINE DONOR SUPPORT AND OUTCOMES IN HEART TRANSPLANTATION: A SINGLE-CENTER ANALYSIS

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Background: Heart transplantation (HTx) donors requiring high-dose catecholamine support, especially norepinephrine (NE), are often considered with caution. This study aims to evaluate the impact of high-dose NE donor support on post-transplant outcomes in HTx recipients in our center.

Methods: We retrospectively analyzed data from 109 HTx recipients transplanted between June 2022 and September 2024 in Bari, Italy. The dataset was stratified based on the NE dose administered to the donor prior to organ procurement, dividing into three groups: Group 1: 0 mcg/kg/min, Group 2: 0.01 to 0.2 mcg/kg/min, Group 3: >0.2 mcg/kg/min. Primary outcome measures included overall survival, 30-day and 1-year mortality, incidence of primary graft dysfunction (PGD), and other secondary outcomes such as prolonged ICU stay, ventilatory support, and renal replacement therapy. Statistical analyses were performed using a multivariate Cox proportional hazards models.

Results: Out of 109 patients, 11 received hearts without NE support, while 89,9 % received hearts supported with NE (Group 2 and 3). No significant differences in overall survival were observed across the groups (Group 2 vs 1: HR 1,11; Group 3 vs 1: HR 0,98; p = 0,656). Similarly, 30-day and 1-year mortality rates did not differ significantly between the groups. However, a higher incidence of prolonged ICU stay was observed in Groups 2 and 3 compared to Group 1 (p = 0,005).

Conclusions: Our findings align with previous studies indicating that the use of NE-supported donor hearts, even at higher doses, may not negatively impact recipient outcomes, provided careful donor selection. The higher incidence of prolonged ICU stays observed in NE-supported groups may reflect the severity of the donors' pre-procurement conditions rather than the direct effect of NE on the organ. Cautiously expanding the criteria for donor heart acceptance to include those supported by higher-dose vasoconstrictors could potentially increase the available donor pool without compromising recipient survival outcomes. In conclusion, high-dose NE donor support is not associated with increased mortality or severe complications in HTx recipients. With appropriate donor selection, these organs may safely contribute to addressing the shortage of donor hearts for transplantation.

EP_277 ACUTE KIDNEY INJURY POST LIVER TRANSPLANT WITH GRAFTS TREATED IN HMP: TRICK ... OR TREAT?

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Background: Many advantages were reported using the machine perfusion (MP) to rescue marginal grafts in the immediate- and long-term outcome. Acute kidney injury (AKI) is a common post-transplant complication using these livers that might compromise patient outcome and amplify the transplant cost. Aim of the study was to analyze the immediate post operative outcomes, including the AKI between patients with MP graft (MP) versus recipients of graft cold stored (noMP), before and after a propensity score matching (PSM).

Methods: From a prospectively maintained database, liver recipients of treated grafts (MP) versus standard cold stored grafts (noMP) of the same period (January 2022- September 2024) were compared. PSM was performed for donor risk index (DRI), macro-steatosis (MaS) > or <30% and recipient MELD, 3:1 (MP vs noMP).

Results: Of 129 transplants, 23MP versus 106 noMP were compared. DRI (2.1 vs. 1.8, p=0.049), donor age (76 vs 65, p=0.01) and presence of moderate macrosteatosis (20% versus 6%) were higher in MP group versus nonMP. Post operatively 35% MP didn't require ICU stay (versus 25% noMP, p=0.04) but had a higher AKI (55% versus 18%, p=0.001). After PSM, 23MP were compared with 68 noMP and MP patients had grafts from higher donor age (75 versus 67, p=0.04), better post operative liver function test and EAD but still high AKI (57% versus 44%, p=0.05). In PSM set, no one needed CVVH/dialysis and both groups were treated with the same immunosuppression protocol. Multivariate analysis showed the recipient pre-transplant creatinine level as the only significant risk factor for AKI (CI:1.84-43.48, OR:9, p=0.011). MaS>30% nearly reached the significant level (p=0.057).

Conclusions: MP remains an important device to rescue marginal livers. In the era of marginal grafts where all efforts aim to increase the donor pool, these recipients might need more post-operative attention to preserve the renal function, even if HMP is used.

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EP_278 17 B - ESTRADIOL THERAPY DURING EX VIVO LUNG PERFUSION IN SHEEP

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Background: Lung transplantation after circulatory death (DCD) is the primary therapeutic and only curative option for end-stage diseases but faces challenges like organ shortages and the risk of primary graft dysfunction (PGD). Ex Vivo Lung Perfusion (EVLP) is a promising solution to improve the viability of donated lungs, potentially expanding the donor pool and addressing transplantation demand. 17β-estradiol (E2) is a potential therapy to decrease the IR induced inflammatory process. Thus, this study aimed to investigate the effect of E2 treatment during machine perfusion.

Methods: Sheep lungs were procured from local abattoir. A warm flush (37°C) was performed, and lungs were kept inflated. There were 2 hours of warm ischemia followed by 3h of static cold storage. Finally, EVLP was performed for 4 hours with pressure-controlled ventilation, a self-made perfusate with the E2 treatment (5mg/L). The lungs were divided in two groups: Control and treated with E2. Lung biopsies were collected, and mRNA was analysed for inflammatory mediators and ATP production. Ventilatory parameters and perfusion pressures were recorded. Hourly gas analyses were performed. Cell damage markers were measured in perfusate.

Results: Control lung homogenates presented a more expressive increase in pro-inflammatory gene expression after EVLP than the treated (E2) group: IL1-β (p=0.0686), IL-6 (p=0.0994). There were no differences between the groups in the dynamic compliance (p=0.4121), pO_2 (p=0.1026) and lactate (p=0.8930). During the perfusion, ASAT and LDH did not differ between the groups (p=0.3060 and p=0.1182). At the end of perfusion, both groups presented similar ATP production(p=0.7442).

Conclusions: Sheep lungs treated with E2 seems to present less inflammatory gene expression in the tissue than the control group, even though at this time point no significant differences were seen in energy production and cell injury markers.

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EP_279 THE IMPACT OF DCD DONATION ON KIDNEY ALLOGRAFT SURVIVAL IS INFLUENCED BY DONOR RACE

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Background: Large scale registry studies have demonstrated that donation after circulatory death (DCD) and donation after brain death (DBD) donor kidney transplants have comparable medium- and long term graft survival. However, these studies do not include donor race in their analyses, a known risk factor affecting graft survival in deceased donor kidney transplants. Additionally, there is growing evidence to suggest potential racial differences in renal ischaemic tolerance. This study aims to address this knowledge gap, evaluating whether donor race modifies the impact of DCD donation on graft survival using a large, multi-centre database.

Methods: A retrospective observational analysis was performed using 261,634 kidney transplant recipients from the UNOS/OPTN database (1987 to 2020), stratified by donor race. Missing data was handled using multiple imputation. Risk-adjusted outcomes were assessed by multivariate cox analysis and visualized using Kaplan-Meier survival curves.

Results: Donor race significantly modified the effect of DCD donation on graft survival. Recipients of DCD kidneys from black donors experienced improved graft survival at 5 (HR 0.89, 95% CI 0.8-1.0, $p < 0.05$), 10 (HR 0.9, 95% CI 0.82-0.99, $p < 0.05$) and 15 years (HR 0.92, 95% CI 0.84-1.0, $p < 0.05$) compared to their DBD counterparts. In contrast, recipients of DCD kidneys from White donors experienced worse graft survival at 15 years (HR 1.08, 95% CI 1.04-1.11, $p < 0.001$), with no differences at 5 and 10 years. The difference in hazard ratios between black and white donors was statistically significant at 5, 10 and 15 years ($p<0.05$).

Conclusions: DCD donation was associated with improved long-term graft survival compared to DBD in recipients of kidneys from Black donors, while recipients of DCD kidneys from White donors experienced reduced long-term graft survival compared to DBD. This highlights a potential role of donor race in modifying the effects of DCD donation on kidney transplant outcomes.

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EP_280 THE IMPACT OF DCD DONATION ON LIVER GRAFT SURVIVAL IS INFLUENCED BY DONOR RACE: AN UNOS STUDY

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Background: As the rates of donation after circulatory death (DCD) within liver transplantation rise globally, efforts to understand the factors contributing to its association with reduced graft survival have intensified. Donor race, particularly donor/recipient ethnicity matching, is known to influence liver transplant graft survival. However, whether donor race modifies the impact of DCD donation on graft survival remains unclear.

Methods: A retrospective analysis was performed on 122,465 liver transplant recipients from the UNOS/OPTN database (1987-2020). Patients were stratified by donor and recipient race. Missing data was handled via multiple imputation. Graft survival outcomes were assessed using multivariate Cox regression and Kaplan-Meier survival curves.

Results: For White donors, DCD donation was associated with worse graft survival at 1 year (HR 1.54, 95% CI 1.41–1.68), 5 years (HR 1.45, 95% CI 1.34–1.57), 10 years (HR 1.68, 95% CI 1.53–1.84), and 15 years (HR 1.69, 95% CI 1.54–1.86) (all $p < 0.001$). For Black donors, DCD donation was associated with worse graft survival only at 1 year (HR 1.31, 95% CI 1.03–1.68, $p < 0.05$), with no significant impact at later time points. The modifying effect of donor race on DCD graft survival was independent of donor/recipient race mismatch in both White and Black donors.

Conclusions: Donor race modifies the impact of DCD donation on graft survival. In White donors, DCD donation consistently worsens outcomes at all time points, while in Black donors, this effect is significant only at 1 year. These effects are not influenced by donor/recipient race mismatch, suggesting that donor race specifically alters the impact of DCD donation on graft survival in liver transplantation.

EP_281 WORLD RECORD FOR KIDNEY PAIRED DONATION IN A SINGLE CENTER: KING FAISAL HOSPITAL EXPERIENCE 2024

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Background: We launched our program in 2016 and in 2024, we performed 135 kidney paired donation (KPD) transplants, thereby surpassing the one-year single center Guinness record of 100 KPD transplants.

Methods: KPD pool consists of HLA incompatible (HLA I) pairs; ABO incompatible (ABO I) pairs; and Compatible Pairs (CP) with poor HLA match. Matching strategies were to provide better HLA class II matches to CP; ABO Compatible or Quasi Compatible (ABOQ) transplants to ABO I; and HLA compatible or ABOQ transplants to HLA I with cPRA < than 80%. In highly sensitized patients (cPRA ≥ 80%), the strategy was either to provide HLA compatible or ABOQ transplants or to allow low risk ABO I or HLA I transplants.

Results: Between January – December 2024, a total of 135 KPD transplants were performed. There were 121 adults and 14 pediatric transplants comprising 30% (135/452) of our LD Kidney transplant pool. 126/135 (95%) transplants were done through direct exchanges (two-five) and the remainder through domino chains. 72/135 (54%) of KPD transplants entered the pool as HLA I; 34/135 (25%) as ABO I; and 29/135 (21%) as CP. 83/135 (61%) KPD transplant were sensitized; 53/135 (39%) had a cPRA >80%; 32/135 had a cPRA of 95-100%. 21/34 (62%) of ABO I pairs were O recipients of non-A2 donors (A1 or B). 95/135 (70%) of patients received compatible transplants; 15/135 (11%) received ABO quasi-compatible transplants; 2/135 (2%) received low risk ABO I transplants; and 23/135 (7%) received low risk HLA I transplants. The average LKDPI score was -8.4 with an average HLA class II MM of 0.88 and 0.67 for DR & DQ respectively. Moreover, the average Eplet MM load was 22.48 for HLA class II and 10 for HLA DQ. One year actuarial patient survival was 99% and death censored graft survival was 100%. Incidence of ACR was 4.4% (Banff IA – II A) and AMR was 0.74%.

Conclusions: To our knowledge, our annual volume of KPD transplants in 2024 stands as the highest number ever recorded at a single institution. Despite the high immunological risks of our cohort, the short-term outcome data compare favorably to those reported in any LD kidney transplant cohort. Furthermore, the excellent LKDPI scores and HLA class II EpMM loads portend a favorable long-term outcome.

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EP_282 LONG-TERM OUTCOMES OF PAEDIATRIC KIDNEY TRANSPLANTS FROM DCD DONORS: A 33-YEAR COMPARATIVE USA STUDY

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Background: Donation after cardiac death (DCD) is becoming an increasingly common strategy in transplantation and opens the possible donor pool. However, numerous paediatric centres in the UK and several countries in Europe are reluctant to offer DCD kidneys to paediatric recipients. There is only limited data on DCD transplants in the paediatric population. We reviewed the long-term outcomes of paediatric kidney transplants from DCD donors, and compared these to the outcomes of transplants from DBD donors over a 33-year period in the USA.

Methods: Data were retrieved and analysed on kidney transplants from deceased donors in paediatric recipients in 1987-2020 from the United Network for Organ Sharing. Data was compared between paediatric recipients receiving kidney transplants from DBD donors and DCD donors. Data were compared using chi-squared test, t-tests and Kaplan-Meier survival analysis.

Results: Overall, there were 13,127 paediatric kidney transplants from deceased donors, of which 354 were from DCD donors. Patients with transplants from DCD donors were significantly more likely to have delayed allograft function than from DBD donors (20.1% vs 11.9%, p<0.01) however there was no significant difference in the rates of primary non-function (1.1% vs 1.2%, p=0.81). When controlling for era effect, there was no significant difference in graft or patient survival between transplants from DBD and DCD donors (56% vs 55%, p=0.76 and 90% vs 91%, p=0.89, respectively).

Conclusions: We describe the largest cohort of paediatric DCD kidney transplant recipients in the literature. Our data shows that although there are higher rates of delayed allograft function in DCD transplants, the long-term outcomes are equivocal to each other. This shows that kidney transplants from DCD donors are a viable option for children requiring deceased donor kidney transplantation. DCD kidneys should be offered to children equivocally to DBD kidneys as their long-term outcomes do not differ.

EP_283 INTELLIGENT CONSTRUCTION FOR ORGAN DONATION AND PROCUREMENT IN THE FIRST PROVINCIAL OPO IN CHINA

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Background: In China, since the informatic construction of healthcare system has achieved success, the National Health Commission has been calling for the transition from informationization to intelligence. For organ donation and transplantation system, the development direction has been transited from high-speed to high-quality. Thus, in current age, without the support of intelligent system, quality control, management and further improvement can be difficult. Therefore, Shanxi OPO, as the first independent provincial in China, has launched the Shanxi Provincial Organ Donation Intelligence Cloud Management System since 2021 to assist with daily work of donor information reporting & collection, team coordination, and the recording of the entire OD process for traceable data and future analysis. Based on the data provided by the system, we also annually issue scientific report to provide summary of relevant quality indicators of OD & OT so as to continuously improve the quality of procured organs.

Methods: In this study, we introduce how the intelligent system works and analyze how it helps with the improvement of work efficiency.

Results: The service area of the system covers the donor hospitals and transplant centers within Shanxi Province. There are 3 kinds of terminals for different usage. For donor identification and relevant information reports, healthcare professionals can enter the system through our Wechat official account. For OPO personnel, a special mobile APP was created for them to respond, then upload relevant information, data and images for donor evaluation and management. Besides, the whole organ procurement surgery is recorded in the system to guarantee transplantation quality. For personnel of our informatic center, they need to do real-time monitoring and manage system settings. Additionally, specific technician needs to analyze and summarize all the recorded data. Based on which they will develop annual scientific reports for quality control and management.

Conclusions: With the help of the intelligent system, clinical labor costs have been saved and the work efficiency & quality have been improved. Besides, it also helps to improve ability to carry out various scientific research based on the key clinical data collected.

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EP_284 ORGAN DONATION RATES AMONG MUSLIMS INFLUENCED BY DEFINITION OF DEATH BY RELIGIOUS AUTHORITIES

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Background: In the past, death was recognized by absence of breathing and pulse, by public, religious authorities and even medical professionals. In 1968 Harvard Medical School set up an ad hoc committee to define irreversible coma. The committee consisted of several specialties, including neuro-specialists, anesthetists and ethicists. Interestingly it also included a transplant physician, revealing the interest of transplant surgeons. The committee considered loss of all brain functions as the new definition of death, despite continuing cardiopulmonary function with life support machines. A new definition of death was born. The new definition was soon accepted by medical professionals in the west but remained controversial in many eastern societies. Majority of Muslims all over the world, including those residing in western countries, are strongly influenced by religious opinion on defining end of life. This impacts willingness of Muslims to donate organs following brain death. The definition of death by neurological criteria has been controversial among Muslims. religious scholars as well as those working in the medical field. In 1986 Academy of Islamic Jurisprudence, comprising Muslim religious leaders from majority of Muslim countries, discussed brain death with Muslim physicians and accepted it. Unfortunately, their decision was not followed by many religious leaders in several countries, especially those following fundamental interpretation of Islam (Salafi). The influence of those opposing has grown over last decade, especially in Asia and the Middle East and has reflected on deceased donation rates.

Conclusions: Muslim medical community has the responsibility to meet religious leaders to explain brain death and differentiate it from deep coma, which is a main reason for their refusal.

EP_285 THE ROLE OF NEUREGULIN-1 IN LIVER TRANSPLANTATION FROM CARDIOCIRCULATORY DEATH DONORS

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Background: In liver transplantation (LT), the shortage of organs has led to a progressive increase in the use of liver grafts from donors after cardiocirculatory death (DCD). However, grafts with severe steatosis often result in poor postoperative outcomes and, in some cases, are not considered for transplantation due to their pathological condition. This study explores the role of neuregulin-1 (NRG1) in steatotic and non-steatotic liver grafts in liver transplantation from DCD rats.

Methods: Liver grafts from DCDs were transplanted, and the NRG1 pathways were characterized.

Results: NRG1 levels in the liver were elevated in both steatotic and non-steatotic DCD grafts. No changes were observed in p21-activated kinase (PAK1) in DCD grafts, suggesting that it was not modulated by NRG1. Inhibition of NRG1 led to exacerbation of injury and inflammation. The benefits of endogenous NRG1 in liver grafts from DCDs were associated with increased hepatic accumulation of vascular endothelial growth factor-A (VEGFA), while no changes in insulin-like growth factor-1 (IGF1) levels were observed. Exogenous NRG1, together with an increased peroxynitrite generation, induced additional injury and inflammation in DCD grafts, while exogenous VEGFA treatment protected both liver grafts from DCDs. The Id1-Wnt2 signaling pathway, rather than PI3k-Akt, played a key role in the action mechanisms of VEGFA.

Conclusions: Endogenous NRG1 exerts its beneficial effects in liver grafts from DCDs via VEGFA-Id1/Wnt2. Exogenous NRG1 was not useful treatment for liver grafts from DCDs, while VEGFA treatment proved to be a viable and highly protective strategy for both steatotic and non-steatotic liver transplantation from DCDs.

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EP_286 DIFFERENCES IN LIVING KIDNEY DONOR SELECTION IN VERY SMALL, SMALL AND MEDIUM SIZE GERMAN TRANSPLANT CENTRES

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Background: In Germany, 37 transplant centers (TC) performed 2122 kidney transplantations (KT) including 608 living kidney donations (LD) in 2023. 36 centers performed living donation. The high number of TCs in Germany results in small TC size and low numbers of KT per TC. Only two TC in Germany perform >100 KT and only one center >50 LD. 30/ 36 living donation TC's contribute to the German national living donor registry SOLKID-GNR. The aim of the evaluation of registry data was to evaluate, if very small, small or medium size transplant centers accept different donors for living kidney donation.

Methods: The participating 30 centers were categorized according to their caseload in very small (VS) centers with less than 10 LD per year (n=11), small centers (S) with 10-20 LD (n=10) and medium size (M) centers with more than 20 LD per year (n=9). We analyzed the donor demographics of 1020 donors and asked for the immunological risk of the transplantation and the operation technique used.

Results: 209 (21%) LD were carried out in VS, 288 (28%) in S and 523 (51%) in M transplant centers. Donor age, gender, BMI and GFR were similar between VS, S and M transplant centers. The percentage of donors with hypertension (27%) did not differ. VS centers were more likely to accept active smokers (17%), compared to S (14%) and M (10%) centers (p=0.02). M centers performed significantly more ABOi transplantations (28%) compared to S and VS centers (23 and 18%, p=0.02). Both S and M centers performed more immunological high risk donations with e.g. donor specific antibodies (DSA) (both 18%) compared to VS centers (8%, p=0.002). Minimal invasive (MI) operation techniques were more common in M centers (83%) compared to 76% in S and 73% in VS centers (p=0.003). The conversion rate from MI to open procedure was higher in VS and S centers (3.3 and 5.5%) compared to 0.5% in M centers (p<0.001).

Conclusions: There was no difference in living donor selection regarding age, gender, BMI and GFR between VS, S and M transplant centers in Germany. Small centers were more likely to accept active smokers for donation. More frequently medium TCs accepted a higher immunological risk transplantation with presence of DSA and AB0-incompatibility. Minimal invasive techniques were more common in medium TCs and the conversion rates were lower.

EP_287 EFFECT OF ALKALINE PHOSPHATASE IN A PORCINE MODEL OF KIDNEY PRESERVATION AFTER CIRCULATORY DEATH

Juan Miguel Tellez Garcia[1], Thei Steenvoorden[1], Frederike Bemelman[2], Joost Van der Heijden[3], Henri Leuvenink[4], Sandrine Florquin[5], Alessandra Tammaro[6], Liffert Vogt[1]

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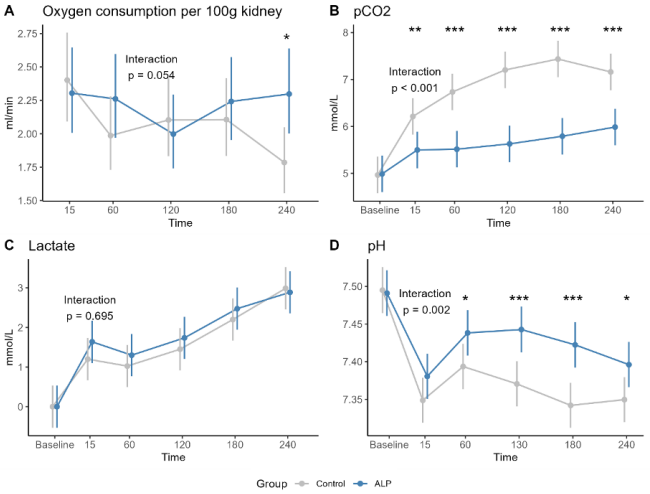
Background: Hypothermic machine perfusion (HMP) ameliorates but does not completely prevent ischemia reperfusion injury (IRI) in deceased-donor kidney transplantation. Alkaline phosphatase (ALP) can reduce IRI-induced kidney injury through the conversion of extracellular adenosine triphosphate into adenosine. The aim of the study was to evaluate if ALP offers protection during donor kidney storage.

Methods: Sixteen abattoir porcine kidneys (eight ALP and eight with placebo) were procured following sacrifice and exposed to 30 minutes of warm ischemia and 24h of HMP. Functional parameters were obtained during 240 minutes of normothermic machine perfusion (NMP). ALP or placebo was supplemented throughout. Tubular necrosis was assessed by a nephropathologist in a blinded fashion. Liquid chromatography–mass spectrometry (LC-MS) was used to analyze metabolites in biopsy tissue.

Results: No differences were detected between the ALP and the placebo group in creatinine clearance or fractional sodium excretion. Urine production was significantly lower in the ALP-treated group. The ALP-treated group showed favorable oxygen use, CO2 production, perfusate pH, and metabolite production (LC-MS), significantly higher levels of intracellular ATP and lower levels of lactate dehydrogenase, but not a lower tubular injury score.

Conclusions: ALP supplementation during and after HMP was associated with lower urine production, reduced energy demand, and improved metabolic function.



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EP_288 ALKALINE PHOSPHATASE AGAINST DELAYED GRAFT FUNCTION IN KIDNEY DONATION AFTER CIRCULATORY DEATH

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Background: Deceased-donor transplantation presents an opportunity to expand the donor pool amidst the continuous growing need for kidney grafts as the incidence of end-stage renal disease increases. Machine perfusion of the graft can ameliorate but not completely prevent ischemia reperfusion injury (IRI) in deceased donor kidney transplantion. Donation after circulatory death (DCD) kidney transplantation specifically, has a high rate of IRI-induced acute kidney injury (IRI-AKI) associated delayed graft function (DGF). Extracellular adenosine triphosphatase (eATP) is a potential critical mediator of this through signaling via inflammatory purinoreceptors. Alkaline phosphatase (ALP) has been shown in both preclinical and clinical research to reduce IRI-AKI through the conversion of extracellular adenosine triphosphatase into adenosine, dampening IRI associated renal damage. At our institution, we successfully conducted a phase 1 pilot randomized, placebo controlled trial (RCT) where ALP was given to patients undergoing living donor transplantation. We are currently conducting a follow-up phase 2 RCT where patients undergoing DCD kidney transplantation are treated with either ALP or placebo.

Methods: Phase 2 trial in adult patients (>18 years) undergoing DCD type 3 kidney transplantation who are neither vegan or strict vegetarian. Eligible patients are randomized to receive either bRESCAP (bovine derived ALP) or placebo. Patients receive a bolus of alkaline phosphatase or placebo before the graft is vascularly anastomosed. Following the bolus, patients continuously receive either medication or placebo intravenously for 72 hours. The cytokine and immune system compartment profiles between the ALP and control treated recipients will be analyzed. Kidney function and incidence of rejection will be monitored until 1 year following the transplantation. The difference between the cumulative incidence of DGF between ALP and placebo treated groups will be the primary outcome. We estimate that the power needed to detect a clinical relevant risk-reduction of 25% in DGF incidence will require around 60-70 trial participants.

Results: The first 16 patients have been treated and an interim analysis of the primary outcome will be conducted after 25 inclusions.

EP_290 CONTINUOUS CREATININE MEASUREMENT VIA MICRODIALYSIS MAY PROVIDE INSIGHTS INTO KIDNEY VIABILITY

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Background: Globally 1-in-5 kidneys procured from deceased donors are discarded pre-operatively, with rates increasing to 50% for organs from older donors and those with comorbidities. Multivariate scoring has been developed to quantify potential viability, but these only work effectively at population level and do not inform surgeons about likely outcomes from transplanting a specific organ. There is a critical need for objective pre-transplant viability assessment technologies. We have developed a novel approach to the challenge of pre-transplantation viability assessment using a panel of functional and metabolic biomarkers monitored in real-time.

Methods: An interventional feasibility study was conducted involving paired kidneys procured from 8 food-chain pigs. Organs were transported on ice to the research laboratory, where one of the pair was exposed to room temperature for 2 hours to represent extreme warm ischaemic time exposure (“injured kidneys”). Both organs were hypothermically machine perfused for 2 hours (RM3, Waters Medical Systems LLC, Rochester, MN, USA). Microdialysis probes were inserted into the vein and ureter and dialysate creatinine levels were continually quantified in real-time over 30 mins following a bolus of 250uM creatinine into the machine perfusion solution.

Results: 11 usable datasets were recorded. Others were inviable owing to blood foaming, microthrombi, and equipment failure (probe placement, pump failure). In 3 pairs, there were obvious differences in urinary creatinine clearance between the injured and uninjured kidneys, with the uninjured organ demonstrating a dynamic rise and decay in urinary creatinine levels beginning within 10 minutes of bolus. Uninjured kidneys also demonstrated dynamic or depleting venous creatinine concentrations. 3 injured kidneys had no dynamic urinary creatinine response, with one showing a rise in venous concentration after bolus.

Conclusions: Continuous paired creatinine measurements from the ureter and vein of kidneys undergoing machine perfusion are possible using microdialysis techniques. The dynamic responses of organs to an arterial creatinine bolus may shed light on pre-operative organ viability.

Conflicts of Interest: Accunea Ltd. is a commercial organisation developing the technology used in this study.

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EP_291 THE STATE OF PAEDIATRIC DECEASED-ORGAN DONATION AT A SOUTH AFRICAN TERTIARY PUBLIC-SECTOR HOSPITAL:A 14 YEAR ANALYSIS

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Background: Solid-organ transplantation (SOT) has been proven to be a highly effective and life-saving treatment modality for children suffering from end-stage organ failure. High paediatric waiting-list mortality has been reported, and children may suffer irreversible physical and psychological effects. Our objectives were to identify in-hospital barriers to organ donation and gain a better understanding of the paediatric donor landscape.

Methods: Retrospective descriptive study of consecutive deceased-donor referrals at Red Cross War Memorial Children's Hospital over a 14-year period,1 January 2007 to 31 December 2020.

Results: During the study period, 156 in-hospital deaths were recorded in the trauma unit and 1 425 in the paediatric intensive care unit. 93 of the 1 581 patients (5.9%) were referred to the on-call transplant co-ordinator as potential organ donors, of whom 69% had been involved in a traumatic accident, including 52% in road traffic collisions. The mean age of the potential donors was 7 years with 60.2% being boys. Initial assessment, 67 of the 93 potential donors (72%) were assessed as eligible for donation of at least one solid organ. The transplant co-ordinator attempted to approach all families for consent; however, five families/next of kin could not be located despite multiple attempts. Among the remaining 62 eligible donors, 44 families/next-of-kin declined consent for solid-organ donation, resulting in a consent rate of 29% (*n*=18). Several families refused consent for religious reasons. One of the consented donors did not proceed to procurement as there were no suitable recipients. Seventeen donors proceeded to theatre, the intention being solid-organ procurement, but in 2 donors the organs were assessed as being unsuitable for transplant. From the remaining 15 donors, a total of 46 organs were procured and successfully transplanted: 14 livers, 30 kidneys and 2 hearts.

Conclusions: During the 14-year study period, only 15 deceased donors could be utilised for SOT, as a result of low in-hospital referral (5.9%) and consent rates (29%). The reasons for low referral and consent rates are complex and often multifactorial, which the current study was not designed to investigate in sufficient detail. Future studies needed for nuances specific to the paediatric deceased-donors.

EP_292 LIVING KIDNEY DONORS REJECTED: EXPERIENCE OF THE UNIVERSITY SAHLOUL HOSPITAL

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Background: The living kideney donor (LKD) constitutes the main source of grafts in Tunisia. Donor selection criteria must ensure donor safety and optimize follow-up care and outcomes for both donors and recipients.

Methods: This is a retrospective study conducted between November 2007 and September 2024, involving 23 donors rejected. The aim of this study was to recognize the reasons for declining LKD

Results: The total number of living donor transplants during this period was 423. Twenty three donors were unable to proceed for kidney donation with a median age of 49 years and a female predominance (56.52%) with a sex ratio of 0.77. The donor-recipient relationship was: parent to child in 12 cases (52.17%), between siblings in 6 cases (26.08%), child to parent in 1 case (4.35%), and between spouses in 4 cases (17.39%). The average number of rejected donors per recipient was 1.3 . The reasons for rejection were: presence of positive donor-specific antibodies (1 case), chronic kidney disease with a glomerular filtration rate (GFR) of 80 ml/min (1 case), recurrent kidney stones (1 case), proteinuria (1 case), microscopic hematuria (1 case), aseptic leukocyturia (1 case), kidney asymmetry (2 cases), vesicoureteral reflux grade IV (1 case), renal artery stenosis (1 case), diabetes (2 cases), an autoimmune disease (5 cases). These diseases were: erythematosus systemic lupus(3 cases) , autommune hepatitis(1 case) celiac disease(1 case) . The other patterns of refusal were severe sleep apnea syndrome (SAS) (1 case), tumor-related cause (1 case), and a cardiac malformation (1 case).

Conclusions: Given the organ shortage, selection criteria should be expanded, but certain contraindications remain indisputable.

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EP_294 VALIDATING A NEW MEASURE OF POTENTIAL LIVING DONORS' READINESS AND ACTIONS TAKEN TOWARDS DONATION

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Background: While measures of readiness to pursue living donation exist for kidney recipients, there are no validated, theoretically consistent measures of readiness to donate a kidney by potential donors. This study developed and validated a new measure of readiness for potential donors and explored its association with taking donation-related actions prior to evaluation and actually donating kidneys 12 months later.

Methods: At five transplant centers, we assessed potential living donors' pre-evaluation readiness to take donation actions using a scale based on the Transtheoretical Model [I am not considering taking actions to see if I can donate a kidney (Precontemplation), still deciding (Contemplation), planning to take (Preparation) and taking actions (Action)]. Participants reported whether they had taken, planned or did not plan to take donation-related actions. We conducted descriptive and chi-squared analyses to examine differences in donor characteristics and actions by readiness level. A univariate logistic regression model estimated the odds of donation by readiness level, reporting odds ratios (OR) and 95% confidence intervals.

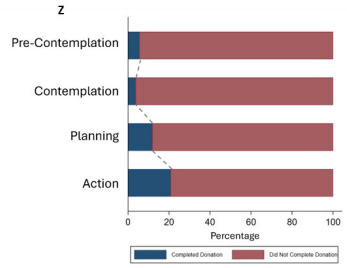
Results: Among 2041 potential living donors (60.9% female, 49.9% White, 18.5% Hispanic, 14.9% Black, 8.3% Asian, 8.4% Other) who began donor evaluation, 374 (18.3%) donated within 12 months. The proportion of patients who took one or more donation-related action was greatest for those in the Action readiness stage when starting evaluation ($p \leq 0.001$, Table 1). Patients taking donation actions at evaluation had 4-times higher odds of donating than those in Precontemplation stage (OR: 4.44 [1.06-18.58]; p=0.041, Figure 1).

Conclusions: Pre-evaluation readiness levels were significantly associated with better preparation, lower dropout rates, and higher donation rates within 12 months. Future studies should assess donor readiness and provide tailored support by readiness stage to encourage donation-related actions and kidney donation.

Table 1 – Proportion of patients who took donation-related actions and donated by Readiness Stage

	Donor Stage				
	Precontemplation (n=36)	Contemplation (n=54)	Preparation (n=382)	Action (n=1,569)	X^2-Test p-value
Took 1+ action before evaluation	26 (72.2%)	41 (75.9%)	**313 (81.9%)**	**1449 (92.4%)**	0.001
Read information about donation	16 (44.4%)	15 (27.8%)	167 (43.7%)	**947 (60.4%)**	0.001
Talked to family about risks/benefits of donation	14 (38.9%)	24 (44.4%)	162 (42.4%)	**960 (61.2%)**	0.001
Talked to recipient about donating	20 (55.6%)	15 (27.8%)	217 (56.8%)	**1063 (67.8%)**	0.001
Thought through how to manage family and work responsibilities when donating	13 (36.1%)	10 (18.5%)	71 (18.6%)	**694 (44.2%)**	0.001
Did not drop out voluntarily before evaluation was complete	23 (63.9%)	18 (33.3%)	232 (60.7%)	**1101 (70.2%)**	0.001
Donated kidneys	2 (5.6%)	2 (3.7%)	**45 (11.8%)**	**325 (20.7%)**	0.001

Figure 1 – Percentage of patients donating kidneys at each level of readiness and univariable logistic regression results.



	Completed Donation	Odds Ratio	P-Value
Pre-Contemplation	2 (5.6%)	[Reference]	---
Contemplation	2 (3.7%)	0.65 [0.09-4.87]	0.678
Planning	45 (11.8%)	2.27 [0.53-9.77]	0.271
Action	325 (20.7%)	**4.44 [1.06-18.58]**	**0.041**

EP_295 FATTY LIVER EXTRACELLULAR VESICLES EXACERBATE HEPATIC ISCHEMIA-REPERFUSION INJURY

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Background: Extracellular vesicles (EVs) play a crucial role in intercellular communication and are involved in fatty donor liver ischemia-reperfusion injury (IRI). However, the mechanisms by which fatty liver-derived EVs contribute to IRI remain unexplored.

Methods: Fatty liver mice models were established by feeding high-fat diets (HFD), and IRI models were created through surgical procedures. EVs from the liver tissues of HFD-induced fatty liver mice (HFD-EVs) and normal mice were extracted and purified. Normal mice were intravenously injected with HFD-EVs and subjected to the IRI model. In vitro, primary mouse hepatocytes and the AML12 cell line were subjected to hypoxia-reoxygenation experiments to simulate IRI. After co-incubation with HFD-EVs, ROS accumulation was measured using a fluorescent probe, and cell apoptosis was assessed by TUNEL staining. Mitochondrial membrane potential and morphology changes were observed using JC-1 and MitoTracker staining.

Results: Oil Red O staining of liver sections from HFD-induced fatty liver mice showed significant fat deposition. After IRI, serum ALT, AST, and LDH levels were significantly elevated, and liver sections exhibited more severe damage compared to normal mice. In fatty liver mice after IRI, the expression of Caspase-3 and Bax was significantly increased, while Bcl-2 expression was notably decreased. Compared to normal liver EVs, HFD-EVs had a higher protein content, and proteomic analysis indicated that HFD-EVs activated mitochondrial-mediated apoptosis pathways. In normal mice injected with HFD-EVs, IRI resulted in more severe liver damage. Liver sections showed more pronounced damage, and Western blotting revealed a significant increase in Caspase-3 and Bax expression, with a decrease in Bcl-2 expression. In vitro, hepatocytes exposed to HFD-EVs under hypoxia-reoxygenation conditions exhibited greater ROS accumulation and higher TUNEL-positive rates. JC-1 and MitoTracker staining showed a significant decrease in mitochondrial membrane potential and morphological changes, while Western blotting indicated increased release of cytochrome c.

Conclusions: Fatty liver-derived tissue EVs exacerbate hepatic ischemia-reperfusion injury by activating mitochondrial-mediated apoptosis pathways.

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EP_296 SODIUM AND LACTATE DURING HYPOTHERMIC OXYGENATED LIVER MACHINE PERFUSION IMPROVE RISK STRATIFICATION

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Background: Hypothermic oxygenated machine perfusion (HOPE) has been shown to enhance post-transplant outcomes in liver transplantation (LT). However, a significant limitation is the absence of biomarkers to evaluate graft viability during perfusion. Currently, there are no universally accessible and easily interpretable metrics for real-time monitoring of HOPE.

Methods: This study conducted a retrospective analysis of outcomes for 158 patients who underwent LT following HOPE at our institution from 2018 to 2023. HOPE was performed using standardized protocols and the University of Wisconsin machine perfusion solution. Blood gas analyses were carried out at 30-minute intervals during the first 120 minutes of perfusion. Data on hospitalization and clinical outcomes were collected and analyzed prospectively. Early allograft dysfunction (EAD) was assessed based on the Olthoff criteria.

Results: Among the 158 liver transplant recipients, 44 (27.8%) developed EAD. Grafts that later exhibited EAD showed significantly lower sodium concentrations throughout HOPE, while lactate levels were notably higher at 60 and 90 minutes. At the 90-minute mark, sodium and lactate levels demonstrated the strongest predictive capacity for EAD, with area under the receiver operating characteristic (AUROC) values of 0.741 and 0.633, respectively. Optimal thresholds were identified at 85 mmol/L for sodium and 4.3 mmol/L for lactate. Stratification using these cut-offs revealed distinct risk groups: a low-risk group (high sodium, low lactate) had an EAD incidence of 17.6%, while the high-risk group (low sodium, high lactate) experienced a significantly elevated EAD rate of 69.2%.

Conclusions: Evaluating sodium and lactate levels at 90 minutes during HOPE offers a straightforward method to stratify donor liver grafts by the risk of EAD prior to transplantation. Implementing this 90-minute pre-transplant assessment using widely available blood gas analysis tools could enhance donor organ selection and improve clinical outcomes for LT recipients.

EP_297 INFLUENCE OF SHORT COLD STORAGE AND LONG HYPOTHERMIC MACHINE PERFUSION ON OUTCOMES OF KIDNEY TRANSPLANTATION

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Background: Hypothermic machine perfusion (HMP) reduces delayed graft function (DGF) and improves kidney graft survival from extended-criteria donors (ECD). If it is not possible to apply HMP immediately after retrieval, cold storage (CS) remains the method of choice. However, as referral center, we receive grafts, which were discharged elsewhere using CS. We apply HMP and gain time to find appropriate recipient. Results of short CS and long HMP are unclear. We evaluated impact of combined short CS followed by long HMP and solitary CS on kidney outcomes in single-center experience.

Methods: We compared 50 recipients with mean age 51 (range: 17-76) whose grafts were preserved in CS before kidney transplantation (KTx) (group A) and 75 recipients with mean age 52 (range: 19-76) whose grafts were preserved in CS followed by HMP (group B). Total ischemia time (TIT) was 1092 min (SD±520) in group A. In group B TIT was 1510 min (SD±443) including 253 min (SD±162) for CS and 1256 min (SD±386) for HMP. TIT was significantly longer in group B ($p<.05$). All donors were brain-dead with significantly more ECD in group B (9/50 vs. 28/75, $p<.05$). We evaluated incidence of primary graft non-function, DGF, creatinine clearence (Cr) at discharge, at 3 and 6 month follow-up.

Results: PNF (1/50 vs 5/74, p=ns) and DGF incidence (23/50 vs 27/74, p=ns) were comparable in group A and B, respectively. Cr at discharge [1,98 mg/dL (SD±1,18) vs 2,11 mg/dL (SD±1,09), p=ns], in 3 month follow-up [1,7 mg/dL (SD±1,09) vs 1,69 mg/dL (SD±0,86), p=ns] and in 6 month follow-up [1,45mg/dL (SD±0,75) vs 1,46 mg/dL (SD±0,57), p=ns] were similar in group A and B, respectively. Both groups demonstrated significant Cr decrease from discharge to 6th month was observed ($p<.05$).

Conclusions: Short CS followed by long HMP is comparable to solitary CS on early and mid-term graft survival and provides additional time with no harm to the graft. Further observation is necessary to determine long-term outcomes.

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EP_298 DONOR WITH OUT OF HOSPITAL CARDIAC ARREST TREATED BY CPR. MID-TERMS OUTCOMES

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[1]University of Bari; Aouc Policlinico di Bari; Cardiac Surgery Unit, [2]Università Degli Studi di Bari; Cardiac Surgery Unit, [3]University of Bari; Aouc Policlinico di Bari; Cardiac Surgery, [4]University of Bari; Aouc Policlinico di Bari

Background: Cardiac transplantation is the gold standard for the treatment of advanced heart failure refractory to medical therapy. The number of patients on the waiting list exceeds the number of available donors. The use of DBD donors with out-of-hospital cardiac arrest (OHCA) treated with CPR with preserved ejection fraction may be a valuable resource to allow the donor pool to be increased.

Methods: Retrospective study conducted at the Policlinico of Bari, in the South of Italy, from March 2022 and December 2024. The population was divided into two groups: recipient from a donor with OHCA treated with CPR (n=30) and recipient from a donor without cardiac arrest (nOHCA) (n=139). The pre-operative characteristics of the two populations were superimposable. The following were analyzed in the post-operative period: the incidence of PGD, the use of ECMO, CVVH and survival in recipients based on the donor used.

Results: The time of cardiac arrest in the donor treated by CPR was 27,12 minutes (±7.23). 12 patients (40,00%) with donor with OHCA required post-operative ECMO compared with 49 recipients (38,28%) from donors without cardiac arrest (p=1,00). For primary graft dysfunction (PGD) the percentages was symylar between two groups: 11 patients (36,67%) in OHCA group and 49 patients (38,28%) in nOHCA groups (p=1,00). Post-CVVH (Continuous Venovenous Hemofiltration) was necessary in 16 patients (53,33%) belonging to OHCA groups and in 65 patients (50,78%) belonging to nOHCA groups (p=0,96). Kaplan Meier curves showed log-rank=0,87 with p-value=0,34.

Conclusions: The cardiac arrest donor treated with CPR with preserved ejection fraction is an important resource in cardiac transplantation to reduce the gap between patients on the list and donor availability. According to our study, the outcome does not depend on the donor used but on the characteristics of the recipient

EP_299 URINARY EXTRACELLULAR VESICLES IN SHORT-TERM FASTING AND KIDNEY TRANSPLANTATION

Christiaan Oudmaijer[1], Martijn van Heugten[2], Sebastian Beckmann[3], Daphne Komninos[4], Rutger Ozinga[5], Kimberly Smit[5], Wilbert Vermeij[5], Jan Hoeijmakers[5], Jan IJzermans[6], Ewout Hoorn[7]

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Background: Urinary extracellular vesicles (uEVs) contain kidney-specific molecules, including RNA. Whether the transcriptome of uEVs directly reflects gene expression in human kidney tissue is unknown.

Methods: For this proof of concept study, an urine sample was collected just before kidney donor nephrectomy and kidney cortex biopsies were collected during this procedure. uEVs were isolated using a differential ultracentrifugation protocol. RNA in uEVs and tissue samples was sequenced, and results were cross-correlated.

Results: Three out of 8 uEV samples RNA were of sufficient quality and these were sequenced and analyzed. Correlation analysis revealed significant associations between the uEV and kidney transcriptome in the expression of relevant kidney-specific genes.

Conclusions: Our findings confirm the proof of principle that uEV cargo reflects expression at kidney tissue level. Our data also emphasizes the importance of pre-analytical procedures to improve successful RNA sequencing. Optimization of uEV isolation and combining RNA-sequencing with proteomic analysis can pave the way towards the application of uEVs as “liquid biopsy”.

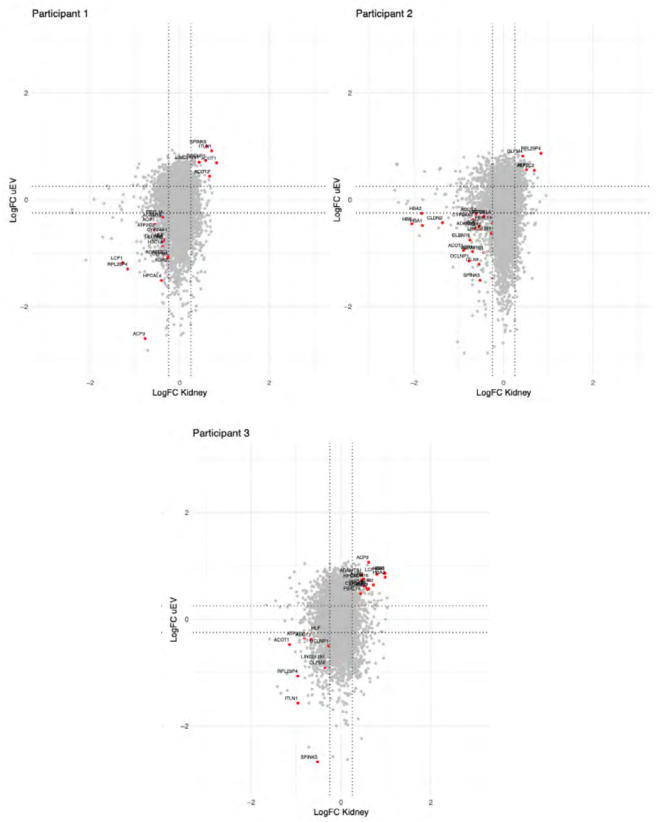

Figure 1: Scatterplots of log2 fold changes (LogFC) of RNA expression in urinary extracellular vesicles (uEV) vs. kidney tissue in the three participants.

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EP_300 FATIGUE IN LIVING KIDNEY DONORS COMPARED TO A GERMAN GENERAL POPULATION SAMPLE

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Background: Developing clinically relevant fatigue symptoms is a potentially severe complication in living kidney donors (LKD). So far, it remains unclear whether fatigue scores in LKD after donation fundamentally differ from those of general population samples. The association between sociodemographic and donor-specific parameters and fatigue in LKD is poorly understood.

Methods: Fatigue scores of 358 LKD, on average 7.67 years post-donation, were compared to the results of 1896 subjects from the German general population in five strata of age and sex. Fatigue was evaluated using the Multidimensional Fatigue Inventory (MFI-20). Relationships between the five MFI-20 subscales and sex, age, and educational level were observed. The association between donor-specific variables and fatigue levels was also analyzed.

Results: LKD reported lower fatigue scores compared to the German general population sample. LKD aged 65-74 and above reported significantly lower fatigue scores. Female donors aged 45-54 years showed significantly higher general fatigue scores than the corresponding subgroup of the general population sample. Multiple regression analyses in the general population sample revealed associations between female sex, lower educational level, and higher age with higher values in most MFI-20 subscales. In LKD, years since donation, partnership, and recipient group were not strongly related to fatigue. Higher fatigue scores were associated with more regret regarding the donation, a worse relationship with the recipient, a more negatively perceived recipient's health, less perceived family support, and more financial burden.

Conclusions: Fatigue symptoms are less prevalent, particularly in older donors, and predictors of fatigue detected in the general population sample are less relevant in the donor sample. Middle-aged female donors might have a higher risk of developing fatigue. This group may require more intense exploration and support before and after donation.

EP_301 CASE OF SUCCESSFUL MULTIORGAN DONATION AFTER HYDROGEN SULFIDE INTOXICATION AFTER INDUSTRIAL ACCIDENT

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Background: Hydrogen sulfide is a toxic gas commonly found in the environment and generated as a by-product in industries such as oil refining and sewage treatment. Hydrogen sulfide poisoning occurs through inhalation, with high-level exposure being associated with fatal toxicity. The primary mechanism of toxicity involves mitochondrial inhibition of aerobic metabolism, leading to lactic acidosis, oxidative stress, and ultimately cell death. The cortex, basal ganglia, and brainstem are particularly sensitive to hydrogen sulfide. At concentrations above 1000 ppm, inhibition of the respiratory center can cause apnea, even after only a few breaths.

Case report:A 41-year-old worker was brought to the emergency department after a hydrogen sulfide pipeline explosion and successful CPR. The patient was found unconscious and without respiration at the scene of the explosion. He underwent approximately 10 minutes of resuscitation, although the exact duration of CPR remains unknown due to the circumstances of the industrial accident. Upon arrival at the hospital, the patient presented with pulseless electrical activity, and three doses of 1 mg adrenaline were administered before return of spontaneous circulation (ROSC) was achieved. On arrival at the emergency department, the patient was areflexic with bilateral mydriasis. A CT scan revealed severe cerebral edema. The patient was admitted to the ICU. Initial laboratory results showed mild liver impairment (AST and ALT <90 U/L), acute kidney injury (AKIN 1), and hyperlactatemia. During observation, lactate levels gradually decreased, and there was no evidence of progression in liver or kidney injury. Subsequent laboratory results essentially ruled out ongoing mitochondrial damage. Brain death was declared less than 24 hours after admission, based on neurological evaluation and cerebral angiography.

The patient's organs were successfully transplanted into six recipients, including the heart, two split liver grafts, pancreas, and two kidneys. All organ transplants showed survival at one and three years, with sufficient graft function. No delayed graft function was observed.

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EP_302 NORMOTHERMIC MACHINE PERFUSION MITIGATES ACUTE REJECTION OF RAT RENAL ALLOGRAFT

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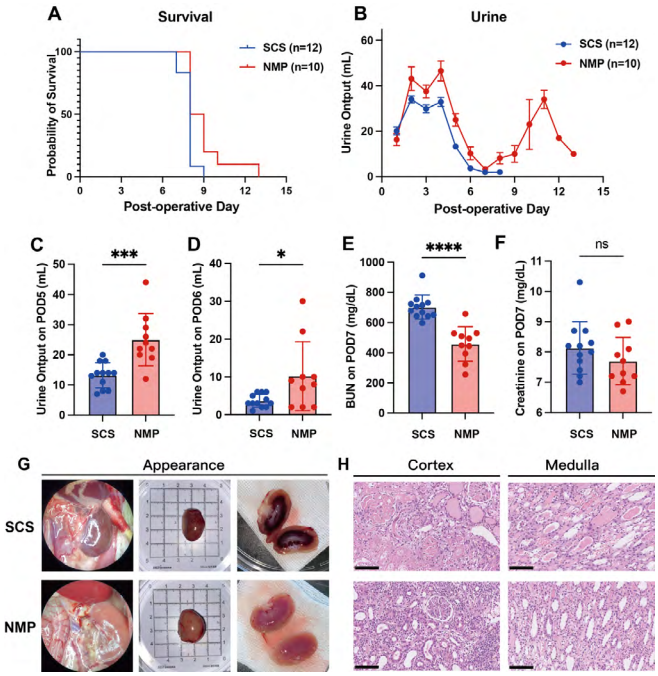
Background: Normothermic machine perfusion (NMP) has been extensively applied in clinical transplantation, indicating promising outcomes.

Methods: Male Brown Norway (BN) and Lewis rats (280 to 320 g) were used for all experiments. The left kidney from BN was procured. The renal grafts were perfused at 37ºC in the NMP group and preserved in HCA-II solution at 4ºC in stable cold storage (SCS) group. The preservation time was 3 hours. Lewis rats underwent bilateral nephrectomy and received the BN grafts. Then, we compared each group's graft function, survival rates, and graft histology on postoperative day (POD) 5.

Results: The median survival time of the NMP group was significantly longer than that of the SCS group (8.5 vs 8.0 days, *P*=0.0157, Figure A). Moreover, the urine volume of the NMP group from 2 to 7 days after surgery was significantly higher than that of the SCS group (Figure B - D), and the blood urea nitrogen on POD7 was significantly lower in the NMP group than in the SCS group (Figure E). On POD5, the allografts in the SCS group presented a mottled color, while those in the NMP group showed only slight swelling (Figure G). Microscopically, both the SCS and NMP groups exhibited extensive mononuclear lymphocyte infiltration, but obvious extensive peritubular capillary bleeding and infarction were observed in the SCS group (Figure H).

Conclusions: NMP can significantly prolong the survival time of recipients and remarkably improve the early function of transplanted kidneys.



NMP Prolongs the Survival Time of Recipients in the Acute Rejection Model and Improves the Early Function of Transplanted Kidneys

(A) Survival of recipients in the SCS group and the NMP group; (B) Urine output of recipients in the SCS group and the NMP group; (C) Urine output of recipients on POD5, SCS = 13.25 ± 4.18 ml, NMP = 25.00 ± 8.67 ml, *P* = 0.0005; (D) Urine output of recipients on POD6, SCS = 3.67 ± 1.73 ml, NMP = 10.20 ± 9.13 ml, *P* = 0.0241; (E) Serum BUN of recipients on POD7, SCS = 702.4 ± 79.88mg/dl, NMP = 459.0 ± 114.2 mg/dl, *P* < 0.0001; (F) Serum creatinine of recipients on POD7, SCS = 8.13 ± 0.87mg/dl, NMP = 7.70 ± 0.78mg/dl, *P* = 0.2374; (G) Appearance of renal allografts; (H) Microscopic changes of the transplanted kidney under HE staining, scale bar 100μm.

EP_303 THE IMPACT OF NEPHROTOXIC ANTIBIOTICS ON KIDNEY GRAFT VIABILITY DURING HMP: A PRECLINICAL STUDY

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Background: The shortage of donor kidneys is a critical global issue. Marginal donors, including those with infections, offer a potential solution but pose risks of donor-derived infections (DDI). Donors with proven positive blood and urine cultures for multidrug-resistant Gram-negative bacteria are currently contraindicated for kidney procurement due to the high risk of transmitting infections to recipients. Ex vivo treatment of septic kidneys represents a potential method to not only prevent DDI but also enable the utilization of these previously unsuitable donors. This study aims to evaluate whether the use of nephrotoxic antibiotics—tigecycline and gentamicin—during hypothermic machine perfusion (HMP) damages porcine kidney grafts.

Methods: A minipig model was used for kidney procurement and perfusion. Kidneys were perfused with or without antibiotics for 4 hours (c. = 600 mg/l) and analyzed histopathologically. Immunohistochemical markers (MCM2, MPO, iNOS, Annexin V, M30 Cytodeath) were assessed to evaluate proliferation, inflammation, and apoptosis. Antibiotic concentrations in perfusate were measured by high-performance liquid chromatography.

Results: Histopathological analysis revealed no significant tissue damage between treated and control groups. Immunohistochemical markers showed that kidneys perfused with antibiotics had higher inflammation, increased apoptosis, and lower cell proliferation than control group. However, the overall condition of treated kidneys improved compared to their pre-perfusion state. Antibiotic concentrations in the perfusate decreased minimally after 4 hours, indicating sustained delivery.

Conclusions: This study demonstrates the potential for using tigecycline and gentamicin during HMP without causing significant histopathological damage. Despite observed adverse effects, HMP with ATB improved post-perfusion kidney condition Sustained antibiotic levels suggest effective ATB delivery, which could improve infection suppression. These findings support HMP combined with antibiotics as a strategy to prevent donor-derived infections and enable the safe use of marginal donors with multidrug-resistant Gram-negative bacterial infections. Further research is required to evaluate the clinical applicability of this approach.

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EP_304 UNEQUAL DONOR/RECIPIENT AGE MATCHING DOES NOT AFFECT LONG-TERM IMMUNOLOGICAL OUTCOMES: WHICH MECHANISMS ARE WE MISSING?

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Background: Donor/recipient (D/R) mismatch seems not to affect late immunological and survival outcomes after Heart Transplant (HT), and so does unequal D/R age matching on long-term outcomes. The aim of this study is to analyze the effects of unequal D/R age matching on the clinical and immunological outcomes in a 10-year-single-center study and to investigate the possible predictor factors.

Methods: Clinical and hemodynamic data of all patients who underwent HT at our Institution between January 2012-December 2023 were retrospectively collected. Patients <50 years were selected and matched into 2 groups according to their D/R age (recipient<50years+donor<50years Group 1, recipient<50years+donor>50years Group 2) and then analyzed in terms of thirty-day mortality, cardiac allograft vasculopathy (CAV), acute cellular rejection (ACR) and antibody mediated rejection (AMR), incidence of malignancy, and long-term overall survival.

Results: Among 116 patients, Group 1 included 88 (male D/R 57%/74%, median age D/R 22/24 years), and Group 2 28 (male D/R 32%/54%, mean age D/R 56/44 years) patients, respectively. Donor coronary artery disease did not differ between the two groups. Recipient gender differed between the two groups (p=0.011). Preoperative inotropes and tMCS in recipients, did not differ between the two groups (p=0.227 and p=0.204). Thirty-day mortality was not significantly different among the 2 groups (p=0.560). At 10-year follow-up time, CAV>1 and malignancies were higher in Group 1, whereas there was no statistical difference in ACR and AMR. Long term overall survival did not differ in the two groups.

Conclusions: Our experience shows that unequal D/R age matching in recipients <50 years does not affect early late immunological outcomes and overall survival in HT patients, it even seems to protect from the incidence of CAV and malignancies. Aging-related biological mechanisms and endogenous organ reprogramming should be investigated to explain this finding.

EP_305 AWARENESS AND PERSPECTIVE OF LIVING DONATION AMONG KIDNEY TRANSPLANT CANDIDATES

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Background: Live donor kidney transplantation offers superior outcomes for end-stage renal disease, yet significant recipient-level barriers persist, particularly in ethnically diverse populations. While research largely focuses on donors, limited attention has been given to recipient perspectives. This study explores awareness and attitudes toward living kidney donation (LKD) among kidney transplant candidates to identify opportunities for improving education and care.

Methods: A single-center survey was conducted from March to September 2024. An anonymous 10-question survey assessed demographics, LKD awareness, willingness to accept kidneys from family or altruistic donors, and reasons for reluctance. A total of 89 transplant candidates referred in for transplant assessment responded.

Results: Among the candidates surveyed, 51% were from an ethnically diverse population. Overall, 87% were aware of LKD, with awareness higher among younger recipients (100% for ages 18–29) and White participants (100%) compared to older recipients (84% for ages 65+) and Asian/Asian British participants (60.9%). Reluctance to seek family donations was common, particularly among Asians (63.6%) and those aged 50–64 (46.7%), with concerns about burdening family and cultural beliefs being key factors. While 85% were willing to accept kidneys from altruistic donors, acceptance rates for children's or partner's kidneys were notably lower, especially among Asian participants (15% and 26.1%, respectively).

Conclusions: The findings reveal significant ethnic and cultural disparities in LKD awareness and willingness. Tailored education, culturally sensitive communication, and peer-support programs are critical to addressing these barriers and promoting equitable access to live donor kidney transplantation.

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EP_306 LIVER TRANSPLANTATION FROM VERY OLD DCD DONORS: A SINGLE-CENTRE EXPERIENCE

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Background: Donation after circulatory death (DCD) has expanded the pool of organs for liver transplantation (LT). Following positive outcomes from selected cases, there is growing interest in expanding the use of marginal DCD donors, particularly those of advanced age.

Methods: We report our experience with DCD-LT from donors over 75 years, comparing results with those from donors under 75 years during the same period.

Results: From November 2021 to September 2024, our center performed 35 DCD-LTs: 9 from donors over 75 years and 26 from donors under 75 years. The two groups were similar in terms of age, BMI, and cirrhosis severity (median age: 63 vs. 61 years, p = 0.46; BMI: 23.2 vs. 24.8, p = 0.27; MELD Na: 17 vs. 17, p = 0.86). All DCD cases used regional normothermic perfusion (NRP), and ex situ machine perfusion (MP) was used in 5/9 (56%) of DCD >75 and 15/26 (58%) of DCD <75. Functional warm ischemia time was similar (37 vs. 38 minutes), while cold ischemia time was longer in the <75 group (252 vs. 164 minutes, p = 0.42). One case of primary non-function occurred in the DCD <75 group. Early allograft dysfunction rates were similar (22.2% vs. 23.1%). The DCD <75 group had a higher peak ALT (699 vs. 436 U/L, p = 0.08) and a higher rate of acute kidney injury (34.6% vs. 11.1%, p = 0.23). With a median follow-up of 12 months (range 3–25 and 0–43 months), biliary stricture rates were 11% vs. 23% (p = 0.42).

Conclusions: Our initial experience suggests that liver transplantation from elderly DCD donors (>75 years) yields acceptable results and is not inferior to standard DCD donors when appropriate patient selection and modern preservation technologies are used.

EP_307 NO LIMIT FOR DCD DONOR AGE IS POSSIBLE

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Background: Liver Transplantation (LT) represents the treatment of choice in various liver disease, the increasing use of grafts harvested from extended criteria donor (ECD) and donors after circulatory death has the goal to reduce the gap between donors and recipients. However, the use of DCD grafts is usually limited to recipients with low MELD score and/or absence of technically complex surgical procedure to reduce the risk of graft dysfunction.

Methods: Herein we report the first case of LT performed using graft harvested from an 86 years-old DCD donor in a patient with symptomatic polycystic liver disease (PLD). Liver retrieval was performed according to standard technique, NRP lasted 208 minutes, arterial lactates were 11.9 mEq/L at the beginning of NRP and decreased to 5.7. AST and ALT remained stable within normal values during all the procedure. NRP flow remained stable between 2.5-3 L/min during all procedure. Liver biopsy revealed microsteatosis 5%, macrosteatosis 5%, liver fibrosis F1 and absence of necrosis. LT was performed using veno-venous bypass associated to portal cannulation, as a standard procedure in our center in patients with PLD, to avoid hemodynamic instability during liver mobilization and reduce splanchnic congestion. In our case, due to adhesion related to previous cystic infection, liver was not detachable from inferior vena cava and for this reason inferior vena cava replacement was performed. Arterial and portal anastomosis were performed in a standard fashion while biliary continuity was restored with an hepatico-jejunostomy due to discrepancy between the two bile ducts. Cold Ischemia Time (CIT) was 255 minutes of which 165 minutes of Hypothermic Oxygenated Perfusion.

Results: Post-operative course was marked by acute cellular rejection treated with steroids and bowel occlusion treated by emergency laparotomy. Patient is currently alive with normal graft function one year after liver transplantation.

Conclusions: It seems that the use of elderly DCD donor could provide acceptable results in LT.

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EP_308 IMPACT OF ECMO FOLLOWING CARDIAC ARREST ON ORGAN DONATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Organ donation following cardiac arrest (CA) increasingly contributes to the donor pool. Extracorporeal membrane oxygenation (ECMO) is used in CA for cardiopulmonary resuscitation (ECPR), as well as for in situ organ preservation in donation after circulatory death (DCD). In the present study, we performed a systematic review and meta-analysis to assess the impact of ECMO use following CA on organ donation.

Methods: We searched three electronic databases (PubMed, Scopus, and Web of Science) and included single-arm and comparative studies (comparing ECMO with other in situ organ preservation techniques). The organ use rate was calculated and the quality of the included studies was assessed.

Results: We included 64 primary observational studies (16 comparative). The number of included studies increased over time. The most common clinical scenario was controlled DCD (n=42), followed by uncontrolled DCD (n=23), and ECPR (n=7). Multiorgan donation occurred in 86% ECPR, 43% controlled DCD, and 21% uncontrolled DCD. A non-statistically significant higher organ use rate was observed with ECMO when compared with other in situ preservation techniques [RR 1.11 (95% CI, 0.99-1.26)]. The overall quality was 'good' in 44, 'fair' in 1, and 'poor' in 19 studies.

Conclusions: The use of ECMO in organ donation following CA is increasing, being more frequently described in controlled DCD than in uncontrolled DCD. ECPR is an emerging group that most frequently results in multiorgan donation. More studies are needed to confirm the increase in the donor pool and the organ use rate promoted by the utilization of ECMO following CA.

EP_309 IMPACT OF NORMOTHERMIC MACHINE PERFUSION IN DECEASED DONOR LIVER TRANSPLANT FOR HEPATOCELLULAR CARCINOMA

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Background: Normothermic and hypothermic oxygenated machine perfusion (NMP and HOPE) are used to reduce the deleterious effects of ischaemia-reperfusion injury (IRI) in liver transplantation. Their ability to modulate the IRI is believed to have a favourable impact on recurrence of hepatocellular carcinoma (HCC). Oncological implications of normothermic perfusion are not well investigated. This retrospective study looked at any impact the normothermic machine perfusion may have on the oncological outcomes of patients transplanted for HCC.

Methods: This is a retrospective review of patients who underwent liver transplantation for known HCC between January 2015 to December 2022 at Addenbrookes Hospital, Cambridge. Incidental HCC, concomitant cholangiocarcinoma, redo, and multi organ transplants were excluded. The cohort was divided into two groups for outcome comparison: livers with static cold storage (SCS) and NMP. Primary outcome of the study was 2-year disease free survival. We also looked at the vascular and biliary complications, 30-day re-exploration rate, clinically significant rejection and 2-year graft survival.

Results: Total 110 patients were eligible for the analysis, 45 donations after brain dead (DBD) and 65 donations after circulatory death (DCD). Forty-five liver grafts (41%) underwent NMP with median perfusion duration of 478 minutes (IQR 412-556). The median waiting time for liver transplant was 163 days (IQR 69-335) and 78% recipients received bridging therapy. There were two cases (3%) of recurrence within first two years in the SCS group (one hepatic only, one with both hepatic and extra hepatic) and four recurrences (9%) in NMP group (two graft recurrences, and all had extrahepatic disease). This was not statistically different (p=0.224). The SCS and NMP group did not significantly differ in the secondary outcome measures with equivalent one-year (95 and 97%) and two-year (87% and 91%) graft survival rate, respectively (table 1).

Conclusions: Within the limits of small sample size and short follow up time, normothermic machine perfusion did not seem to have any oncological implications on deceased donor liver transplantation.

Table 1

Parameters	SCS (n=65)	NMP (n=45)	p-value
DCD (%)	42 (64%)	23 (51%)	0.15
UKELD	51 (48-54)	51 (48.5-53)	0.88
AFP before transplant (kU/l)	5 (4-15.5)	5.5 (4-11)	0.74
NMP duration, min	-	478 (412-556)	NA
Preop HCC characteristic			
Number of L4/5 lesions	1 (range 0-5, IQR 0)	1 (range 0-5,IQR 1)	0.28
Size of largest lesion (mm)	24 (15-30)	22 (17-29)	0.88
Explant histopathology			
Number of lesions	2 (1-3)	3 (1-4)	0.13
Size of largest lesion (mm)	27 (20-35)	25 (18-30)	0.09
Biopsy proven rejection (%)	15 (23)	13 (28.8)	0.59
Biliary complications (%)	9 (13.8)	5 (11)	0.67
NAS (%)	10 (17.8)	7 (15)	0.98
Re-exploration, 30-day (%)	18 (27.7)	9 (20)	0.35
Hospital Stay- days	15 (12-23.5)	14 (11.5-23.5)	0.59

Values are medians (interquartile range) or number (percentage)

UKELD- United Kingdom end stage liver disease; Alpha-fetoprotein (AFP); NAS (Non-anastomotic biliary stricture (NAS)

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EP_310 ABO INCOMPATIBLE DUAL GRAFT LIVING DONOR LIVER TRANSPLANTATION USING MODIFIED EXTENDED LEFT LATERAL GRAFT

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Background: Liver transplantation is a life-saving procedure for patients with end-stage liver disease, but the availability of suitable donor grafts remains a significant challenge. Innovative surgical techniques are essential to expand donor options while maintaining favorable outcomes for both donors and recipients.

Methods: A 54-year-old male with hepatitis B-related cirrhosis underwent an ABO-incompatible dual graft liver transplantation. The procedure included a modified right lobe graft from one donor and a modified extended left lateral graft from another donor, employing a novel surgical technique in which the middle hepatic vein (MHV) was excluded from the donor grafts to minimize donor morbidity. In the recipient, MHV reconstruction was performed using an allograft (donor-derived vein) to ensure optimal venous outflow and graft function. This approach was designed to prioritize donor safety while achieving an adequate graft-to-recipient weight ratio (GRWR). Post-operative management involved plasma exchange and immunosuppressive therapy to prevent rejection and minimize complications.

Results: The dual graft transplantation achieved a GRWR of 1.27, ensuring sufficient graft volume for the recipient. Post-operative recovery was uneventful, with no significant complications. The recipient demonstrated normalized liver function within weeks, and both donors recovered fully without long-term sequelae.

Conclusions: This case demonstrates the effectiveness of a modified dual graft technique in addressing the challenges of limited graft availability while ensuring a sufficient graft-to-recipient weight ratio (GRWR). By prioritizing donor safety and optimizing recipient outcomes, this method offers a promising strategy for managing high-risk liver transplant cases. It also highlights the potential for expanding donor options and improving the applicability of dual graft techniques in complex clinical scenarios.

EP_311 EFFECT OF AGE, BMI AND GENDER ON OUTCOMES FOLLOWING LIVING DONOR NEPHRECTOMY; A SINGLE CENTRE STUDY

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Background: The average age and body habitus of living kidney donors is increasing. Current literature on long-term outcomes for donors with such demographics is limited. The primary aim of this study was to assess the effect of age, BMI and gender on post-operative outcomes following living donor nephrectomy (LDN).

Methods: Pre and post-operative data were retrieved from all patients who underwent LDN at a single UK institution between 2014 and 2024.

Results: Over a 10-year period, 339 patients underwent LDN, of which complete data was available for 314 patients: 63 right (20.1%), 251 left (79.9%); median age 49-years (range 23 -77); 136 (43.3%) males; and median BMI 26.8 (range 18.5-32.8). 33 (10.5%) had controlled hypertension (HTN) pre-donation. Median FU was 63 months (range 10-131). There was 1 conversion to open procedure, 27 (9%) developed surgical site infections, 49 (16%) UTI, 26 (8%) an ileus and 13 (4%) hernias. Mean eGFR (+/-SD) pre-donation was 89.5 (+/-12.9) ml/min. This declined to 54.6 (+/-10.0) at 1-2 days post-op, and recovered to 57.7 (+/-11.1), 58.8 (+/-10.8) and 61.5 (+/-11.1) ml/min at 3-months, 1-year and 5-years post-donation respectively. When analyzed using a generalized linear mixed-effects model, eGFR steadily increased by 0.76 ml/min/1.73 m^2 per year (CI 0.59 to 0.93, p<0.0001) over 7 years of follow up. When analyzed for age, gender, BMI, pre-donation HTN, starting eGFR, initial eGFR reduction and nephrectomy side, the rate of functional recovery was significantly reduced for donors >65y, those with a starting eGFR <70ml/min and those with an initial eGFR drop >40ml/min. 42 (13.4%) patients developed new or increasing requirements for existing HTN, and 11 (3.5%) developed proteinuria. Using multiple cox regression analyses, increasing age was associated with an increased risk of developing new/worsening HTN, and a pre-operative eGFR <70ml/min was associated with an increased risk of developing proteinuria.

Conclusions: Living donor nephrectomy results in an initial eGFR decline followed by a 7-year recovery period. Increasing age is associated with HTN and a slower recovery in renal function. Lower pre-operative eGFR is also associated with a slower recovery and a greater risk of developing proteinuria. This study warrants further research to continue to ensure donor safety.

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EP_312 AVOIDING LIVER GRAFT RECOOLING AFTER NORMOTHERMIC MACHINE PERFUSION: THE FIRST WORLDWIDE EXPERIENCE

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Background: Normothermic machine perfusion (NMP) of the liver represents a widely used alternative method of preservation and graft function assessment in liver transplantation (LT). Cooling the organ slows metabolic activity but cooling and rewarming can induce cellular stress, similar to ischemia-reperfusion injury.

Methods: The study aims to show the safety of not cooling the graft at the end of NMP. A secondary aim is to demonstrate that avoiding graft cooling leads to better post-LT outcomes, including evaluating graft and patient survival. This is a retrospective analysis of all 37 LT consecutively performed in our center after NMP over a period from September 2018 to April 2024. For the first 15 cases of the series (group A), once disconnected from the NMP, the liver underwent re-cooling with 1 liter of perfusion fluid (Ringer's lactate) at 4 °C after NMP, while in the subsequent 22 cases (group B), the graft was directly implanted.

Results: Recipients' median MELD score was 22 (IQR: 15-24) for Group A, and 14 (IQR: 8-20) for Group B (p=0.03). No other statistically significant difference was found among the recipients' characteristics. Donors (12 DCD and 25 DBD) had a mean age of 64 years (IQR: 53-74), without statistically significant differences between the two groups. One case of graft primary nonfunction (7%) group A, and 23 patients experienced early allograft dysfunction, of whom 10 (67%) in group A and 13 in group B (59%, p=0.74). The two groups were homogeneous in terms of all the other post-LT variables analyzed. A non-significant difference (22% vs. 18%, p=0.65) was observed in terms of postoperative biliary complications; no cases of ischemic colangiopathy were observed.

Conclusions: Our findings suggest that the approach of not recooling the liver graft after NMP seems to be safe. This may be due to the protective effect on the graft cells from the second thermal shock. However, the study is limited by a small sample size, needing to expand the population and probably also to perform prospective randomized trials to confirm our findings.

EP_313 SHORT STORAGE AND WASHING OF ERYTHROCYTES ENHANCE LIVER FUNCTION IN NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) extends liver preservation time and assesses graft viability for transplantation. Red blood cells (RBCs) are integral to the perfusate, enabling gas exchange essential for metabolism. Storage lesions in RBCs impair oxygen kinetics, energy reserves, osmoregulation, and waste removal. Washing RBCs enhances their morphology and removes waste, offering a standardized starting point for NMP. This study investigates the effects of RBC storage duration and washing on liver functionality during viability assessment in NMP.

Methods: Between November 2020 and November 2023, 37 liver NMPs were analyzed. Perfusions used young RBCs (n=10, storage duration 11–21 days), old RBCs (n=17, storage duration 22–31 days), and washed RBCs (n=10, storage duration 12–31 days). Primary outcomes included functionality in viability assessment criteria: perfusate (glucose, lactate, pH), bile (pH), and differences (delta) between perfusate and bile (glucose, bicarbonate, pH).

Results: In starting perfusate, washed RBCs exhibited higher pH (p=0.043), and lower lactate (p=0.003) and glucose (p<0.001). After commencing perfusion, perfusate lactate was higher with old RBCs (fig 1A, p<0.001). Washed RBCs reduced bile (p<0.001) and perfusate (p=0.009) glucose during NMP, though delta glucose remained unchanged (fig 1B, p=0.164). Young RBCs yielded higher delta pH compared to old (fig 1C, p<0.001) and washed RBCs (p=0.004), and higher delta bicarbonate compared to old RBCs (fig 1D, p<0.001). Utilization rates were 90%, 70.6%, and 90% for young, old, and washed RBCs (p=0.323), with similar post-transplant outcomes, including graft survival and patient survival.

Conclusions: Young and washed RBCs perform better in viability assessment criteria compared to old RBCs. Washed RBCs improved perfusate conditions but did not surpass young RBCs in overall viability assessment. RBC quality is critical in NMP and may influence transplantation decisions.

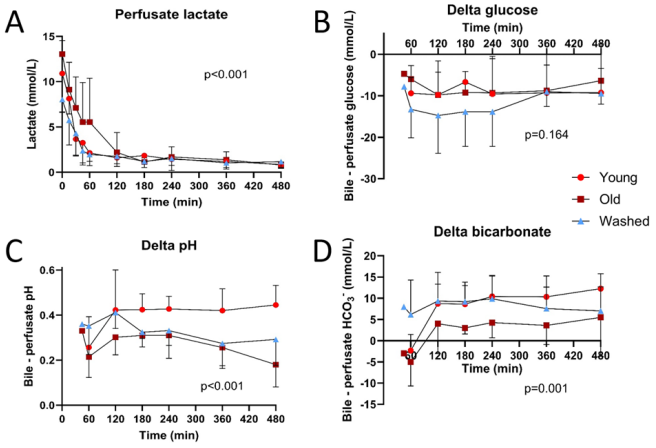

Figure 1: Viability assessment criteria during normothermic machine perfusion of the liver, comparing young, old and washed red blood cells.

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EP_314 PROFESSIONALIZING THE ORGAN PERFUSIONIST; THE NEW EDUCATIONAL PROGRAM FOR ORGAN PERFUSINISTS

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Background: Organ perfusion between donation and transplantation—to improve organ quality, test viability, or prolong preservation for logistical reasons—has become indispensable in the field of organ transplantation. The role of the organ perfusionist has evolved significantly, especially with rapid developments in machine perfusion that revealed the need for a new professional: the organ perfusionist (OP). OPs are integral to organ perfusion and normothermic regional perfusions (NRP), and oversee all logistical aspects related from donation to transplantation. This integration enhances coordination and efficiency within the transplantation process.

Methods: To accommodate the education for this profession, the first international training course for organ perfusionists is established in Groningen, The Netherlands. This educational program covers liver-, lung-, kidney- and heart perfusion as well as NRP. Since 2022, 42 organ perfusionists have successfully completed the program.

Results: Last year, the educational program was redesigned, and the education is now based on the transplantation chain, covering everything of relevance for the OP. Additionally, we have examined from an educational perspective how to prepare students for their professional practice by stimulating critical thinking skills and actively involving them in the processing of theory. We have implemented a flipped classroom approach, where students acquire the theory through self-study before class, while the teaching sessions are used for interaction and practical application, thereby enhancing the transfer of theory to practice. Overall, the program takes 10 months, and involves 11 (online) course days, exercises, and two skills weeks at the University Medical Center Groningen, The Netherlands.

Conclusions: By the end of the program, graduates are equipped with knowledge about organ donation, organ anatomy, perfusion strategy, perfusion circuit, abnormalities and canula dynamics, backtable training, in vivo and ex vivo organ function, perfusion parameters, viability testing and decision making, troubleshooting, perfusion report and transplantation.

EP_315 LONG-TERM SURVIVAL AFTER LIVING DONOR LIVER TRANSPLANT WITH HEMASHIELD GRAFTS FOR MIDDLE HEPATIC VEIN RECONSTRUCTION

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Background: Due to the limited availability of homologous vein allografts, prosthetic vascular grafts, such as Hemashield grafts, are used for middle hepatic vein (MHV) reconstruction in living donor liver transplantation (LDLT). MHV reconstruction is critical for maintaining adequate venous outflow in the graft, which directly influences graft survival and patient outcomes. This study aimed to evaluate the long-term outcomes and patency rates of Hemashield grafts.

Methods: This retrospective, single-arm study analyzed patients who underwent adult LDLT at Asan Medical Center between January 2018 and December 2019, focusing on those who received Hemashield grafts. The primary endpoints were the patency of the Hemashield grafts and patient survival.

Results: Among 755 adult LDLT recipients, 147 underwent MHV reconstruction using Hemashield grafts. The mean recipient age was 56.5 ± 7.6 years; the mean Model for End-stage Liver Disease (MELD) score was 15.2 ± 8.6; and the graft-recipient weight ratio was 1.16 ± 0.26. Two patients (1.4%) required MHV conduit stenting due to early thrombosis of the Hemashield graft. The 3-month, 1-year, and 3-year patency rates of the Hemashield grafts were 79.9%, 54.4%, and 40.9%, respectively. The survival rates for the patent group were 96.3%, 89.1%, and 83.6%, while the occluded group had survival rates of 93.1%, 82.3%, and 78%. The log-rank test p-value was 0.306, indicating that patency did not significantly affect survival.

Conclusions: Hemashield grafts used for MHV reconstruction demonstrate high short- and long-term patency rates, resulting in favorable survival outcomes. Therefore, Hemashield grafts can be considered a preferred prosthetic material for MHV reconstruction in LDLT.

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EP_316 KIDNEY DENERVATION PRIOR TO BRAIN DEATH DOES NOT PREVENT BRAIN DEATH-INDUCED KIDNEY INJURY

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Background: Brain death (BD) negatively impacts transplant outcomes. Still, the pathophysiology of kidney damage caused by BD is poorly understood, especially concerning the contribution of the sympathetic nervous system. We aim at investigating whether renal denervation (DNRV) performed prior to BD induction attenuates kidney injury.

Methods: Renal denervation (DNRV) was performed on the left kidney of rats using a method adapted from Eriguchi and Tsuruya. This procedure involved the dissection of renal nerve fibers and the application of 10% phenol in ethanol to the renal artery. BD was induced via intracranial pressure elevation using a Fogarty catheter. BD was confirmed by the absence of pupillary reflexes, a positive apnea test, and a Cushing reflex. Kidney norepinephrine (NE) levels, tubular damage (extent of acute tubular necrosis - ATN), and kidney injury biomarkers (Casp3, Ki67, KIM1) were compared to the paired contralateral non-denervated kidney (CTL). Additionally, kidney samples were subjected to high-throughput RNA sequencing (Illumina®). Paired differential expression analysis followed by pathway enrichment analysis were performed using DESeq2 in R and IPA (Qiagen®), respectively.

Results: Renal denervation effectively reduced kidney NE levels 6h *post* BD (DNRV: 1.64 pg/mL [1.44–2.01] vs. CTL: 2.16 pg/mL [1.81–2.79], p = 0.0312, confirming the suppression of sympathetic input. No significant differences were observed in ATN extent (DNRV: 50% [25–55] vs. CTL: 60% [45–70], p = 0.13), serum creatinine increase (DNRV: +0.040 ± 0.011 mg/dL/h vs. CTL: 0.053 ± 0.022 mg/dL/h, p = 0.13), or expression of injury biomarkers. RNA sequencing data detected no significant differences between DNRV and CTL kidneys.

Conclusions: Although renal denervation effectively reduced the sympathetic input, it did not prevent BD-induced kidney injury in our rat model. These findings suggest that neurogenic mechanisms play a limited role in BD-associated kidney damage.

EP_317 THE VALUE OF ANONYMOUS CONTACT - GRATITUDE LETTERS

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Background: In 2021 an improvement plan was established to achieve national publicity and uniformity. It implied that anonymous contact between family and recipients could be established via the organ donation coordinator (ODC). The impetus for the improvement plan came from various media. Those media covered situations in which the relatives of post-mortem donors were surprised, disappointed and sometimes even agitated that they had received little or no notice from the recipients of the deceased donor's organs[1]. The experience of ODC's in the Netherlands shows that receiving a letter from organ recipients is perceived positively by the relatives. This usually appears to provide comfort during a period of mourning and to be helpful in processing grief and loss. The improvement plan can prevent negative publicity about organ donation and thus indirectly have a positive effect on registrations in the Dutch Donor Register.

Methods: A pilot project at Radboud University Medical Center in 2020 showed a doubling of letters by kidney recipients; by properly informing the recipient, discussing the possibility of writing a letter, and offering support in writing.

Results: This above led to an interactive presentation at the Dutch Congress of the NTV in March 2021, where "the importance of anonymous contact" was discussed. That kicked off the improvement plan to implement above mentioned actions as starting points in every Dutch transplant hospital. After the launch in 2021, a number of UMCs have seen an increase in the number of gratitude letters received. Nationwide, you see a total number of letters in 2022 of 121, in 2023 of 156 and 2024 of 176 gratitude letters.

Conclusions: The increase in letters in most of the transplant hospitals varies per donated organ and per hospital. However, the absolute numbers are not a goal; it is about the contribution of writing or receiving a letter in the mourning process. Receiving an organ from a deceased donor and losing a loved one are both profound life events. Both writing and receiving a gratitude letter contribute to coping with this.

1. Volkskrant 26-4 2019, RTL nieuws 11-12 2017, AD 2-2-2019

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EP_318 TRANSFORMING TRANSPLANTATION: DRONE DESIGNS AND THEIR POTENTIAL APPLICATIONS

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Background: Drones offer a promising solution to logistical challenges in organ transplantation, where minimising cold ischaemia time is critical. By reducing transport times and carbon emissions, drones could transform transplant logistics. This review examines drone designs and their use in organ transport, emphasising potential advancements like AI-assisted navigation and portable machine perfusion systems.

Methods: A systematic review of literature was conducted from January 2015 to December 2024, identifying studies on drone use and designs in organ transport across human and animal trials.

Results: Three studies highlighted the feasibility of drones for organ transport: • Kidney Transport (Scalea et al., 2021): A human kidney was transported 2.8 miles, maintaining integrity and reducing cold ischaemia time. • Lung Transport Simulation (Sage et al., 2022): Drone-based lung transport demonstrated viability under urban conditions. • Rat Liver Transport (Enjoji et al., 2023): An experimental study preserved liver viability post-transport. Two potential drone designs emerged as optimal for specific scenarios:Potential Future Advancements: • **AI-Assisted Navigation:** Could optimise routes, monitor environmental factors, and adapt to obstacles in real time. • **Machine Perfusion Integration:** Heavy duty drones (payload capacity >30kg) could be used to extends cold ischaemia time for hearts (4–6 hours) and livers (6–8 hours), enhancing transport outcomes. Lighter organs like kidneys, with longer cold ischemia times (8–12 hours), may benefit less.

Conclusions: Drones represent a transformative advancement in organ transport, offering faster, more efficient, and potentially sustainable solutions. Combining drones with portable machine perfusion systems could improve outcomes for organs with shorter cold ischemia times whilst reducing waste and carbon emissions. Scaling eco-friendly drone operations and overcoming regulatory challenges are critical to achieving widespread adoption, aligning this innovation with global healthcare sustainability goals.

Feature	Hexacopter	Octocopter
Design	Lightweight, agile; compact structure	Heavy-duty, stable; reinforced for larger payloads
Best Use	Urban transport; short distances	Long-range inter-city/regional flights
Payload Capacity	5kg - 10kg, suitable for light organs (e.g., kidneys, lungs)	10kg - 20kg - suitable for heavy organs (e.g., livers, hearts)
Energy Source	Electric	Hybrid (electric + gas)
Sustainability Features	Lower energy usage, reduced carbon footprint	Higher energy efficiency for long-range transport
Advantages	Lower cost, agile in urban environments	Robust, efficient for long distances
Limitations	Restricted range, weather-sensitive	More expensive, less agile

EP_319 PROGNOSIS OF THE KIDNEY TRANSPLANT PATIENT: THE ROLE OF "TRADITIONAL" RISK

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Background: Kidney transplant is the therapeutic option of choice in patients with kidney failure. Currently, the number of kidney transplants performed per year is constantly growing in Italy. However, the risk stratification of transplant patients remains an important research question because renal prognosis (risk of graft failure, GF) is still suboptimal, particularly in those who have been transplanted for many years. Furthermore, while the prognostic role of immunological risk factors is well defined, that of the traditional risk factors of chronic kidney disease (CKD) i.e. anemia, hypertension, proteinuria, mineral-bone disease, hyperkalemia, previous cardiovascular event (CVD) and smoking is still little studied.

Methods: We designed an observational cohort study, enrolling patients undergoing kidney transplant, followed in 6 Nephrology Centers in Italy. The baseline visit of the patients was collected 12 (±2) months after the intervention, i.e. after achieving a stable clinical and biohumoral picture. Demographic and clinical information was collected at the baseline visit. Follow-up continued until the onset of GF. The risk categories were created according to the KDIGO-2024 guidelines. GF incidence rates were calculated by the Poisson method. The adjusted risk of GF was calculated by Cox regression.

Results: Overall we studied 757 transplant patients, with an average age of 45.9 ± 11.3 years and 66.5% male. Stage distribution was: 54.5% G1-2, 21% G3a, 18.6% G3b, 5.8% G4. The incidence rate of GF, in a mean follow-up of 6.4±3.6 years, was significantly higher in the presence of anemia (risk ratio, rr 1.9, p=0.0002), hypertension (rr 1.8 p=0.0018), proteinuria (rr 1.7, p=0.006), hyperphosphatemia (rr 2.0 p=0.048), smoking (rr 2.0, p=0.034). Cox multivariate analysis showed that, proteinuria (HR 1.42, 95%CI 1.14-1.78), anemia (HR 1.46, 95%CI 1.0-2.12), CVD (HR 1.66 95%CI 1.10-2.50) and smoking (HR 2.26, 95%CI 1.16-4.41) were significantly associated with GF.

Conclusions: Risk factors for CKD progression also play a significant role in kidney transplant patients. Such evidence is essential for the management of the transplanted patient during nephrological follow-up.

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EP_320 SECONDARY LIVER PERFUSION: A "STRESS TEST" MODEL TO INVESTIGATE ORGANS FAILING CLINICAL PERFUSION

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Background: The donor liver shortage has created an urgent need to utilize higher-risk grafts for transplantation. Normothermic machine perfusion (NMP) enables *ex vivo* graft assessment before usage and could safely expand access. Still, it remains unclear which NMP performance metrics predict an organ's inability to withstand reperfusion injury in a recipient. Proposed metrics like lactate clearance often fail to differentiate dysfunctional grafts. The question remains: are we discarding organs rightly? Our aim was to investigate viability criteria by reanimating Liver X, declined for transplantation after NMP.

Methods: Liver X was procured from a 40-year-old, brain death donor. The liver was transported on ice with 6 hours of cold ischemic time (CIT) before undergoing 12 hours of NMP. Due to its performance during NMP, the liver was declined for transplant. We sought to model how Liver X would have performed *in vivo* to determine whether perfusion parameters rightly guided its discard. We implemented another round of cold ischemia and reanimation, termed secondary perfusion. Liver X was subjected to 1.5 hours of CIT and 7.5 hours of NMP. Evaluation metrics were consistent with those of primary NMP.

Results: *In situ*, the liver showed homogenous coloration (Fig. 1A), though steatosis was found on biopsy (Fig. 1B-C). During primary NMP, Liver X showed low arterial flows, persistent acidosis, and no glucose utilization (Fig. 1D-F). During secondary NMP, flows remained low, acidosis worsened, and lactate clearance was impaired (Fig. 1G-I). Metabolic deficits during primary perfusion were aggravated by the secondary stress of our model.

Conclusions: Results indicate that Liver X would have posed risk for nonfunction in a recipient. Determining markers that accurately identify such grafts during perfusions with conflicting results is critical. We propose that livers declined after NMP undergo "stress testing." Organs failing this secondary perfusion would confirm unsuitability and help validate existing NMP criteria. Any recovering functionality would provide insight into refining parameters to reduce unnecessary graft discard. This model could enable multi-center studies to define donor liver risk profiles alongside perfusion criteria, offering data from marginal organs excluded from current research.

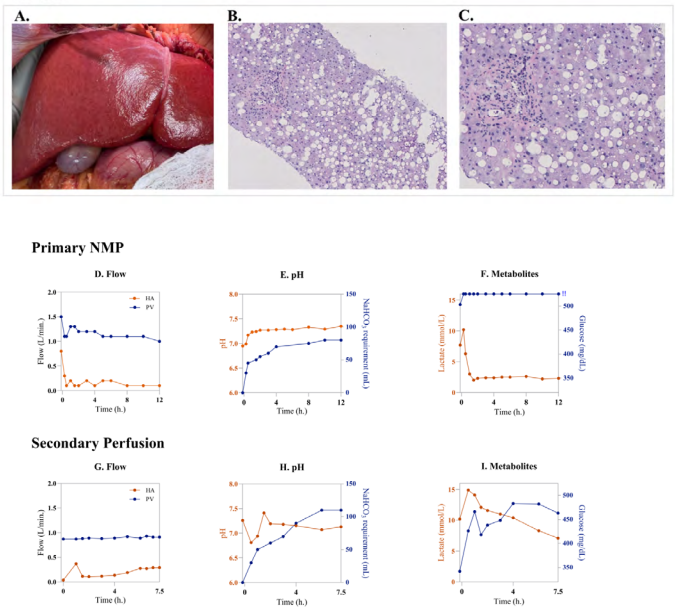

Figure 1: Assessment of the liver. **A:** Gross imaging of the liver *in situ* at donor hospital. **B, C:** Histological imaging of the liver from an *in situ* biopsy at donor hospital, stained with hematoxylin & eosin and imaged at 10x and 20x, respectively. **D, G:** Hepatic artery (HA) and portal vein (PV) flow rates of the liver during NMP. **E, H:** Perfusate pH and total 5% sodium bicarbonate (NaHCO3) requirement of the liver during NMP. **F, I:** Perfusate lactate and glucose levels during NMP. **!!:** Glucose levels exceed measurable range (>525 mg/dL). Created with GraphPad Prism 10.3.1.

EP_322 IMPLEMENTATION OF KIDNEY FUNCTION MEASUREMENT USING IOHEXOL PLASMA CLEARANCE TO IDENTIFY POTENTIAL LIVING KIDNEY DONORS

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Background: When identifying potential living kidney donors, precise kidney function measurements are necessary. Estimation using a creatinine-based formula is very error-prone. One possibility for measuring GFR (mGFR) is to use plasma-iohexol-clearance. Based on kidney function, a decision can be made as to whether living donation is possible or not. As a rule, a living donation is rarely carried out for a patient at less than 75 ml/min per 1.73 m2. In our living donation program between 2014 and 2019, we systematically established mGFR using plasma-iohexol-clearance.

Methods: All patients were given 5 ml of iohexol (Accupaque 350). After 3h, 4h, and 5h, blood samples were taken from the patients and the iohexol concentrations in the blood samples were determined in the central laboratory (mGFR). Based on the elimination kinetics of iohexol, kidney function (mGFR) was then determined precisely.

Results: Evaluation for kidney donation was performed in 46 patients. 24 patients had an $eGFR_{CKDEpi}$: > 90 ml/min/1.73m^2. This was confirmed with mGFR in 23 cases. One patient had a kidney function of 78 ml/min/1.73m^2. This potential donor (female, 54 kg, 165 cm) was not further prepared for a kidney transplant because there was a too great difference in relation to the recipient (male, 79 kg, 177 cm). 16 patients had an eGFR of ≥75-89 ml/min/1.73m^2. An mGFR function of >90ml/min/1.73m^2 was identified in 8 of these patients. 3 potential donors had an mGFR of ≥60-74 ml/min/1.73m^2, although only one was considered as a donor because the mismatch of age/sex/body size was minimal. 5 patients had an mGFR of ≥75-90 ml/min/1.73m^2. One donation could not be made due to a large age/weight mismatch. 6 patients had renal function in the range ≥ ml/min/1.73m^2. Two patients had kidney function ≥75-90 ml/min/1.73m^2 and were eligible for donation. The other patients were no eligbile. All living kidney donations (46) were successful

Conclusions: Accurate kidney function measurement for living kidney donors is essential in order to limit the potential risks for donors to a minimum. The kidney function measurement, which has a significantly higher precision, enables the identification of patients who are suitable for a potential living donation. Iohexol clearance measurement is a simple method that can be carried out in a centralized manner.

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EP_323 BARRIERS AND FACILITATORS TOWARD DECEASED ORGAN DONATION AMONG MUSLIMS IN QATAR

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Background: Since the first organ donation in Qatar in 1986, over 25% of the total adult population has pledged to donate organs after death. However, Qatar's diverse, predominantly Muslim population presents challenges, as evidence shows Muslims are less likely to donate. Therefore, this study examined barriers and facilitators to deceased organ donation among Arab and non-Arab Muslims in Qatar.

Methods: A qualitative approach was undertaken guided by the social constructivist worldview and used comparative purposive sampling. The study included Qataris and Egyptians as Arab-Muslims and Pakistanis and Bangladeshis as non-Arab-Muslims in Qatar. Transcripts were coded both inductively and deductively using framework analysis in NVivo v.20.

Results: Following the analysis, five overarching themes have been identified that influences the collective nature of the decision toward deceased organ donation which encompasses: 1) individual, 2) family, 3) religion, 4) community and 5) healthcare system, with religion and family playing key roles. The varying schools of thoughts among the religious leaders played an important role in the decision-making which hindered family discussions and decisions to register or consent. However, the participants had a very positive view and trust toward the healthcare system in Qatar. Often the expatriate population compared what was happening back in their home country related to inequity and mistrust in organ donation which negatively influenced their decision-making.

Conclusions: In collectivist societies, strategies and policies should adopt a whole-system approach, addressing religion, culture, family, and trust in the healthcare system. This requires intervention at various societal levels to ensure inclusivity and relevance. Although extensive, such an approach would lead to more effective outcomes if guided by robust, diverse research and evidence.

EP_324 INFLUENCE OF FAMILY DYNAMICS IN CONSENT TOWARD DECEASED ORGAN DONATION IN TWO DIVERSE REGIONS WITHIN INDIA

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Background: In India's deceased organ donation system, where families have the final say on the deceased's wishes, the influence of family dynamics and communication has been underexplored. This study examines the influence of families in deceased organ donation decisions, based on the perspectives of transplant coordinators from two regions in India.

Methods: A qualitative study was conducted with fourteen transplant coordinators from northern and southern India, and the data were analysed using framework analysis in NVivo v20.

Results: In India, decisions regarding deceased organ donation are often collective, involving not only the immediate family, who hold legal authority, but also extended family and friends. In such a context, families frequently tend to "veto" the deceased's organ donation decision due to the absence of prior conversations, conformity-oriented communication, and inconsistent hospital family approaches. Such collective decision-making posed challenges for transplant coordinators, who must navigate complex family dynamics. Early involvement of coordinators has proven beneficial, enabling them to identify key decision-makers, provide grief counselling, and improve understanding of organ donation. However, approaches varied across centres; some offered supportive environments with private rooms for discussions, emotional support, and collaboration from medical and management teams, which facilitated the donation process.

Conclusions: To achieve self-sufficiency in deceased organ donation within each country, it is crucial to learn from nations with higher consent rates. However, equally important is identifying the factors that enable certain centres to effectively support families in making informed decisions. Additionally, standardising culturally competent practices plays a key role in this process which could potentially reduce the refusal rates and thereby enable self-sufficiency.

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EP_325 IMPACT OF TRIIODOTHYRONINE (T3) ON CELLULAR ENERGETIC STRESS AND MITOCHONDRIAL DYSFUNCTION IN A RAT DCD MODEL OF EVLP

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Background: Ischemia/reperfusion injury (IRI) remains a critical challenge in lung transplantation, significantly contributing to PGDand CLAD. Cellular energetic stress and mitochondrial dysfunction are key drivers of ischemic injury exacerbation. Given their anti-oxidative and metabolic effects,thyroid hormones have the potential toreduce IRI-dependent mitochondrial failure.

Methods: An established rat model of EVLP was used. After procurement, lungs were either immediately perfused for 3h (n=10) or exposed to 2h-ischemia (1h-warm+1h-cold), followed by3h-EVLP (n=10). T3 (EVLP+T3 and ischemia+EVLP+T3, n=5 each) or an equal volume of saline (EVLP and ischemia+EVLP, n=5 each) were directly added to the perfusion fluid.Lung hemodynamics and airway pressure were monitored throughout the procedure.Perfusate samples were collected at time intervals, biopsies were taken at the end of EVLP. Lungsamples collected from rats in resting conditions were used as reference (Native, n=5)

Results: No significant differences were detected in hemodynamics, airway pressure, or gas-analysisacross treatment groups.T3 administration failed torestore the ATP depletioninduced by ischemia (Figure, p=0.026), and provided no protection in pulmonary energetic charge.Mitochondrial DNA (mtDNA)perfusate concentrations increased over EVLP, in both lungs exposed to ischemiaand in immediately perfused organs (p<0.05). mtDNA release tended to be greater in lungs treated withT3.The oxidative marker 8OHdG likewise rose over the EVLP procedure, with the highest release in the EVLP+ischemia+T3 group (p=0.029). Consistently, greaterlevels of cell death markers were detected in T3-treated lungs compared to untreated organs. Gene expression analysis of lung biopsies showed induction of apoptosis-related genes in T3-treated lungs.

Conclusions: Despite promising results of T3 in other contexts, such as lung fibrosis and ventilator-induced injury,our evidence indicate that ex vivo administration of T3 does not improve bioenergetic dysfunction in ischemic lungs. On the contrary, hormone treatment in this setting appears to exacerbate injury. These results suggest caution in developing T3-based treatments for isolated lungs.

EP_326 INCREASE IN THE USE OF EXPANDED CRITERIA LIVING DONORS TO FACILITATE PREEMPTIVE KIDNEY TRANSPLANTATION FOR OUR PATIENTS

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Background: Spain currently has the highest percentage of deceased donors per million population worldwide (50 pmp 2023). Despite this, the median dialysis time on the transplant list was 20.6 months in 2023. Young patients and blood group O recipients have this time increased. The living donor is the best solution to offer them a preemptive kidney transplant. In recent years, the number of living donors with expanded criteria has been growing significantly in our area to facilitate this objective.

Methods: Using the Catalan Registry of Kidney Patients, we describe the characteristics of 2.510 living donor kidney transplants performed in Catalonia between the years 2000 and 2023 in order to observe the changes in the acceptance criteria of these donors.

Results: The following table shows the increase in the number of expanded criteria living donors according different characteristics. There is also a parallel growing in the preemptive transplants performed.

Conclusions: The progressive introduction of living donors with expanded criteria has allowed the constant increase in anticipated kidney transplantation in our patients. The excellent long-term outcome of these grafts in the recipients (10-year patient survival 86.4%, death censored graft survival 82.9% and graft survival 72.2%), as well as the preservation and stability of the donor's kidney function in follow-up over the years allows us to increasingly consider them as a first option for renal replacement treatment that prevents our patients from starting dialysis.

Living donors	2000-2005	2006-2010	2011-2015	2016-2020	2021-2023	Total	p-value
n	175	481	778	639	510	2583	
>70 years	2.9 %	2.9 %	4.8 %	8.5 %	8.6 %	149	0,000
CKD EPI <70	5.2 %	6.3 %	5.89 %	3.8 %	16.8 %	199	0.000
Proteinuria > 150 mg/24 h	1.4 %	5.4 %	5.6 %	3.6 %	6.4 %	79	0.151
Hypertension	6.9 %	8.8 %	11.7 %	14 %	18.0 %	309	0.000
Diabetes Mellitus II	0 %	0.6 %	0.1 %	0.3 %	1.5 %	13	0.006
Donor lithiasis	3.1 %	1.6 %	2.6 %	5.8 %	2.9 %	72	0.004
Preemptive TX	34.9%	43.8%	47.1%	57.6%	57.8%	1262	0.000

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EP_327 LONGTERM EX SITU NORMOTHERMIC KIDNEY PERFUSION

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Background: Marginal grafts are increasingly considered for transplantation due to the widening gap of available donor grafts and waiting recipients. Graft assessment and repair prior to implantation are therefore essential to minimize the risk of failure. Normothermic perfusion has not been widely evaluated for kidney grafts, with existing perfusions limited to 2 days. The aim of this study was to develop a long-term (>3 days) normothermic *ex situ* swine perfusion model in kidney grafts.

Methods: Swine kidneys were retrieved with minimal injury. After cannulation, organs were perfused at 37°C for up to several days in a newly designed normothermic ex situ device with automated blood gas and glucose regulation, addition of nutrition, antibiotics, and vasodilators. Kidney biopsies, urine and perfusate samples were taken daily for analysis as well as markers of viability.

Results: In total 17 kidneys were perfused. Four kidneys were perfused for 3 or more days. Viability was maintained up to 4 days without histological evidence of glomerular and minimal to moderate tubular necrosis. We observed upregulation of ki67 and pH3 in tubular cells with mean values of up to 14.2% and 2.2% respectively. This expression of ki67, a proliferation associated protein, correlated with the duration of ex situ perfusion.

Conclusions: This is the first report of normothermic kidney perfusion for up to 4 days with unprecedented observation of upregulated ki67 and pH3 after multiple days of perfusion. These preclinical results open the door for development of long-term perfusion protocols for discarded human grafts while also hinting at limitations and challenges.

EP_328 DETERMINATS OF ARTERIAL STIFFNESS IN KIDNEY DONORS POST-NEPHRECTOMY

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Background: Kidney donation leads to a decrease in glomerular filtration rate (GFR) after nephrectomy. Although kidney donors are not at a higher risk of end-stage renal disease compared to non-donors, there are concerns about a potential increase in cardiovascular risk, due to accelerated aortic stiffness, an independent factor for cardiovascular disease and all-cause mortality. Our study investigated the determinants of arterial stiffness in kidney donors post-nephrectomy.

Methods: We conducted a cross-sectional study of 107 kidney donors, who are under regular follow-up at our Outpatient Donor Clinic, with at least one year after nephrectomy. Arterial stiffness indices, including pulse wave velocity (PWV) and augmentation index (AIx), were measured using the Mobil-O-Graph device, along with intima-media thickness (IMT).

Results: Among kidney donors, 65.4% were female. The mean age was 62.4±9.8 years and the mean estimated glomerular filtration rate (eGFR) was 61.1±13.2ml/min/1.73m2. Individuals were followed for a median time of 3.2 (1, 24) years. Hypertension, obesity and tobacco use were reported in 28%, 20.6% and 32.7% of donors respectively. The Mean PWV was 8.5±1.6m/s, mean AIx was 27.5±7.3 and mean IMT was 0.69±0.2mm. Univariate analysis, revealed a significant inverse correlation between PWV and eGFR, with higher PWV levels observed in donors with advanced CKD stages. Donors with CKD3b had significantly higher PWV compared to individuals with CKD stage 1, 2, and 3a (p=0.005, p=0.0001 and p= 0.016 respectively). AIx was strongly associated with female gender and the number of antihypertensive medications (p< 0.001 and p= 0.011, respectively). IMT was inversely associated with eGFR (p = 0.02). No correlations were found between age or comorbidities and arterial stiffness.

Conclusions: Kidney function seemed to be an important determinant of cardiovascular risk, expressed by PWV and IMT one-year post-donation. In accordance with studies in the general population systemic stiffness, expressed by AIx, appeared to be related to gender and anti-hypertensive treatment among kidney donors.

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EP_329 FREQUENCY AND REASONS FOR LIVING KIDNEY DONOR EXCLUSION IN A LIVING KIDNEY TRANSPLANT PROGRAM IN GREECE

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Background: Acceptance criteria of living kidney donors (LKD) have been expanded. However, their utilization rates are not adequately recorded in the literature. We aimed to record the frequency, reasons and impact of LKD exclusion from donation within a transplant program in Greece.

Methods: LKD and recipient couples, evaluated at our center between 2014 and 2024 and excluded from transplantation, were retrospectively studied. Demographic, immunological, renal and imaging parameters and comorbidities of the candidate LKD were recorded. Recipients' outcome after their donor's exclusion was also examined.

Results: Between 2014 and 2024, 792 candidate LKD were evaluated at our center. 196 (24.7%) were excluded from donation. 64.8% (127/196) of the excluded LKD were women, the mean age was 59.4±10.6 years (34.7% were older than 65 years), mean BMI 27.7±4.9 and mean measured GFR 93.7±19.8ml/min. 25.5% (50/196) were obese, 37.7% (74/196) hypertensive and 10.2% (20/178) diabetic. Glomerular haematuria was recorded in 27% (53/196) and proteinuria in 15.3% (30/196). Kidney biopsy was performed in 17.8% (35/196). ABO or HLA incompatibility was observed in 20.9% (41/196) and 23.5% (46/196) respectively. Reasons for LKD exclusion was the presence of renal disease in 28.1% (55/196), HLA incompatibility in 22.9% (45/196), the presence of ≥2 risk factors for kidney disease in 15.3% (30/196), ABO incompatibility in 12.2% (24/196), abnormal scintigraphic findings in 11.2% (22/196), abnormal angiographic findings in 10.2% (20/196), nephrolithiasis in 5.6% (11/196), malignancy in 5.6% (11/196), cirrhosis in 0.5% (1/196) and monoclonal gammopathy in 0.5% (1/196). In 12% of the excluded LKD, ≥2 exclusion criteria coexisted. Of 103 candidate kidney recipients of excluded LKD with adequate follow up, 34 (33%) were transplanted from a deceased donor, 11 (10.7%) from another LKD while 55 (53.4%) remained on the waiting list and 3 (1.5%) died.

Conclusions: During the last decade, in our transplant center, only 24.7% of LKD were excluded from donation after thorough evaluation. This low discard rate contributed to the increase of the kidney transplantation activity in the country.

EP_330 USE OF CILASTATINE FOR THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY IN RENAL TRASPLANTATION IN AN ANIMAL MODEL

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Background: Cilastatin, a dehydropeptidase I inhibitor of the apical membrane of the tubular epithelium, protects against nephrotoxic damage by stabilizing cholesterol rafts and reducing apoptotic pathways. We set out to evaluate the nephroprotective capacity of cilastatin against cold ischemia and reperfusion damage in a rat model of renal transplantation.

Methods: Lewis-Lewis isogenic kidney transplantation with a prolonged cold ischemia (29h) was performed. Two study groups were established: control (n=9) and cilastatin treatment (n=14). In the treatment group, cilastatin (150 mg/kg-dose) was administered to the donor rat 24h and 30 minutes before kidney procurement and to the recipient rat at transplantation and 24h after implantation. Blood samples were obtained throughout the post-transplantation period to assess renal function. After 47 hours post-transplantation, the rats were sacrificed and the kidney grafts were processed for histological analysis: morphological analysis by haematoxylin-eosin (H/E) staining and immunohistochemistry (IHC) for KIM-1 (marker of renal damage), caspase 3 (marker of apoptosis) and CD68 (macrophage marker). Gene expression analysis with real-time PCR was also performed for of Bcl2 and caspase 3, KIM1, NGAL, PAI1 ,MCP1 and CD68.

Results: All rats survived to the end of the study. Cilastatin treatment significantly reduced creatinine (6.61±0.48 vs 5.21±0.40, P=0.0436). Semi-quantitative analysis of renal damage in H/E showed a significant reduction in the Cilastatin-treated group. IHC showed a significant reduction of KIM1, caspase 3 and CD68 in the Cilastatin-treated rats. Gene expression analysis demonstrated a propensity for the reduction of Bcl2, caspase 3, KIM1, NGAL and PAI1 molecules (Figure 1).

Conclusions: Cilastatin reduced the damage induced by prolonged cold ischemia and reperfusion in the isogenic kidney transplantation rat model, although further studies are needed to confirm this finding.

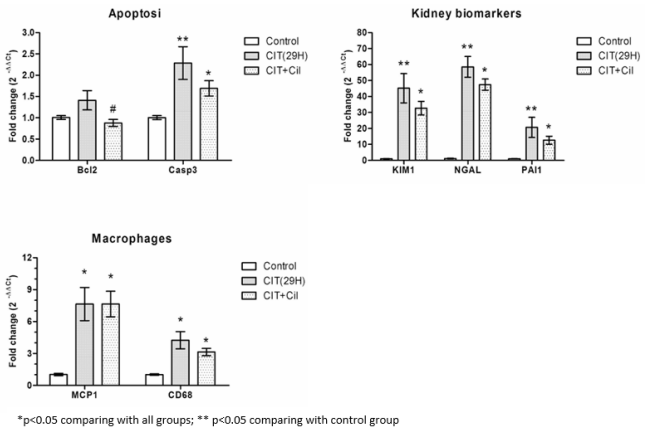

Figure 1. Gene expression analysis using RT-PCR

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EP_331 PROTEINURIA IN DECEASED KIDNEY TRANSPLANT DONORS FOR PREDICTION OF CHRONIC TRANSPLANT LESIONS

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Background: Proteinuria is an established biomarker in native kidney disease, there is, however, a lack of data on its significance for assessing organ quality in the setting of deceased kidney donors. Donor urinary protein-to-creatinine ratio (UPCR) has been associated with the extent of chronic lesions in pre-transplant kidney graft biopsies in a prospective single center study. Validating this association in a larger multicenter cohort and assessing its value in addition to known clinical predictors might help to improve evaluation of organ quality and organ utilization.

Methods: We are currently conducting a prospective observational multi-center study recruiting 300 consecutive adult deceased kidney donor and kidney graft recipient pairs procured and transplanted in all four Austrian transplant centers. The primary aim is to validate donor UPCR for assessing graft quality of kidney grafts from deceased donors by examining the association of donor UPCR with the extent of chronic lesions in pre-implant kidney grafts (glomerulosclerosis, arteriosclerosis/arteriolosclerosis, interstitial fibrosis and tubular atrophy = total chronic lesion score). The secondary objective is the evaluation of donor UPCR for the prediction of graft function after one year, and building of a donor urine biobank. The study in currently ongoing; the expected end of study is by the last quarter of 2027.

Results: The trial centers at Vienna, Linz, Graz and Innsbruck have started including patients and samples in January 2023, March 2024, April 2024 and June 2024, respectively. To date, 125 donor-recipient pairs have been included, with an estimated inclusion of the last patient by July 2026.

Conclusions: While proteinuria in donor reports is often noted semi-quantitatively and not linked to graft quality, a preliminary study has shown that a quantitative and qualitative assessment of donor proteinuria can predict chronic graft damage. Confirming these findings through a large multicenter study, alongside known graft quality predictors, could help develop better prediction models for graft quality. These models have the potential to enhance pre-implant risk assessment and organ utilization. Establishing a large comprehensive donor urine bio-database will enable further research.

EP_332 ESPANDING THE LIVING KIDNEY DONOR POOL, 3RD ACT: REFRAMING THE EVALUATION PROCESS IMPROVES DONOR RECRUITMENT

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Background: Donor demand is still rising and only a proportion of prospective live kidney donors (LD) succeeds in donating. To improve donor recruitment and yield we analysed our LD study process focusing on causes of exclusion and evaluation time.

Methods: From January 2015 to September 2024, we evaluated 526 potential LD. LD were divided in two groups based on causes of exclusion. Data were obtained by review of an electronic database.

Results: Of 526 prospective donors, 200 (38%) successfully donated during the observation period, 292 (55,5%) were excluded, 34 (6,5%) were actively undergoing evaluation at the time the survey was concluded. Of the 292 excluded donors, 51,7% were genetically related, 56.5% female, median age 56 yrs (22-81), BMI 25 kg/m2 (18-42). The reasons for exclusion were medical (n=156) 53%, (n= 94) 32% nonmedical, (n=26) 9% HLA/AB0 incompatibility non accepting paired donation and unknown (n=16) 6%. Medical cause of exclusion were nephropathy (39%), CV disease (14%), diabetes (12%), hypertension (11%), cancer (7%), obesity (3%). Among non-medical reasons, the leading cause was psychological (52%), in most low motivation. Based on these data we reframed the evaluation protocol introducing a dedicated LD case manager and improved the dedicated multidisciplinary network. Over the past six years, the time needed for LD evaluation decreased from 293.5 to 154 days, yielding a 47% reduction in total evaluation time, while pre-emptive transplant candidates made it to be transplanted before dialysis in 70% vs 44 % in the previous era.

Conclusions: A dedicated donor/recipient study pathway that reduces study time can encourage donation and increase the number of pre-emptive transplants. Multidisciplinary evaluation and center expertise help expand the donor pool to include marginal candidates.

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EP_333 THERAPEUTIC MILD HYPOTHERMIA IN BRAIN DEAD DONORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Delayed graft function (DGF) can be up to 50% in deceased donor kidney transplants, and is associated with diminished long-term graft function, and increased patient morbidity and hospitalization. The use of therapeutic hypothermia (core temperature 34-35oC) has shown to impact DGF, especially in extended criteria donors (ECD), as shown in randomised controlled trials (RCTs). The aim of this review is to identify the effect of mild hypothermia on DGF.

Methods: Articles in English language published after 2000 were searched in PubMed, Embase, Cochrane Library, Europe PubMed Central, Directory of Open Access Journals, and ClinicalTrials.gov. Search MeSH terms included donors, living/organ donors, brain/cardiac/circulatory dead/death, induced mild/moderate hypothermia, effect of hypothermia on kidney/renal function, renal/kidney transplantation. Inclusion criteria included age >18 years old, mild hypothermia of 35oC, and DGF as a primary outcome. The authors evaluated RCTs where mild hypothermia was used in kidney donors, and DGF was the primary outcome. Citation identification, study selection, and data extraction were independently undertaken by 2 reviewers. A consensus method was used to resolve disagreements concerning the assessment of the methodologic quality of the RCTs.

Results: The search identified 6 studies that examined mild hypothermia in brain death donors; 5 studies (2606 patients) met the inclusion criteria. The observed log odds ratios of individual studies ranged from -0.58 to -0.08. The estimated average log odds ratio was -0.3220 (95% CI: -0.4545 to -0.1894) with p value of <0.0001. There was no significant heterogeneity (Q test I2=0.0006%). Two studies reported greatest impact on DGF in ECD kidney recipients (hypothermia vs normothermia; p ≤0.031 and p ≤0.003).

Conclusions: The present systematic review provides further evidence that therapeutic mild hypothermia can improve DGF rates with more beneficial effect on ECD kidneys.

EP_334 SUCCESSFUL INTERNATIONAL ADOPTION OF INTEROPERABLE AND SECURE DIGITAL ORGAN MANAGEMENT PLATFORM

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Background: It is well understood that costly inefficiencies exist in the current fragmented donation and transplantation ecosystem. Outdated paper processes and systems operating in silos without seamless sharing of key data can lead to errors, compliance issues, time-intensive processes, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.

Methods: A donation organization responsible for managing country-wide donation and transplant adopted a comprehensive, modern, digital interoperative platform (previously adopted around the world) to manage the donation workflow, shifting from the previous paper process. The platform is a modern web-based system which provides advanced communication tools and has the potential to securely interface with external systems such as hospital EMRs.The donation organization, together with the software provider, coordinated updates to the workflow, processes, and policies, and organized comprehensive training sessions to ensure full compliance and oversee change management of the implementation.

Results: The comprehensive secure donation platform streamlines the clinical workflow by providing: 1) access to the latest chart information across multiple staff; 2) real-time and retrospective data quality tools to flag potential errors; 3) auditing and additional reporting and compliance tools; 4) notifications and alerts to team members upon key case updates; 5) scheduling and assignment coordination; and more. Implementation of the donation platform has resulted in a positive impact in donation outcomes due to the efficiencies gained.

Conclusions: As the donation organization continues using the new platform they look forward to upcoming reporting on the qualitative benefits of transitioning to the modern software as well as potentially expanding across the donation-transplantation ecosystem with interfacing capabilities.

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EP_335 IMPACT OF PRE-OPERATIVE HAEMODIALYSIS ON TRANSPLANTED KIDNEY FUNCTION

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Background: Hypotension and electrolyte disturbances are known short term consequences of haemodialysis (HD). However, little is known of its effects on kidney transplantation in this acute setting. The aim of this study is to show if HD immediately before transplantation has an effect on the short-term graft outcomes.

Methods: This is a single centre retrospective analysis of deceased donor kidney transplants between 2019 to 2023. Only patients with in-centre HD were included. Data was collected on the last pre-operative HD sessions. The outcomes measures (DGF, serum creatinine up to 3 months and complications) were stratified according to the time lapse between HD session to the initiation of surgery.

Results: 172 patients were included. 103 were males and the mean age was 56.02±11.37 years. The mean duration of HD was 196.28±44.58 minutes and the mean volume removed was 1.259±0.9273 litters. 84 patients developed delayed graft function and received at least 1 HD session post-operatively. The mean time from the HD to the initiation of transplantation was 1525±1016 minutes. No statistically significant effect was observed on the DGF when the HD cut off was 3,6,12 or 24 hours from the initiation of the transplantation (p 0.0577, p 0.4363, p 0.8511 and p 0.8580 respectively); 4- and 12-weeks post-transplant function was also not significantly different.

Conclusions: Although HD can significantly alter the hemodynamic parameters of the patients before an operation, we couldn't elicit any direct relationship with the short-term post-transplant outcomes. Hence, pre-transplant HD appears safe even when instituted soon before the surgery.

EP_336 LIVING LIVER DONATION AFTER BARIATRIC SURGERY: CHALLENGES, OUTCOMES, AND IMPLICATION FOR DONOR MANAGEMENT

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Background: The increasing prevalence of obesity and metabolic syndrome has led to a surge in bariatric surgery among potential living liver donors. However, the implications of prior bariatric surgery on donor liver morphology, function, and regeneration post-donation remain underexplored.

Methods: We conducted a retrospective review of six living liver donors with a history of bariatric surgery who underwent donor hepatectomy at our centre. We analysed donor selection criteria, preoperative assessments, perioperative management, and postoperative recovery, focusing on liver regeneration, metabolic adjustments, and potential complications. Morphological and histological findings from preoperative imaging and intraoperative assessments were also examined to evaluate the effects of bariatric surgery on the donor liver.

Results: Preliminary observations suggest that prior bariatric surgery introduces unique considerations in donor evaluation, including altered liver morphology, steatosis, and vascular adaptations. Perioperative management was tailored to address potential nutritional deficiencies and altered gastrointestinal anatomy. Postoperative recovery was generally uneventful, with early indications of adequate liver regeneration and no significant long-term complications in this cohort except for one donor who had undergone a Roux-en-Y bypass surgery. However, subtle variations in the regenerative capacity and metabolic profile of donors with prior bariatric surgery were noted, warranting further investigation.

Conclusions: Bariatric surgery presents novel challenges and opportunities in the context of living liver donation. While our initial experience indicates that these donors can be safely managed, careful preoperative evaluation, surgical planning, and postoperative follow-up are crucial to optimise outcomes. Further data collection and analysis are underway to better understand the long-term implications of bariatric surgery on donor liver function, recovery, and regeneration. Our findings aim to inform clinical guidelines and facilitate safe expansion of the living donor pool.

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EP_337 DONOR LIPASE AND AMYLASE DO NOT PREDICT PANCREAS TRANSPLANT OUTCOMES, AN OPTN REGISTRY NATIONAL COHORT STUDY

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Background: Simultaneous pancreas-kidney (SPK) transplantation improves quality of life in people with diabetes and end-stage renal disease, and limits the progression of diabetes related complications. Many surgeons remain reluctant to accept the pancreas of a donor with raised serum lipase and amylase, due to concern of potentially inferior outcomes. We aim to establish whether donor serum lipase and amylase predict pancreas transplant outcome.

Methods: This retrospective cohort study utilised the Organ Procurement and Transplantation Network data registry on all adult SPK transplantation (2010-2023). Adjusted regressions models assessed the effect of donor serum lipase and amylase on 1-year pancreas transplant outcomes.

Results: 10,451 SPK recipients were included. Median peak donor lipase was 38 (Figure 1A; IQR 18- 92, max 2985) and median amylase was 84 (Figure 1B; IQR 45-168, max 2831). Neither donor peak serum lipase, nor amylase, had a significant impact on pancreas graft survival when adjusting for multiple confounders (aHR=1.019; 0.980-1.059, and aHR=0.986; 0.943-1.031, respectively). Interaction terms were included to assess whether the impact of peak lipase/amylase on outcome differed based on trend; there was no evidence that lipase/amylase trend altered the impact on outcome (p=0.250 and p=0.492, respectively). Restricted cubic splines (Figure 2) were used to assess the relationship between these enzymes and pancreas graft survival without assuming linear relationships; these confirmed that neither lipase, nor amylase, had a significant impact on pancreas transplant outcome.

Conclusions: Donor lipase and amylase do not predict transplant outcomes. Therefore, raised donor serum lipase and amylase should not be considered a barrier to organ utilisation. The use of pancreas grafts from donors with raised lipase/amylase is a simple approach to prevent donor organ discard and expansion of donor pool.

EP_338 MIT-001 ATTENUATES RENAL DAMAGE CAUSED BY RENAL ISCHEMIA-PERFERFUSION INDUCED RENAL FIBROSIS

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Background: Ischemia-reperfusion injury (IRI) is a significant contributor to the development of renal fibrosis, a hallmark of chronic kidney disease (CKD). During CKD progression, ischemia-reperfusion (IR) increases inflammatory responses, leading to ferroptosis and fibrosis. MIT-001 has been shown to mitigate necrosis and inflammation in various organ injuries. This study investigates whether MIT-001 can reduce CKD-induced renal fibrosis by suppressing inflammation and reactive oxygen species (ROS) in an IRI mouse model, along with the underlying mechanisms.

Methods: Eight-week-old male C57BL/6 mice were divided into groups based on IR induction and MIT-001 administration. IR was induced via 24-hour renal IRI. Kidney tissues and blood samples were collected one, three, and seven days after MIT-001 treatment. HK-2 cells treated with TGF-β were used for in vitro studies.

Results: Blood urea nitrogen and serum creatinine levels were significantly decreased in MIT-001-treated IRI 3-day and 7-day mice compared to untreated IRI 3-day and 7-day mice. Regarding antifibrotic effects, the expression levels of F4/80, collagen IV, alpha-smooth muscle actin, and transforming growth factor-beta were markedly reduced, while E-cadherin expression was increased in the kidneys of MIT-001-treated IRI 3-day and 7-day mice. Regarding anti-ferroptosis effects, increased levels of xCT, SLC7A11, and GPX4, as well as a reduction in 4-HNE, were observed in MIT-001-treated IRI 3-day and 7-day mice. Additionally, regarding anti-inflammatory effects, lower levels of HMGB1 and nuclear factor kappa B were detected in the kidneys of MIT-001-treated IRI 3-day and 7-day mice compared to untreated IRI 3-day and 7-day mice.

Conclusions: These findings confirm that IR induces kidney damage and fibrosis. MIT-001 serves as a protective agent against IRI-induced renal fibrosis by reducing inflammation, ferroptosis, and oxidative stress in IRI mice.

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EP_339 INNOVATIVE APPROACHES TO BETA-CELLS RESEARCH

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Background: Diabetes mellitus is a significant global health challenge, driven by insufficient insulin secretion from pancreatic beta-cells and leading to chronic hyperglycemia with severe complications. However, challenges such as donor scarcity, cell functionality preservation, and post-transplantation issues limit current therapeutic options. This study explores the potential of phytoecdysteroids and experimental models for beta-cell transplantation.

Methods: Beta-cells were isolated from Wistar rats through mechanical and enzymatic dissociation and cultured under sterile conditions. Phytoecdysteroids, including ecdysterone, turkesterone, and polypodin B, were added to the culture medium to evaluate their effect on insulin secretion using ELISA. A rat model of diabetes was developed via pancreatectomy, followed by beta-cell transplantation. Isogenic and allogenic cell suspensions were transplanted into diabetic rats, and glucose and insulin levels were monitored post-transplantation.

Results: Phytoecdysteroids significantly enhanced insulin secretion in cultured beta-cells. Ecdysterone exhibited the strongest effect, increasing insulin levels to 164.0 mU/L, 1.5 times the basal secretion. Turkesterone and polypodin B also showed stimulatory effects, though less pronounced. In the transplantation model, beta-cells restored glucose homeostasis in diabetic rats. Glucose levels dropped to 7-7.8 mmol/L within three hours post-transplantation, while insulin levels increased to 30-41 mU/L by day three. Control rats without transplantation exhibited persistent hyperglycemia (>18 mmol/L). These findings underscore the efficacy of phytoecdysteroids in enhancing beta-cell function and the potential of beta-cell transplantation in diabetes management.

Conclusions: Phytoecdysteroids, particularly ecdysterone, are promising agents for enhancing insulin secretion and improving beta-cell functionality. The developed rat model of diabetes and successful transplantation of beta-cells demonstrate the feasibility of this approach for restoring glucose regulation. These findings pave the way for innovative therapies targeting sustainable and effective treatment options for diabetes.

EP_340 EARLY AND LONG-TERM RENAL OUTCOMES OF LIVING KIDNEY DONORS AFTER NEPHRECTOMY FOR TRANSPLANTATION

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Background: The ability of the remaining kidney to compensate for baseline renal function (RF) is essential to assess the degree of morbidity associated with living donor kidney transplantation (LDK). One year after donation, the residual kidney can compensate for up to 70% of pre-nephrectomy RF. Aim of the study was to evaluate the short-term (1m) and long-term (1y) trend of renal function after nephrectomy in living donors (LDK) and the factors involved in the compensation of basal RF.

Methods: We evaluated 24 LDK [M/F:37.5%/62.5%; 49.17±10.36y; BMI 24.03±4.24kg/m2], 3 with borderline hypertension. Basal eGFR estimated with CKD-EPI formula was 98.30±11.24ml/min/1.73m2 (Fig.1). Post donation follow-up at 1, 6 and 12 m. We considered Renal Compensation Rate (RCR)= (eGFR one year post nephrectomy/baseline eGFR)*100. The sample was then divided in ? or <70% of RCR.

Results: Mean eGFR decreased immediately after nephrectomy of approximately 40 ml/min (35%) with eGFR 62.86±12.48 ml/min, stable at 1 year (Fig.2). No donor developed ESRD. At 1 year, the average RCR was of 64.09±10.09%. 5/24 (20%) of LDK compensated ? 70% of the baseline renal function. Younger age and male gender were found to be possible predictive factors of the compensation rate at 1 year. No association was found between compensation of renal function, basal GFR and comorbidities (Fig. 3).

Conclusions: Living kidney donation is a safe procedure. In our experience, age and gender affect the evolution of post-nephrectomy renal function after the same period of follow-up. Knowing the differences in compensation capacity between different subgroups of LKD is useful for correctly informing future donors.

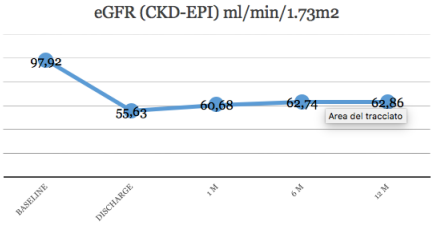

Fig.1

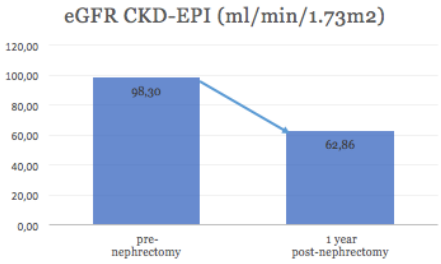

Fig.2

	RCR at 1 y < 70%	RCR at 1 y ≥ 70%	P value
N	19	5	
Age, years	51,84±8,51	39±11,31	**0.01**
Male gender, n (%)	5 (26,3%)	4 (80%)	**0.02**
Hypertension, n (%)	2 (10,5%)	1 (20%)	0.56
Dyslipidemia, n (%)	9 (47,4%)	1 (20%)	0.27
BMI, Kg/m²	25,63±4,48	24,36±2,64	0.63
Obesity, n (%)	4 (21 %)	0 (0%)	0.26
Basal sCr, mg/dl	0,79±0,12	0,91±0,16	0.07
Basal eGFR CKD EPI, ml/min	96,63±10,13	105,4±13,22	0.10
Basal Scintigraphy, ml/min	103,59±20,45	106,12±11,94	0.68
Remaining kidney GFR, ml/min	51,58±6,04	49,44±7,68	0.51

Fig.3

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EP_341 CROSS-SPECIES TRANSCRIPTOMIC COMPARISON OF HUMAN VERSUS MURINE DONOR KIDNEYS AFTER CIRCULATORY DEATH OR BRAIN DEATH

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Background: This study compares the transcriptome of pre-implantation human kidney biopsies and murine kidneys to assess the relevance of rat models of kidney donors after brain death (DBD) or circulatory death (DCD).

Methods: We analyzed 10 human preimplantation kidney biopsies (5 DCD and 5 DBD) and 16 rat kidneys (9 DCD and 7 DBD) with matched criteria (i.e. 14-hour cold ischemia; <10h *post* brain death (DBD) or 20 minutes of warm ischemia (DCD)). Samples were subjected to high-throughput RNA sequencing (Illumina®). Differential expression analysis followed by pathway enrichment analysis were performed using DESeq2 in R (version 4.4.0) and Ingenuity Pathway Analysis (Qiagen®).

Results: Principal component analysis (PCA) showed a separation between the DBD and DCD groups, in both humans and rats. In humans, PC1 and PC2 accounted for 32% and 20% of total variability, respectively. Murine data showed 60% and 9% for PC1 and 2, respectively. In humans, 503 genes were down-regulated and 338 up-regulated in DBD vs DCD. In rats, we had 2144 down-regulated genes and 1950 upregulated. Pathway enrichment analyses showed that 5 of the 10 major pathways enriched in each model were common to both species, including acute response signaling, IL10, IL17 and IL6 signaling, and JAK kinase signaling. The “Tox and Functions” analysis revealed a common positive enrichment for “mesangial cell proliferation” and “proximal tubular toxicity” in human and murine DBD compared to DCD biopsies.

Conclusions: Our rat models mimic the transcriptomic characteristics of human biopsies from DBD and DCD donors. This concordance makes these animal models useful to study the mechanisms of per-transplant lesions and test preconditioning strategies suited to each type of donor.

EP_342 LONG-TERM OUTCOMES OF RENAL TRANSPLANTATION FROM EXPANDED CRITERIA LIVING DONORS

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Background: In the last decades, we have witnessed a steady increase in the use of donors with expanded criteria in Spain, initially from deceased donors and later from living donors. All of this aims to decrease the waiting time to be transplanted for our recipients. There is considerable concern regarding the long-term outcomes associated with expanded criteria living donors, particularly when faced with the decision between a preemptive transplant using a living donor with expanded criteria or a standard deceased donor after an extended period on the waiting list.

Methods: Using the Catalan Registry of Kidney Patients, we analyze and compare the long-term results obtained using standard living donors (<70 years old and >70 ml/min CKD-EPI), standard deceased donors (45-60 years old, CKD-EPI>70 ml/min, no diabetes), expanded living donors (>70 years old or CKD-EPI<70 ml/min) and expanded criteria deceased donors (>70 years old or CKD-EPI<70 ml/min) during the period 2000-2023.

Results: The following table shows the results obtained with these different categories of donors

Conclusions: Our data confirm that living donors provide better long-term patient and graft survival rates in the kidney transplant population. Notably, the results are superior when using a living donor with expanded criteria compared to a standard deceased donor. When comparing outcomes between expanded criteria living and deceased donors, the differences are significantly in favor of living donors.

Living donors	Standard living donor	Expanded living donor	Standard deceased donor	Expanded deceased donor	p-value
n	1968	129	2851	2407	
Patient survival (10 years)	86.15%	81.54%	72.8%	32.9%	p=0,0432
Graft survival (10 years)	74.5%	63.9%	57.2%	24.0%	p=0,0424
Death censored graft survival (10 years)	85.6%	79.3%	73.6%	64.1%	p=0,0733

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EP_343 CELL-FREE DNA DURING NORMO- AND HYPOTHERMIC MACHINE PERFUSION DOES NOT PREDICT POST-TRANSPLANT KIDNEY FUNCTION

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Background: Machine perfusion may offer the opportunity to assess the quality of marginal donor kidneys upon transplantation. During perfusion, cellular components are flushed out into the perfusate. One of these components is cell-free DNA (cfDNA), which is released upon active secretion, inflammation, or cell death from tissue injury. Studies showed that cfDNA origin - either nuclear or mitochondrial - can be indicative of graft (dys)function. This study quantified cfDNA concentration and origin during normothermic- and hypothermic machine perfusion (NMP, HMP) of transplant kidneys and evaluated its association with post-transplant graft function: immediate function (IF), delayed graft function (DGF), and primary non-function (PNF).

Methods: Perfusate was collected from 41 NMP and 51 HMP deceased donor kidneys immediately after the graft was removed from machine perfusion. cfDNA was isolated using the QIAamp Circulating Nucleic Acid kit and quantified with the dsDNA High Sensitivity Assay on a Qubit 3 fluorometer. Mitochondrial and nuclear cfDNA were quantified by qPCR, using synthetic gene fragments for absolute quantification. cfDNA concentration and copy numbers were corrected for the perfusion time.

Results: A significantly higher cfDNA concentration was observed during NMP (7.8 ng/µL) compared to HMP (0.09 ng/µL; $p < 0.001$). Regardless of perfusion type, the majority of cfDNA originated from mitochondria, with a 24-fold difference during HMP ($p < 0.001$) and a 13.8-fold difference during NMP ($p < 0.01$). Additionally, nuclear and mitochondrial cfDNA copy numbers were 7.3-fold and 4.1-fold higher, respectively, during NMP compared to HMP ($p < 0.001$). Finally, no significant differences in cfDNA concentration or nuclear and mitochondrial copy numbers were observed across IF, DGF, and PNF kidneys (Figure 1).

Conclusions: In our study, we did not find differences in perfusate cfDNA concentration and nuclear or mitochondrial copy numbers between IF, DGF, and PNF kidneys. Therefore, perfusate cfDNA measurements cannot be used as a tool to predict graft function.

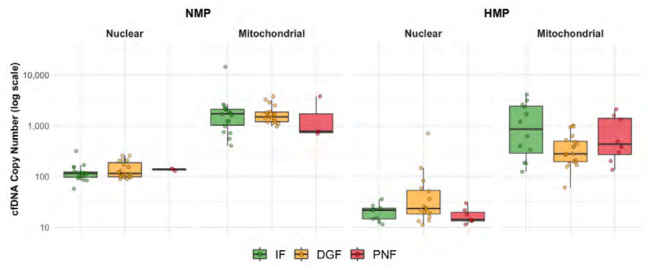

Figure 1: Perfusion-time corrected copy numbers of nuclear and mitochondrial cfDNA during NMP and HMP for different post-transplantation graft functions (IF, DGF, PNF).

EP_344 INFLUENCE OF HYPOTHERMIC AND NORMOTHERMIC MACHINE PERFUSION ON RENAL INTEGRITY USING A MURINE MODEL OF MACHINE PERFUSION

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Background: While normothermic MP (NMP) is well established for liver transplantation, the optimal MP protocols for kidney perfusion are still being debated. To gain insight into the impact of current MP protocols on renal integrity and potential inflammation, we established a kidney MP model that allows for both hypothermic (HMP) and normothermic (NMP) perfusion of murine kidneys.

Methods: Kidneys were perfused in a pressure-controlled manner at 80 mmHg, with the perfusate oxygenated with carbogen (95% O2, 5% CO2) to a level of > 600 hPa. In the HMP setting, a cell-free perfusate was used to maintain stable perfusion for 60 minutes. All grafts remained viable at the end of the HMP period with a stable vascular resistance of 30 ± 10 mmHg/ml/min and a flow rate of 3 ± 1 ml/min. NMP was performed with a perfusate substituted with 30% human erythrocytes, allowing perfusion for one hour with a stable vascular resistance of 35 ± 10 mmHg/ml/min and a flow rate of 2.5 ± 1 ml/min ($p < 0.001$ for flow rate and vascular resistance, respectively, HMP versus NMP). During NMP, all kidneys exhibited metabolic activity.

Results: Notably, kidneys subjected to NMP showed a greater incidence of tubular injury compared to those subjected to HMP. When comparing the cellular composition of the perfusates, significantly lower frequencies of B cells and dendritic cells (DCs) were identified in NMP perfusates, while higher frequencies of neutrophils were detected. Although there were no differences in the overall frequencies of T cells in HMP or NMP perfusates, higher frequencies of regulatory T cells (Tregs) were present in HMP perfusates. Overall, renal macrophages were preferentially present in the tissue during perfusion compared to B cells, neutrophils or NK cells. NMP also induced mRNA upregulation of P-selectin and ICAM-1, the latter also being upregulated on glomerular endothelial cells.

Conclusions: Our study using a small animal model demonstrates significant differences in renal injury, cellular composition of retained cells in perfused grafts, and intragraft activation during either HMP or NMP perfusion, allowing for a comprehensive analysis of MP protocols on renal integrity. In addition, the availability of this model will facilitate the testing of novel therapeutic agents for organ regeneration during MP.

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EP_345 RETROPERITONEOSCOPIC DONOR NEPHRECTOMY-A CRITICAL APPRAISAL

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Background: Laparoscopic donor nephrectomy is the standard of care for kidney retrieval in renal transplantation. Retroperitoneoscopic donor nephrectomy(RDN) has the advantage of direct vascular access and avoidance of peritoneal transgression. The aim of this study is to assess the outcome of RDN in voluntary kidney donors.

Methods: This study was a prospective observational study from 1st January 2023- 31st march 2024 with a sample size of 50 voluntary kidney donors who underwent RDN. Data were collected with regards to donor characteristics, warm ischemia time, operative time, estimated blood loss, length of the hospital stay, post-operative complications, return to work ,post operative serum creatinine of donor and recipient.

Results: RDN was successfully performed for all the donors. In our study 37 were female and 13 were male donors. Left RDN was performed in 46 (92%) and right RDN was performed in 4(8%) donors. Single renal artery was present in 38(76%) and double renal artery was found in 12(24%) donors. Single renal vein was found in 49(98%), circumaortic and retro aortic renal vein was found in one case each (2%). The mean operative time was 181.2±35.27 minutes (110-260 min.). Mean warm ischaemia time(WIT) was 165.6±44 seconds (100-300seconds). Estimated blood loss was 37.6±12.7 ml (20-80 ml). The mean duration of hospital stay was 1.45±0.63(1-3) days. Return to work was in 9.76±2.03 days (6-15 days) All the grafts functioned well with mean serum creatinine of the recipient at 1 week ,3 months ,6 months as 1.18,1.19,1.3 mg/dl respectively.

Conclusions: Retroperitoneoscopic donor nephrectomy is a safe and feasible alternative to laparoscopic donor nephrectomy with good donor and recipient outcomes.

EP_347 40 YEARS OF TRANSPLANT COORDINATION IN CATALONIA: A STORY OF 30000 LIVES

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Background: Catalonia has been a pioneer in most transplants in Spain. Clínica Barraquer performed in 1926 the first cornea trasplant. Hospital Clínic carried out the first kidney transplant in 1965 and the pancreas transplant in 1983. One year later, arrived the first liver transplant at Hospital Bellvitge and the first heart transplant at the Sant Pau Hospital. In 1984, the Health Departament of Catalan Government created the Transplant Programme, an innovative initiative in Spain to order the incipient world of non-renal transplants.

Methods: The Transplant Programme created the authorised hospital network for donor detection, the different transplant programmes and defined the role of the hospital transplant coordinator, the key figure of the Spanish Transplant Model, a reference in the world. One year later, in 1985, was set up the first coordination office for organ exchange between hospitals. During these early years, from 1985 to 1989 (ONT creation), the Barcelona office coordinated the organ exchange between Catalan hospitals but also hospitals from the rest of Spain.

Results: The transplant activity figure shows the increase from less than 200 transplants before 1984 to 1,344 interventions in 2024. Currently, with 165 transplants per million of population (pmp), Catalonia is the region with the highest transplant activity in Spain and could be in the world. In terms of cadaveric donation, we observed different patterns: increasing trend during the first period (1989-1997), stabilization or light decrease until 2012, due to the brain death decline, and finally, a sustained increase until today, thanks to cardiac donors programs. In 2024 Catalonia obtained 381 real donors, with a donor rate of 47 pmp donors, slightly lower of global Spain.

Conclusions: 40 years later, and with more than 30,000 organ transplants performed by Catalan hospitals, Catalonia and Spain are world leaders and referents in donation. This mean to give life and hope to thousands of people.

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EP_348 PAEDIATRIC KIDNEY TRANSPLANT: A 12-YEAR FOLLOW-UP OF PIONEERING MACHINE PERFUSION IN LATIN AMERICA

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Background: Scientific evidence shows that preserving kidneys from deceased donors (DD) with hypothermic machine perfusion (HMP) reduces the incidence of Delayed Graft Function (DGF), the need for dialysis within the first week post-transplant. DGF has been associated with complications such as rejection, increased length of hospital stay and lower survival rates for both grafts and patients. However, this technology is not yet widely used in Latin America, and there are few publications on the use of HMP for paediatric kidney recipients. This study evaluates the use of HMP in DD kidneys for paediatric transplantation and compares the outcomes with those of static cold storage (SCS) in short and long-term post-transplant scenarios.

Methods: This retrospective cohort study analyzed data from all paediatric recipients of DD kidney transplants performed between June 2012 and June 2024 in a Brazilian public hospital and was approved by the local Ethics Committee. The exposure factor in this longitudinal observational analysis was the use of HMP to preserve kidneys. Data were collected by a systematic review of medical charts and electronic databases. All DD were brain-dead and next of kin provided written informed consent that was freely given.

Results: Medical records of 240 kidney transplanted children whose grafts had been kept only in SCS (n=130) or in HMP (n=110) before surgical implantation were reviewed. Regarding donors' characteristics, traumatic brain injury was the most prevalent cause of death in both groups and the average age was 15 years. Final serum creatinine was 1 mg/dL in the SCS group and 1.4 mg/dL in the HMP group. Regarding recipients' characteristics, there were no statistically significant differences between groups. Among clinical outcomes, DGF stood out in 29% of transplanted children whose grafts had been placed in SCS while it was observed in only 12% of children in the HMP group. Also, number of dialyses sessions, length of hospital stay and serum creatinine at one year post-transplant, as well as graft loss at 3, 6 and 12 years post-transplant were significantly higher in the SCS group.

Conclusions: In this study, HMP proved to be a protective factor against DGF and prolonged hospital stay, and it improved long-term graft survival in paediatric patients undergoing kidney transplantation.

EP_349 NORMALISATION PROCESS THEORY AND THE IMPLEMENTATION OF A RENAL PRE-TRANSPLANT NORMOTHERMIC MACHINE PERFUSION SERVICE

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Background: Normalisation Process Theory (NPT) provides a framework to analyse and assess the progress of complex healthcare interventions, whilst describing the social and logistical requirements for it to be an effective intervention. Normothermic Machine Perfusion (NMP) has been developed as a clinical service, to enable viability assessment and potential reconditioning of kidneys prior to transplantation. The developing technology in renal transplantation has no nationally defined criteria for when it should be used and places the organ at increased risk. This has made the implementation of the service challenging and dependent on the specific staff involved in the decision-making process.

Methods: NMP as a clinical service was assessed with NPT in the form of semi-structured focus groups and interviews, utilising specific topic guides structured to the four constructs of NPT: Coherence, Cognitive Participation, Collective Action and Reflexive monitoring. The transcripts were analysed using *NVivo* qualitative data analysis software.

Results: Due to the developing nature of this new technology and lack of published evidence, there is no clearly defined role for NMP along with no shared understanding within the department, but it is clear the service has potential value to renal transplant recipients. The delivery of the service has been limited to a few key individuals who are not always available, making the implementation fractured. There was a lack of clear training for those not directly involved with NMP and it has been difficult to obtain adequate financial support from the management team. There is a clear impression that the use of the technology can improve outcomes and is a worthwhile endeavour but this needs to be reviewed and audited in a systematic way.

Conclusions: The absence of full-time staff and clear guidelines on when to utilise the service has led to the poor implementation, with inadequately defined roles and uncertainty on how the service can be used. Guidelines need to be created on both a local and national level to ensure the service is used efficiently and a clinical trial could be utilised to ensure the service is used consistently. There needs to be defined revenue streams to support this endeavour, with sufficient managerial input and support.

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EP_350 EFFECT OF ANAKINRA (IL-1 RECEPTOR ANTAGONIST) ON PORCINE KIDNEYS DURING MACHINE PERFUSION

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Background: Donor shortages and poor post-transplant outcomes highlight the need for better organ recovery and preservation. Machine perfusion (MP) offers a therapeutic platform to improve the viability of marginal and discarded kidneys for transplantation. Anakinra, an IL-1 receptor antagonist, has show potential in modulating cytokine storms and mitigating inflammation. We hypothesize that Anakinra administration during either hypothermic machine perfusion (HMP) or Normothermic Machine Perfusion (NMP) could protect the kidneys against ischemia-reperfusion injury (IRI) in a porcine model of donation after circulatory death.

Methods: Eighteen porcine kidneys were obtained from a local slaughterhouse and allocated into three groups: Control group: 24 hours of HMP followed by 6 hours of NMP; HMP+Anakinra group: 24 hours of HMP, with Anakinra (100 mg/kg) administered after 12 hours of HMP, followed by 6 hours of NMP; NMP+Anakinra group: 24 hours of HMP followed by 6 hours of NMP, with Anakinra (100 mg/kg) administered after 1 hour of NMP. All kidneys underwent 30 minutes of warm ischemia. Physiological measurements and samples (tissue, perfusate, urine) were collected for analysis. Data were compared using two-way ANOVA with Tukey's post-hoc test for multiple comparisons.

Results: At the end of the 6-hour of NMP, the HMP+Anakinra group exhibited significantly lower levels of cytokine IL-1β in perfusate samples (p=0.01), as well as reduced total protein in urine (p=0.01) and lower lactate (p=0.006) compared to the Control group. No significant differences were observed in perfusate flow rate, fractional sodium excretion, weight gain, ASAT, or LDH among groups. However, a trend toward higher creatinine clearance was observed in both Anakinra-treated groups compared to the Control group.

Conclusions: These initial results suggest that Anakinra administration during HMP may protect the kidney against IRI reducing inflammation and tissue injury. While results for NMP administration were less conclusive, trends observed warrant further investigation to optimize dosing strategies and therapeutic timing.

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EP_351 OPTIMIZING LUNG TRANSPLANTATION FROM UNCONTROLLED-DCD DONORS ACROSS DISTANCES

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Background: The success of lung transplantation from donation after circulatory death (DCD) relies heavily on the proper preservation, assessment, and timing. The distance between the donor and transplant center plays a crucial role in minimizing ischemic times and ensuring the organs remain viable, particularly in uncontrolled-DCD donors. When no suitable recipients are available at the closest transplant center, collaboration between hospitals becomes key: it facilitates organ's transport over distances, widening donor pool and addressing regional disparities in organ access.

Methods: We report a successful bilateral lung transplantation involving an uDCD donor. The lungs were procured from a donor who died of aortic dissection (Cardio-Circulatory arrest at 6:35 a.m. and perfusion starting at 11 a.m.), at the University Hospital of Siena and placed in an Organ Care System (OCS-lung) for evaluation (from 12:30 p.m. to 6 p.m.). Due to the unavailability of suitable recipients at the nearest transplant center, after confirming the organs' viability, they were transported to Milan (360 km away). Cold static preservation (10 degrees) was maintained overnight, until the implantation the day after (2:20 p.m. and 5:58 p.m. for the right and left lung respectively). Lungs were transplanted into a 61-year-old recipient affected by pulmonary bronchiectasis, with no operative complications, no need of ECMO support and no post-operative signs of PGD. The recipient was extubated on the second and discharged on the 17TH post-operative day.

Results: The use of advanced technologies, such as the OCS and cold static preservation at 10°C, enhances the ability to assess and prolong the preservation time of uDCD lungs. This extends the donor pool over longer distances, enabling lung transplantation to be conducted in a more flexible, semi-elective manner.

Conclusions: These strategies ensure that viable organs can be transplanted even when a suitable recipient isn't available locally, thereby addressing regional disparities in organ access.

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EP_352 IMPACT OF DONOR KIDNEY VOLUME AND RECIPIENT BODY SURFACE AREA ON OUTCOMES IN LIVING DONOR TRANSPLANTATION

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Background: Renal transplantation is the preferred treatment for end-stage renal disease (ESRD), offering the best quality of life and long-term survival outcomes. Donor kidney volume (KV), reflecting nephron mass, and recipient body surface area (BSA), representing metabolic demand, are key factors in graft function. Mismatches between KV and BSA may lead to hyperfiltration injury, compromising graft outcomes. Larger donor KV has been linked to better outcomes in recipients with higher BSA, yet standardized guidelines for integrating KV and BSA in organ allocation remain limited. This study examines the impact of KV-to-BSA ratio on post-transplant outcomes, hypothesizing it improves graft survival and function.

Methods: This retrospective study at Mahatma Gandhi Medical College, Jaipur (Oct 2022–July 2023), included 244 living donor kidney transplants. Donor Kidney Volume (DKV) was measured via preoperative CT, and Recipient Body Surface Area (BSA) was calculated using the Mosteller formula. The kidney volume-to-BSA ratio (Vol/BSA) was determined for each pair. Graft function at 12 months post-transplant was assessed using eGFR. A linear regression model adjusted for variables ($p<0.15$) was followed by multivariate analysis. The Vol/BSA ratio was categorized into tertiles, and variables were compared across these tertiles.

Results: Among 244 donors, 77.5% were females (mean age 49.56 years, BSA 1.66 m²). Recipients: 13.9% females (mean age 36.05 years, BSA 1.65 m²). Post-transplant mean eGFR: 68.91 ml/min/1.73 m²; serum creatinine: 1.42 mg/dL. Multivariate analysis showed recipient age, female status, (Figure. 1)and Vol/BSA ratio significantly impacted eGFR (Table.1). Mean eGFR by Vol/BSA tertiles: • Lowest: 60.95 ± 25.81 ml/min/1.73 m². • Middle: 69.67 ± 25.83 ml/min/1.73 m². • Highest: 75.95 ± 33.36 ml/min/1.73 m² ($p = 0.004$). The difference in eGFR across tertiles was statistically significant ($p = 0.004$).

Conclusions: Our study demonstrates that a larger donor kidney volume relative to the recipient's body surface area (BSA) is associated with improved post-transplant outcomes. These findings underscore the importance of meticulous donor-recipient matching to enhance transplant success and reduce complications.

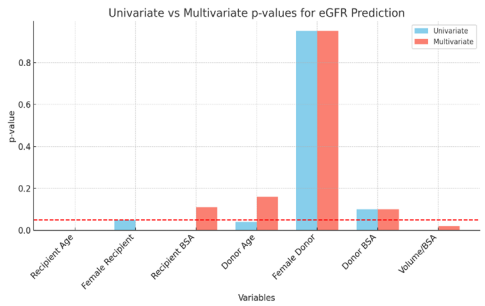

Figure.1

Variables	Volume/BSA ratio			p-value*
	Low (48.61 to 99.38) n = 81	Middle (99.39 to 125.35) n = 80	High (125.36 to 210.46) n = 83	
Recipient age (in years), mean ± SD	38.25 ± 10.97	35.92 ± 11.75	34.02 ± 11.84	0.06
Female recipient, n (%)	05 (6.2)	14 (17.5)	15 (18.1)	0.04
Recipient BSA (m^2), mean ± SD	1.76 ± 0.17	1.64 ± 0.18	1.56 ± 0.19	0.01
Donor age (in years), mean ± SD	51.12 ± 11.59	48.62 ± 10.22	48.94 ± 1.10	0.27
Female donor, n (%)	70 (86.4)	65 (81.3)	54 (65.1)	0.003
Donor BSA (m^2), mean ± SD	1.63 ± 0.16	1.65 ± 0.18	1.70 ± 0.18	0.04
Post operative Serum Creatinine (mg/dl), mean ± SD	1.58 ± 0.71	1.44 ± 0.65	1.24 ± 0.76	0.07
Post-operative eGFR	60.95 ± 25.81	69.67 ± 25.83	75.95 ± 33.36	0.004

Table.1

EP_353 GUINNESS WORLD RECORD OF ORGAN DONATION & INCREDIBLE JOURNEY OF HAYAT - UNITED ARAB EMIRATES

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Background: In recent years, the UAE has established a robust deceased donor organ donation and transplantation program. Hayat, which means life in Arabic, is the National Human Organ and Tissue Donation and Transplantation Program, created in September 2020 under the supervision of the Ministry of Health and Prevention -MOHAP. In addition to establishing appropriate legislation, the training of health professionals has carried out awareness-raising activities in a multicultural society, including the voluntary registration of donation intentions.

Methods: Establish a new global registry for the largest number of online organ donation records in a one-hour period in the Guinness book. Different segments of society were invited in advance, encouraging them to spread the word in their communities for people to sign up at a specific date and time. Entries were monitored live by Guinness auditors in an auditorium. The time count was started, and the records were monitored. Access was made through the home page https://mohap.gov.ae/en/hayat

Results: Before the start of the online challenge, 21,357 residents of various nationalities were registered in the Hayat registry. After an hour, another 4,010 registries were added, and the number increased to 25,367, setting a new world record for recording donation intentions in a period of one hour. Currently, more than 30 thousand registrations have been made.

Conclusions: The establishment of donation and transplant programs requires clear institutional strategies, government support with specific legislation and regulation, specialized health care team training, to broad communication support. Social awareness actions can be useful for publicizing these programs, in addition to motivating interest in the subject of organ donation as part of health care programs.

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EP_354 LIVERWEIGHTGRAFT-CT: ARTIFICIAL INTELLIGENCE PROTOCOLS IN THE ASSESMENT OF WEIGHT OF GRAFTS FOR LIVER TRANSPLANTATION

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Background: An accurate assessment of graft weight and volume prior to liver transplantation is crucial to optimize organ allocation and ensure effective transplantation. Our study aims to employ artificial intelligence (AI) protocols on donor CT scans to achieve highly precise predictions of these parameters.

Methods: We identified and analyzed morphological parameters and available CT images from 76 donors within our center in Turin over the past four years. For each donor, we ensured the availability of organ weight measured at the conclusion of bench surgery. The data from 50 donors, along with total liver volumes obtained from their baseline CT scans, were used to train an AI software developed by our center in collaboration with the Polytechnic University of Turin. The software was subsequently employed to estimate the graft weight for the remaining 26 donors, and its results were compared with the known actual liver weight. Finally, the same technique was applied to evaluate the volume and weight of eight split grafts performed at our center, for which both CT and actual weight data were available. In the secondary analysis, we combined CT data with biopsy results from all transplanted livers to stratify volume data based on the presence of steatosis. Additionally, donor morphological parameters were integrated to enhance the precision of weight and volume predictions.

Results: The error between the AI-estimated weight and the actual weight averaged 4% for whole livers and 6.5% for split grafts.

Conclusions: The preliminary results of this study are promising . Increasing the number of cases to further train the AI model is expected to improve these outcomes

EP_355 FLUID MANAGEMENT IN LIVING KIDNEY DONOR NEPHRECTOMY ON THE DONOR AND RECIPIENT OUTCOMES: A META-ANALYSIS

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Background: Living kidney donor nephrectomy offers an avenue of treatment for patients suffering end stage renal disease. This procedure offers superior outcomes compared to other forms of renal replacement therapy such as dialysis and kidney transplantation from cadaveric donors. Living donor nephrectomy also does not pose significant risks to the donors. However, appropriate fluid hydration is paramount for the successful outcome for both the donor and recipient. Overhydration is associated with renal interstitial edema which is detrimental to both the recipient and the donor. Underhydration, however, is also detrimental as this can lead to acute kidney injury to both the recipient and donor. This study aims to find out the ideal fluid management during living donor nephrectomy for the optimal outcome for both the donor and recipient.

Methods: This study was a meta-analysis conducted in alignment with the PRISMA-P guidelines for systematic reviews and meta-analyses. It focused exclusively on adult patients who have undergone donor nephrectomy. The search strategy involved utilizing electronic databases such as The Cochrane Library, PubMed, Google Scholar, HERDIN and ScienceDirect. Keywords including “intraoperative fluid”, “fluid management”, “donor nephrectomy”, “postoperative serum creatinine”, and “postoperative graft function” will be used to identify relevant studies.

Results: Three studies were included in the meta-analysis. The overall pooled mean difference showed no significant difference in the change in creatinine after nephrectomy in donors who had restrictive versus liberal volume fluid management (MD=1.83, 95%CI= -4.27 to 7.93, p=0.58). Also, no significant difference in the change in creatinine after nephrectomy in recipients who had restrictive versus liberal volume fluid management (MD=45.94, 95%CI= -64.03 to 155.90, p=0.41). The overall pooled risk ratio showed no significant difference in the risk of delayed graft function (RR=0.90, 95%CI=0.25 to 4.37, p=0.88).

Conclusions: In the meta-analysis, results showed that there were no significant differences seen in the creatinine levels of both kidney donors and recipients among the groups receiving different fluid management protocols. Also, it did not negatively affect graft function from a safety perspective.

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EP_356 FIRST REPORTED CASE OF KIDNEY TRANSPLANTATION FROM A DONOR WITH FAMILIAL HYPERKALAEMIC HYPERTENSION

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Background: Familial hyperkalaemic hypertension (FHHt; Gordons syndrome) is a rare monogenic cause of hypertension. It is due to mutations that lead to activation of the sodium chloride cotransporter (NCC) in the distal tubule, resulting in hypertension, hyperkalaemia, metabolic acidosis, and hypercalciuria. The mainstay of treatment is NCC inhibition with a thiazide diuretic. Use of kidneys from donors with FHHt has not been reported before.

Methods: A 27-year-old male with known FHHt, ankylosing spondylitis, and rheumatoid arthritis became a donor after brain death after suicide. Both kidneys were transplanted. We report their clinical outcomes, focusing on recipient physiological changes.

Results: The left kidney was transplanted into a 22-year-old female with end stage kidney disease (ESKD) due to Alport's syndrome. HLA mismatch was 010 and she required one session of dialysis 5 days post-transplant. She was initiated on a thiazide diuretic 7 days post-transplant after graft function and is now 13 months post-transplant with good graft function (creatinine 107umol/l), normokalaemia, and normotension. She has had recurrent urinary tract infections leading to a reduction of immunosuppression, but no rejection episodes. The right kidney was transplanted into 31-year-old male with ESKD of unknown cause. HLA mismatch was 110 and he had primary graft function. 5 weeks post-transplant he developed hypertension, hyperkalaemia and metabolic acidosis. He was subsequently initiated on a thiazide diuretic (Bendroflumethiazide) with normalisation of physiological derangement. He had graft dysfunction at week 6 with acute tubular injury and prominent tubular calcium on transplant biopsy (**Figure 1a**). 26 weeks post-transplant he was diagnosed with post-transplant lymphoproliferative disease (PTLD), with involvement of the transplanted kidney (**Figure 1b&c**), developed sepsis and died.

Conclusions: We report the first cases of kidney transplantation from a deceased donor with FHHt. Physiological changes in recipients were successfully managed with thiazide diuretics. Whether the development of recurrent UTIs or PTLD was associated with FHHt, or its treatment, is unknown.

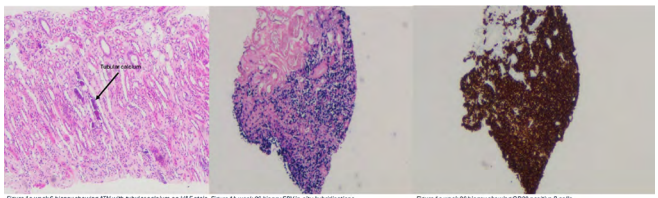

Figure 1a week 6 biopsy showing ATN with tubular calcium on H&E stain Figure 1b week 26 biopsy EBV in-situ hybridisations Figure 1c week 26 biopsy showing CD20 positive B cells

EP_357 OPTIMIZING ORGAN DONATION- A SOCIODEMOGRAPHIC AND PROCEDURAL ANALYSIS OF 110 EFFECTIVE DECEASED ORGAN DONORS IN 2024

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Background: Organ donation involves various steps, with sociodemographic and procedural factors significantly affecting outcomes. Analyzing these variables can help optimize the donation process and identify areas for improvement. This study aimed to assess sociodemographic factors, procedural timelines, and family consent dynamics to improve organ donation in the UAE.

Methods: A retrospective analysis of 110 deceased organ donors was conducted in 2024. The study focused on the following variables: a) Sociodemographic Variables: Gender, Age; b) Genetic Variable: ABO Blood Group; c) Process Variables: Time from Death Declaration by Neurological Criteria to Organ Retrieval, Time to Repatriate the Donor's Body, Family Consent Dynamics.

Results: The average donor age was 45 years (range: 20–85). Gender distribution was 83.8% male and 16.2% female. Donors came from diverse nationalities: 32 from India, 23 from the Philippines, 17 from Bangladesh, 18 from Pakistan, and others. Blood group distribution: O+ve (42.7%), A-ve (2.7%), A+ve (26.4%), AB (5.5%), B-ve (0.9%), and B+ve (21.8%). The average time from death declaration to obtaining family consent was 5.2 days (O- 13 days). The average time from organ retrieval to body repatriation was 20.6 days (range: 3–56 days), reflecting logistical delays.

Conclusions: This study highlights key areas for improving the organ donation process, including reducing the time to secure family consent and improving body repatriation timelines. These timeframes are gradually decreasing. The diversity in donor nationalities emphasizes the need for tailored communication strategies, such as multilingual support and culturally sensitive approaches during family interactions.

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EP_358 A SAFE METHOD FOR EVALUATING POTENTIAL DECEASED ORGAN DONOR INCREASES THE NUMBER OF ORGANS FOR TRANSPLANTATION.

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Background: The number of utilized deceased organ donors and the quality of transplanted organs can be affected without an effective, reproducible clinical-laboratory evaluation methodology that guarantees traceability.

Methods: We developed a clear and safe method, based on 2 fundamental principles: 1) Up-to-date knowledge of absolute contraindications for organ donation and, 2) Decision-making based on three questions, which can be repeated throughout the organ donation process (Since the identification of the PD until the results of the organ biopsy or other complementary study after the organ retrieval) seeking to minimize the infectious and cancer diseases risk transmission. Absolute contraindications were categorized into 4 groups: A) Serological, B) Cancer: Solid and haematological tumours, C) Infectious diseases, D) Biological risk for transmission of infectious diseases and cancer. The decision-making questions were 3: 1) What was the cause of death by neurological criteria (DNC)? ; 2) Are there any absolute contraindication for organ donation? 3) Are there any relative contraindications for organ donation? Each PD was subjected to the same methodology. The questions were answered after knowing: a) Clinical History of the PD, b) Cause of DNC, c) Results of laboratory tests, d) Previous illnesses, e) Physical examination and, f) Biological risk behaviour. The set of information was evaluated following this methodology by a group of doctors since 2022 to 2024. This method was applied in the United Arab Emirates Organ Procurement Organization.

Results: 2021 was the year before this methodology. 2021: 39 effective donors (ED) were obtained, and 147 transplants (TX) were performed. 2022: 55 ED were obtained and 203 TX were performed (increase of 41% and 38%, respectively). 2023: the number of ED increased to 85 and 262 TX (54% and 30% increase, respectively). 2024: the number of ED increased to 110 and 307 TX (29% and 17% increase, respectively).

Conclusions: This methodology used proved to be useful and reproducible and can directly contribute to the increase in donors and organs. The repetitive nature of different doctors involved in donor validation generated a flow of decision making. As it is an easily reproducible methodology, it can be implemented by OPOs and hospitals dedicated to organ donation.

EP_359 EXPERIENCE REPORT: THE IMPACT OF IN-HOSPITAL ORGAN DONATION COORDINATORS ON ORGAN DONATION IN DUBAI HOSPITALS (2022-2024)

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Introduction / Background: Organ donation is a vital component of global healthcare systems. In Dubai, significant advancements have been achieved between 2022 and 2024 through the introduction of In-Hospital Organ Donation Coordinators (ODCs) and enhanced training programs for healthcare workers (HCWs). These initiatives aimed to streamline the donation process, increase referrals, and boost organ retrieval rates.

Objectives: This study evaluates the impact of ODCs and HCW training on organ donation outcomes in Dubai hospitals, focusing on referrals, consents, and organ retrieval rates.

Methods: A retrospective review of organ donation data (2022–2024) analyzed referrals, consents, and retrievals to assess the role of ODCs and HCW training.

Results: From 2022 to 2024, organ donation saw significant growth: • Referrals rose from 149 to 321 (+115.4%). • Consents increased from 26 to 62 (+138.5%). • Organs retrieved grew from 73 to 178 (+143.8%). Year-over-year growth: • **2022–2023:** Referrals +55.7%, consents +80.8%, retrievals +91.8%. • **2023–2024:** Referrals +38.4%, consents +31.9%, retrievals +27.1%. Improvements are attributed to ODCs' role in case management and HCW training, which enhanced donor identification, family communication, and process efficiency.

Discussion: ODCs played a crucial role in improving organ donation outcomes by educating HCWs and providing operational support. Training programs enhanced HCWs' ability to identify donors and initiate timely referrals, contributing to increased referrals, consents, and organ retrievals.

Conclusion: ODCs and HCW training have significantly boosted organ donation rates in Dubai. Continued investment in these initiatives is essential to sustain progress and save more lives.

Key Data Overview

Year	Number of Referrals	Increase (%) Since Previous Year	Number of Consents Obtained	Increase (%) Since Previous Year	Total Organs Retrieved	Increase (%) Since Previous Year
2022	149	—	26	—	73	—
2023	232	55.70%	47	80.77%	140	91.78%
2024	321	38.36%	62	31.91%	178	27.14%

Total Increase (2022-2024): • Referrals: 115.4%. • Consents: 138.46%. •Organs Retrieved: 143.84%. This report highlights the transformative role of ODCs and HCW training in creating a more organized and effective framework for organ donation in Dubai.

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EP_360 HEPATIC ARTERIAL BUFFER RESPONSE IS PRESERVED IN EX SITU PERFUSED WHOLE AND HEMI PORCINE LIVERS

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Background: The hepatic arterial buffer response (HABR) describes compensatory flow changes in the hepatic artery in response to changes in portal venous blood flow. When portal flow decreases, hepatic arterial flow increases to maintain total liver flow. This is primarily to maintain constant hepatic metabolism of products of digestion. Ex situ perfusion systems aim for a physiological environment to maintain normal liver function. Understanding how to best achieve this including through manipulation of vascular flows is critical to its success.

Methods: We investigated the effect of portal venous pressure (PvP) modulation on livers perfused using the OrganOx *metra*. Six whole livers and four right hemi-livers from circulatory death donors were perfused for up to 24 hours. PvP was reduced to 12mmHg by occlusion of the portal inflow line using an adjustable pinch valve in three whole and two hemi-livers. Hepatic arterial resistance and portal-to-arterial blood flow ratio was calculated at hourly intervals.

Results: PvP modulation reduced hepatic arterial resistance at all time points beyond 9 hours of normothermic machine perfusion. Hepatic arterial resistance (mean±SE) with vs without PvP modulation was 99±9 vs 198±27 mmHg/L/min at 12 hours of perfusion (p=0.005). Total hepatic blood flow was similar at all time points beyond 1 hour despite portal modulation. The ratio of portal to arterial blood was significantly lower with portal modulation at all time points except 1 and 7 hours.

Conclusions: PvP modulation reduces hepatic arterial resistance in ex situ perfused livers and maintains total hepatic blood flow. PvP modulation increases the proportion of total blood flow to the hepatic arterial system compared to the portal venous system. Many ex situ perfusion protocol aim for physiological ratios of portal:arterial blood flow (3:1) however oxygen delivery to the portal venous system is higher than in vivo due to supraphysiological oxygenation of portal venous blood. In perfused livers where portal blood is highly oxygenated it may be desirable to lower the portal:arterial blood flow ratio to improve oxygen supply to the biliary epithelium (arterial supply). We demonstrate that the portal:arterial blood flow ratio can reproducibly be lowered whilst maintain total hepatic blood flow by reducing PvP.

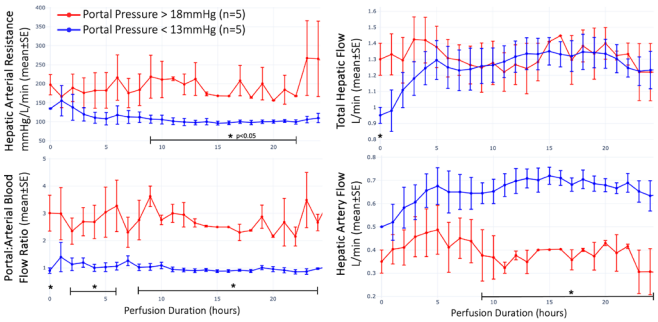

Figure 1. Effect of portal venous pressure modulation in porcine livers (n=10) on hepatic arterial resistance, portal:arterial blood flow ratio, total hepatic blood flow and hepatic artery blood flow

EP_361 HYPOTHERMIC VS NORMOTHERMIC MACHINE PERFUSION IN HUMAN KIDNEY GRAFT RECONDITIONING: A META ANALYSIS

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Background: Hypothermic machine perfusion (HMP) has been widely accepted as a preservation strategy for suboptimal donor kidneys. Normothermic machine perfusion (NMP) is a new preservation method which might offer similar or better outcomes. This study presents a systematic review and meta-analysis comparing HMP and NMP in graft assessment, reconditioning, and optimisation in the clinical settings.

Methods: Databases (Pubmed, Science Direct, Cochrane, and EBSCOhost) were searched using pre-specified MeSH keywords with Boolean operators. In addition, a hand-search strategy was used to identify additional articles. The selection of studies was done by four reviewers. Studies which fulfilled the inclusion criteria underwent full-text review. The quality of included articles was conducted using Newcastle-Ottawa Scale (NOS).

Results: A total of 2 studies from an initial 38 publications were selected. In the clinical setting, 79 kidneys and 24 kidneys were transplanted following HMP and NMP, respectively. There was no significant difference for HMP vs. NMP regarding post-transplant PNF [Odds Ratio (OR): 2.09; 95% CI: 0.11, 41.64] and DGF [OR: 1.68; 95% CI: 0.63, 4.44]. For secondary outcomes, HMP and NMP had no differences in creatinine level POD 1, 2, 3, 1 week, 1 month, 3 months, 6 months, and 1 year following transplantation [Mean Difference (MD): 4.29; 95% CI: -8.91, 17.48]. Post-transplant EGFR also showed no difference between HMP and NMP in POD 1, 1 week, 1 month, 3 months, 6 months, and 1 year [MD: 0.94; 95% CI: -1.73, 3.61]. Length of stay, 1-year-patient survival, and 1-year-graft survival were also shown no significant differences between the two groups.

Conclusions: In our study, the direct comparison of HMP and NMP kidney perfusion in human kidney transplantation demonstrated no difference towards PNF, DGF, creatinine, eGFR, length of stay, 1-year-patient survival, and 1-year-graft survival.

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EP_362 THE MACHINE PERFUSION EXPERIENCE ON DISCARDED LIVER GRAFTS IN LOW-MID VOLUME TRANSPLANT CENTRE

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Background: Because of donor shortage, about 20% of potential liver transplant (LT) recipients still die during waiting list. To increase potential donor pool, use of Extended Criteria Donors (ECDs) became a widespread practice. Novel machine perfusion (MP) techniques are a useful tool to increase the use of ECD based on their potential to enable graft functional evaluation and organ recovery.

Methods: From January 2018 to December 2024, 22 consecutive discarded liver grafts from brain death donors [median age: 60 (IQR: 50-65) years, median BMI: 25 (IQR: 23-29), median Donor Risk Index (DRI) of 1.8 (IQR: 1.5-1.9)] underwent normothermic (NMP) or hypothermic machine perfusion (HOPE) at Tor Vergata University, Rome. Based on MP parameters, grafts were considered eligible or not for LT. Primary endpoint of the study was the assessment of post LT graft function defined by incidence of Early Allograft Dysfunction (EAD). Secondary aim included evaluation of flow parameters according to different techniques of MP.

Results: 19/22 grafts fulfilled viability criteria and were transplanted (utilization rate of 86%). Seven recipients (36.8%) experienced EAD. Median ALT peak during first 7 days after LT was 881 U/L (IQR: 551-1538). In NMP group (N=4), after the first hour of perfusion, the median hepatic artery and portal vein flow rate were 0,3 L/min (IQR: 0,2-0,4) and 1,0 L/min (IQR: 0,4-1,2) respectively. For HOPE group (N=15), median portal venous flow rate passed from 0,4 L/min (IQR: 0,3-0,6) to 0,5 L/min (IQR: 0,3-0,6) after the first hour achieving 0,6 L/min (IQR: 0,4-0,6) by the end of the process. Median arterial flow rate after 60 minutes was 81 mL/min (IQR: 54-104) and then slowly decreased to 74 mL/min (IQR: 64-87) at the end of HOPE.

Conclusions: We report herein the first Italian MP series of discarded liver grafts in a low-mid volume LT centre. In this setting, results suggest that MP may increase organ utilization rate, but it is effective only in selected ECD grafts.

EP_363 NORMOTHERMIC MACHINE PERFUSION COULD REDUCE DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: Historically, the use of marginal kidneys was limited due to suboptimal preservation methods. Normothermic machine perfusion (NMP) preserves physiological activity during the preservation process, potentially improving graft function and viability, expanding the use of marginal kidneys. While preliminary results are promising, NMP has not yet undergone sufficient clinical trials to determine whether it offers advantages over more widely used techniques. The aim of this systematic review is to assess several outcomes between kidneys that underwent NMP compared to traditional preservation methods after kidney transplant.

Methods: A systematic review was conducted following PRISMA guidelines on 12/20/2024. Randomized controlled trials, case series, and studies comparing NMP with hypothermic machine perfusion (HMP) or static cold storage (SCS) were included. The primary outcome assessed was delayed graft function (DGF). Secondary outcomes included primary non-function (PNF), acute rejection, and one-year graft survival.

Results: Eight NMP studies met the inclusion criteria. Meta-analysis showed significant differences in DGF between NMP (n=220) and control (n=308 [HMP=70, SCS=238]) groups (OR: 0.47 [0.22, 0.99], p<0.05). There were no significant differences between NMP and controls for PNF (OR: 1.07 [0.37, 3.05]) acute rejection (OR:1.60 [0.99, 2.60]), or one-year graft survival (OR:1.03 [0.46, 2.30]).

Conclusions: These findings suggest that NMP yields similar adverse outcome rates compared to traditional methods. Notably, NMP could be associated with reduced rates of DGF. While NMP is a promising technique for renal allograft preservation, further randomized controlled trials are necessary to definitively establish its benefits over conventional preservation methods.

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EP_364 THE EFFECTS OF HYPOTHERMIC VS NORMOTHERMIC MACHINE PERFUSION IN A TRANSLATIONAL PORCINE KIDNEY MODEL: A META ANALYSIS

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Background: This study presents a systematic review and meta-analysis comparing the effects of HMP vs. NMP in a translational porcine kidney model.

Methods: Databases (Pubmed, Science Direct, Cochrane, and EBSCOhost) searching were done using pre-specified MeSH keywords with Boolean operators. In addition, a hand-search strategy was used to identify additional articles. The selection of studies was done by four reviewers. Studies which fulfilled the inclusion criteria underwent full-text review. The quality of included articles was conducted using Newcastle-Ottawa Scale.

Results: A total of 5 studies from an initial 38 publications were selected. 76 porcine kidneys were studied in both HMP and NMP group. NMP had a significant difference in perfusate flow rates compared with HMP [MD 20.09; 95%CI:13.36, 26.82]. For the other perfusion parameter outcomes, HMP and NMP showed no significant difference towards renal resistance index [MD -0.00; 95%CI:-0.53, 0.53), oxygen consumption [MD 1.22; 95%CI:-1.57, 4.01], and urinary output [MD 1.27; 95%CI:-2.21, 4.75]. This study also demonstrated that HMP had no significant difference with NMP on creatinine clearance [MD -2.17; 95%CI:-7.79, 3.45], fractional sodium excretion (FENa) [MD -0.00; 95%CI:-0.11, 0.11], lactate [MD -1.09; 95%CI:-2.51, 0.33], creatinine urine/plasma ratio [MD -9.38; 95%CI:-28.81, 10.05], and pH [MD -0.06; 95%CI:-0.17, 0.05]. Histological parameters, including cytoplasmic vacuolation, tubular dilation, interstitial oedema, epithelial shedding, and loss of tubular integrity, were also comparable between two groups.

Conclusions: In this study, NMP demonstrated to have better perfusate flow rates compared to HMP in translational settings. However, HMP and NMP showed no significant difference on other perfusion parameter outcomes (renal resistance index, oxygen consumption, and urinary output), perfusate analyses (creatinine clearance, FENa, lactate, creatinine urine/plasma ratio, pH), and histological analyses.

EP_365 KIDNEY TRANSPLANTATION FROM DONORS AFTER CARDIAC DEATH WITH 20 MINUTES OF NO-TOUCH PERIOD: SINGLE-CENTER EXPERIENCE

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Background: The use of kidneys from deceased donors after cardiac death (DCD) is now considered a well-established strategy to address shortage of organs. In Italy law requires 20 minutes of no-touch period that prolongs drastically the warm ischemia period, which can affect organ quality. We present our experience with kidney transplants from DCD donors using normothermic regional perfusion (NRP) in situ followed by End-Ischemic Hypothermic Machine Perfusion (EIHP). This combination offers several benefits, mainly reduction in ischemia-reperfusion injury.

Methods: From March 2019 to December 2024, 49 transplants from DCD were performed, including 15 dual kidney transplants (30%). The average age of donors and recipients was 59 (21-81) and 53 (21-73) yo, respectively. Single and double allocation was performed according to our regional guidelines based on age, renal function, and biopsy score data. Donors underwent NRP during procurement, and kidneys were placed in a hypothermic machine perfusion system after bench surgery using two different EIHP systems.

Results: Delayed graft function (DGF) was recorded in 40.8% of cases. In 10% of patients, there was functional DGF (fDGF), while no primary non-function (PNF) was recorded. The mean creatinine at discharge was 2.9 mg/dL (0.9-9.8) and 1.5 mg/dL (0.9-2.9) at 30 days. The average length of stay was 14 days (9-30). The kidneys were perfused in the hypothermic machine for an average of 432 minutes (160-930).

Conclusions: The donation program from DCD donors supported by NRP at procurement and the use of EIHP pre-transplant appears effective and safe. In the absence of PNF, graft survival at 30 days was 100%, achieving optimal organ function. The clinical evaluation of the donor, combined with the physiological response parameters of the organ during normothermic in situ and hypothermic ex vivo perfusion, along with the biopsy score, allows for the implementation of available organs for transplant using this category of donors with reasonable safety.

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EP_366 HYPOTHERMIC VS NORMOTHERMIC MACHINE PERFUSION IN PORCINE KIDNEYS AUTOTRANSPLANTATION MODEL: A META ANALYSIS

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Background: Hypothermic machine perfusion (HMP) is a well-established preservation technique for suboptimal donor kidneys. Recently, normothermic machine perfusion (NMP) has emerged as an alternative approach that may provide comparable or even improved outcomes. This study presents a systematic review and meta-analysis comparing HMP and NMP in graft assessment, reconditioning, and optimization in porcine kidneys auto-transplantation model.

Methods: Online databases (Cochrane, EBSCOhost, Pubmed, and Science Direct) were searched using pre-specified keywords. Additionally, additional articles were identified using a hand-search strategy. The studies were selected by four reviewers. Studies which fulfilled the inclusion criteria underwent full-text review. Newcastle-Ottawa Scale (NOS) was used to assess the quality of included articles.

Results: Two studies were identified from a total of 38 initial publications. In auto-transplantation model, 22 porcine kidneys underwent auto-transplantation, 11 kidneys for HMP and the rest for NMP. Recipient survival was shown comparable between both groups [OR 1.06; 95% CI: 0.12, 8.99]. For perfusion characteristics, both groups demonstrated no significant difference in flow rates [MD -1.72; 95% CI: -3.61, 0.17] and intrarenal resistance index [MD 0.10; 95% CI: -0.49, 0.69]. In perfusate analysis, NMP resulted in better fractional excretion of sodium (FENa) compared to HMP [MD 1.83; 95% CI: 0.22, 3.45]. While, LDH parameter favored HMP group [MD -1.28; 95% CI: -2.31, -0.26]. Both groups showed no significant difference in the peak serum creatinine [MD 0.97; 95% CI: -0.66, 2.60], lactate [MD -5.09; 95% CI: -5.47, -4.71], and glucose [MD 2.47; 95% CI -4.94, 9.89]. Histological analyses, including tubular dilatation, tubular debris, vacuolation, and infiltration, was shown no difference [MD 0.20; 95% CI: -0.37, 0.77].

Conclusions: Porcine kidneys auto-transplantation model, FENa and LDH were shown to have significant difference between the two groups. HMP and NMP had no statistically significant difference for other parameters, such as recipient survival, perfusion characteristics, perfusate analyses, and histological analyses.

EP_367 EVALUATION OF THE PERCEPTION OF MULTIDISCIPLINARY CARE FOR LIVING KIDNEY DONORS FOR PEDIATRIC RECIPIENTS

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Background: The multidisciplinary care of living kidney donors is crucial for ensuring a successful evaluation process and the effective functioning of the program. The Transplant Nurse Coordinator (TNC) must coordinate the activities of the multidisciplinary team and the donor to ensure continuous synergy between all parties. The objective of this study is to assess the effectiveness and efficiency of the multidisciplinary care provided to living kidney donors, with the TNC acting as the organizational leader.

Methods: Donors engaged between May 2023 and June 2024 were included, excluding those who had already completed the donation process. Each potential donor was administered a 13-item questionnaire.

Results: 100% of participants reported receiving clear information on the risks and benefits of donation. The identified support figures were the physician (100%), nurse (67%), and psychologist (67%). Emotional support was considered satisfactory by 66.7% of participants, while 16.7% found it inadequate. In 75% of the cases followed by the transplant center but monitored remotely, participants recognized the need to enhance the communication between the reference center and peripheral hospitals through the continuous presence of a contact person.100% of participants acknowledged the multidisciplinary care.

Conclusions: Our results emphasize the central role of multidisciplinary care in the living kidney donation process. The patients who had direct and continuous contact with the transplant center benefitted from the central role of the TNC as coordinator of the process. It would be advisable to develop a standardized process that introduces the TNC early as the primary contact and outlines the involvement of the multidisciplinary team throughout the process. To improve donor care, proper planning and communication of the steps involved in the process are essential, leveraging the collaboration of various professionals and fostering opportunities for direct interaction with the multidisciplinary team. Strengthening the communication and training network between the transplant center and local services is fundamental to ensure that patients feel comprehensively supported, even when they are not directly interacting with the reference transplant center.

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EP_368 HYPOTHERMIC OXYGENATED PERFUSION WITH HTK SOLUTION: A VIABLE ALTERNATIVE TO UW IN SINGLE-STRATEGY LIVER

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Background: Hypothermic oxygenated machine perfusion (HOPE) improves liver transplantation (LTx) outcomes, with University of Wisconsin (UW) solution as the standard perfusate. Histidine-tryptophan-ketoglutarate (HTK), commonly used as a preservation solution, may eliminate the need to switch solutions during organ processing. This study evaluates the feasibility, efficacy, and cost-effectiveness of HTK for HOPE prior to LTx.

Methods: From May 2023 to October 2024, 23 liver grafts perfused with HTK during retrieval underwent HOPE with HTK solution. A matched cohort of 23 grafts from 150 transplants after HOPE with UW solution (May 2018–May 2023) was identified using donor and recipient criteria, cold ischemia time, and perfusion duration. Outcomes, including early allograft dysfunction (EAD, Olthoff criteria), biliary complications, dialysis, and cost-effectiveness, were analyzed.

Results: Matched cohorts had comparable median cold ischemia times (5.1 hours) and HOPE durations (190 minutes). Postoperative metrics, including ICU stay (HTK: 8 days vs UW: 9 days, p=0.760), hospitalization (HTK: 23 days vs UW: 21 days, p=0.742), and complication index (HTK: 33.5 vs UW: 36.5, p=0.740), were similar. EAD incidence was identical (47.8%, p=1.000). HTK showed reduced trends in biliary complications (13.0% vs 30.4%, p=0.153) and dialysis (17.4% vs 31.8%, p=0.260). HTK use saved approximately €11,000 across 23 procedures, requiring 4 liters per perfusion.

Conclusions: HTK is a viable alternative to UW for HOPE in a single-solution strategy, demonstrating comparable clinical outcomes, significant cost savings, and trends toward fewer biliary complications and dialysis requirements. Larger studies are warranted to confirm these findings and further explore HTK's potential benefits in liver transplantation.

EP_369 DCD LIVER TRANSPLANTATION WITH ELDERLY DONORS: CASE SERIES WITH 92 YEARS OLD GRAFTS

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Background: DCD liver grafts are increasingly used to expand the donor pool for adult transplantation. To improve outcome after DCD liver transplantation, ex situ machine perfusion is used as an alternative organ preservation strategy, with the advantage of dynamic evaluation of the graft. We here report an unprecedented transplantation of an elderly DCD liver graft after hypothermic oxygenated machine perfusion (D-HOPE) in a setting of 20 minutes no touch-time.

Methods: Four grafts were retrieved from 92 y.o. donors. The average total Warm Ischemia Time (tWIT) was 41 minutes while the functional one (fWIT) was 32 minutes. After the retrieval the grafts function was evaluated during D-HOPE for at least 3 hours. Lactates were stable. Arterial and portal perfusion showed a progressive improvement in flow and drop of resistance. The recipients were all cirrotic patients with different etiology (HCV, NASH, alcohol-related) with an average MELD-Na score of 17.

Results: All the transplantations were performed with cava preservation technique and an end-to-end biliary anastomosis. The average total Cold Ischemia Time (tCIT) was 465 minutes.In all cases, postoperative AST, ALT, INR and total bilirubin normalized within a few weeks. No evidence of Early Allograft Dysfunction was demonstrated. The average hospital stay was 17 days. No biliary complication occured, with particular reference to biliary strictures. Nowadays, all the patients are in good condition with a completely normal liver function with a median follow up of 6 months.

Conclusions: This case series reports successful transplantations of elderly DCD liver grafts in a high risk setting due to a long no-touch period. It underlines the role of the sequence NRP-D-HOPE in expanding the donor pool and improving outcome after DCD transplantation.

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EP_370 SCOPE OF ORGAN DONATION FROM NEONATES AND INFANTS: A REVIEW OF FIVE-YEAR MORTALITY IN A NEONATAL INTENSIVE CARE UNIT

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Background: Donor organ shortage limits renal transplants. Neonatal and infant kidney donation remains underutilized despite promising outcomes. This study reviews NICU deaths at Corniche Women and Children Hospital, Abu Dhabi, to assess the feasibility of kidney donation from neonates and infants.

Methods: We reviewed the NICU mortality from 01 Jan 2019 to 31 December 2023. Data were collected retrospectively following approval from the hospital audit department, included all babies born at or after 36 weeks of gestation where a futility of treatment decision was made before death. Cases with an antenatal diagnosis of oligohydramnios, CAKUT, or persistent absence of urine in the foetus's bladder were excluded. We also excluded patients with muti-organ failure involving the kidneys, anuria after birth, death due to sudden deterioration, or the parent's disagreement to donation.

Results: During the study period, there were 297 deaths in the NICU; 57 were born at or after 36 weeks, and 42 fulfilled the inclusion criteria. Three patients (1 male, 2 female) were identified as suitable potential kidney donors, two were diagnosed as brainstem dead, and one anencephaly diagnosed on the antenatal scan. The mean birth weight was 2.97 Kg, and the mean time to death was 10 days following the futility of the treatment decision. The two brain stem dead patients were considered for donation but due to logistic reasons donation didn't occur. In the case of anencephaly, donation was not sought due to ethical uncertainties.

Conclusions: Organ donation is feasible from neonates and infants. Our study may have underestimated the number of suitable potential donors (7%) due to the retrospective nature and stringent exclusion criteria. A prospective audit should be established at a national level. Awareness among the healthcare staff (including NICU and transplant physicians), organ procurement organization and general population is critical to achieving donation from neonates and infants.

EP_371 FACTORS RELATED TO RELATIVES' CONSENT FOR INTENSIVE CARE FOR ORGAN DONATION: RESULTS OF A SPANISH MULTICENTER STUDY

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Background: The implementation of Intensive care to facilitate organ donation (ICOD) in Spain has shown to be a relevant factor for the maintenance of successful donation rates, accounting for 34.6% of deceased donation activity in 2023. Considering the limited available evidence about family consent in the context of ICOD, this study aimed to analyze relationships between consent or refusal to ICOD request and quantitative indicators of concurrent factors.

Methods: A prospective multicenter study was performed with an intentional sample of 47 Spanish hospitals with ICOD program. Hospitals retrieved and registered basic indicators during a 1-year period of n=329 cases of family interviews for ICOD by means of a centralized database. Main indicators included: family decision, reasons in favor/against ICOD consent, patient's will about donation, cause of death, decision-makers profile, relatives' satisfaction with medical attention, perceived family climate and relatives' emotional reactions at the time of interview. Descriptive and inferential analysis were performed.

Results: The reasons most frequently expressed to justify the refusal of ICOD by families were pre-existing opposed will to donate of the patient (47.6%) and ignorance of patient's will (25%). Main reasons expressed by relatives to grant consent were (non-exclusive): following patient's will (38.7%), wish of the own relatives (35.6%), reasons related to solidarity, helping others, usefulness or reciprocity (24.8%). The indicators that showed a stronger relationship with family decision were: knowledge of the patient's will (Likelihood ratio [LR]=216.03; p<.000), satisfaction with medical attention (LR=42.68; p<.000); socio-cultural level of the decision-makers (LR=33.54; p<.000); and family climate (LR=26.54; p<.000). A logistic regression model generated to predict the family decision based on main indicators obtained a 91.8% of accuracy in the classification of cases.

Conclusions: Variables related to relatives' consent for ICOD show a similar profile to other donation procedures, yielding a strong relationship with patients expressed will and relatives' satisfaction with medical attention.

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EP_372 EXPANDING THE DONOR POOL OVER THE AGE OF 70 IN CARDIAC TRANSPLANTATION - A SINGLE CENTER STUDY ANALYSIS

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Background: This study aims to evaluate the feasibility and outcomes of using hearts from donors aged 70 and above, comparing postoperative results with those from younger donors to assess the impact on transplant success and recipient survival.

Methods: This is a single-center, retrospective study conducted at the Cardiac Surgery Unit of the University of Bari. We analyzed data from heart transplant procedures performed between January 2022 and September 2024. The study population included recipients of donor hearts aged 70 years and older (n=14) and a control group of recipients from donors younger than 70 years. We collected and compared preoperative, intraoperative, and postoperative variables, including donor and recipient demographics, clinical characteristics, and outcomes such as 30-day and 1-year mortality rates, incidence of primary graft dysfunction (PGD), and the need for post-transplant extracorporeal membrane oxygenation (ECMO).

Results: Significant differences were observed in the following binary variables: • **Dyslipidemia**: The p-value was 0.0035, indicating a statistically significant difference between the two groups. • **Post-transplant ECMO use**: A p-value of 0.038 showed that recipients of older donor hearts had a higher likelihood of requiring ECMO support post-transplant. • **Primary Graft Dysfunction (PGD)**: A p-value of 0.046 suggested a higher incidence of PGD in recipients of hearts from elderly donors. Donor age ≥70 years was significantly associated with the use of post-transplant ECMO (p-value = 0.018), with a positive coefficient (1.6836), indicating that older donor age increases the odds of needing ECMO. However, other variables such as ischemic time, body surface area (BSA), and preoperative values of bilirubin and glomerular filtration rate (GFR) were not significantly associated with ECMO use or mortality at 30 days or one year. Kaplan-Meier survival curves showed no statistically significant differences in mortality rates between the two groups.

Conclusions: This study suggests that expanding the donor pool to include individuals over 70 years of age is feasible with careful donor selection and adequate postoperative monitoring.

EP_373 PROLONGED PRESERVATION OF LIVERS DONATED AFTER CIRCULATORY DEATH USING DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION

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Background: Liver transplantation with grafts donated after circulatory death (DCD) increases the risk of early graft failure due to ischemia-reperfusion (IR) injury-related complications. A 2-hour period of dual hypothermic oxygenated machine perfusion (DHOPE) has been shown to reduce IR injury-related complications, especially non-anastomotic biliary strictures (NAS). While prolonged DHOPE may safely extend the preservation time for brain-dead donor livers, its safety in DCD livers remains unclear. This study evaluates the safety and outcomes of prolonged DHOPE in DCD liver transplantation.

Methods: Between June 2022 and August 2024, 22 DCD livers underwent prolonged DHOPE (≥4 hours), with a median follow-up of 8 months post-transplant. A 1:1 time-matched control DCD group underwent DHOPE <4 hours. Outcomes included the 7-day peak value of alanine-aminotransferase (ALT;U/L), international normalized ratio (INR), and total bilirubin (µmol/L), as well as graft loss due to primary non function (PNF) or early hepatic artery thrombosis (eHAT) within 2 months. Death-censored graft survival and NAS incidence were assessed at 6 months. Data are presented as medians and ranges.

Results: The total preservation time was 12.0 hours (9.0-23.9) in the prolonged group and 8.8 hours (5.7-10.7) in the controls (p<0.001), with a respective DHOPE duration of 6.4 hours (4.7-19.7) and 3.0 hours (1.3-4.0). Peak laboratory values were comparable between groups: ALT (1525 U/L (440–3997) vs 962 U/L (335–4059), p=0.132), INR (2.2 (1.6–4.3) vs 2.4 (1.3–4.7), p=0.37), and bilirubin (108 µmol/L (23–282) vs 71 µmol/L (9–421), p=0.37). Death-censored graft survival was not significantly different (86% vs 100%, p=0.23), although in the prolonged group, three patients required re-transplantation due to one case of PNF (5%) and two after eHAT (9%). Symptomatic NAS occurred in two patients in the prolonged group (9%) and none of the controls.

Conclusions: Prolonged DHOPE in DCD livers did not result in a significant increase in graft-related complications, including PNF, eHAT and NAS. While graft survival has to be monitored in longer follow-up, it now appears to be safe to extend DCD liver graft preservation. This approach can optimize transplant logistics and facilitate daytime surgeries for high-risk DCD liver recipients.

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EP_374 CAN HYPOTHERMIC OXYGENATED PERFUSION MITIGATE THE IMPACT OF RECIPIENT WARM ISCHEMIA ? - A PRECLINICAL STUDY

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Background: Prolonged recipient warm ischemia (rWI) is an established risk factor for early liver graft failure especially for marginal grafts. End-ischemic Hypothermic Oxygenated Perfusion (HOPE) is now routinely applied to marginal grafts. However, the impact of HOPE in the context of prolonged rWI has not been studied to date.

Methods: Firstly, thermal kinetics of the liver graft during implantation were measured in human liver grafts. Second, based on these data, a rWI porcine model was established by placing the porcine liver graft in a 37°C heated water bath. The temperature was continuously monitored through a probe in the inferior vena cava. A total of 4 study groups were included. All the liver grafts were exposed to 30 min of donor warm ischemia prior to procurement followed by 6h of static cold storage and 2h of ex-situ reperfusion with autologous porcine blood at 37°C to simulate transplantation. We first analyzed the impact of rWI on early ischemia-reperfusion injury by comparing liver grafts exposed to a 60-min rWI period before reperfusion (rWI60), to a group without rWI (SCS). Second, we applied HOPE after static cold storage to each group (namely HOPE and HOPE rWI) to investigate the impact of HOPE on early ischemia-reperfusion injury depending on rWI.

Results: The temperature kinetics of the graft in our experimental rWI model were comparable to those observed in human liver transplantation, reaching a median temperature of 27,8°C after 30min. Porcine liver grafts undergoing rWI compared to livers without rWI had a significant higher transaminase release (218 vs 122 UI/100g/L, p=0,026) and higher lactate ratio levels (1,12 vs 0,39, p=0,039) at the end of reperfusion. In contrast the HOPE rWI group presented with 2.5x lower transaminase release compared to the rWI group (89 vs 218 UI/100g/L p=0.004) although higher than the HOPE group (63 UI/100g/L, p=0.073).

Conclusions: This study shows that rWI increases early hepatocyte injury. In addition, the latter may be mitigated by applying HOPE. The data from this preclinical study reveals a novel protective mechanism of HOPE, which should be further explored in the clinical setting.

Fig 1: (a) Thermal kinetics during rWI of liver grafts in human liver transplantation (n=23) and porcine model (n=11); (b) pictures of the rWI phase in the porcine model; (c) description of the 4 experimental groups

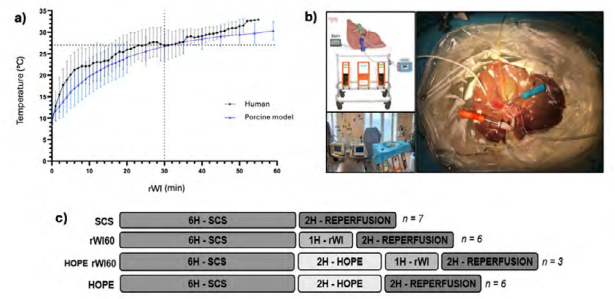

Table 1: AST levels (UI/L/100g) after 120 minutes of ex-situ reperfusion of porcine livers

		p
SCS	**rWI60**	
122 (92-161)	218 (161-249)	**0,026**
rWI60	**HOPE rWI60**	
218 (161-249)	89 (79-94)	**0,004**
HOPE	**HOPE rWI60**	
63 (43-77)	89 (79-94)	0,073

Values are given as median (interquartile interval), Variables were compared using a Mann-Whitney U test. P values < 0.05 indicates statistical significance (in bold)

EP_375 EXPANDING THE DONOR POOL WITH TAKOTSUBO CARDIOMYOPATHY: A SINGLE CENTER STUDY ANALYSIS

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Background: The study aims to explore the feasibility of expanding the cardiac donor pool by including donors with Takotsubo Cardiomyopathy (TS). The analysis focuses on understanding the outcomes of using such donors in heart transplantation, evaluating pre- and post-operative variables, and determining the impact on patient survival.

Methods: This analysis focuses on six donors diagnosed with TS, utilized at the Cardiac Surgery Unit of the Policlinico of Bari between January 2022 and September 2024. Of the six donors, four had classic Takotsubo syndrome, one had the reverse variant, and one had the mid-ventricular variant. The median age of the donors was 30.5 years, with a predominance of female donors (F ratio = 2:1).

Results: Statistical analysis compared patients divided into two groups based on use donor with or without Takotsubo syndrome. Significant differences were found for two preoperative variables: mechanical ventilation (p = 0.00075) and preoperative dialysis (p = 0.0215). This indicates that patients transplanted with TS-affected donor more frequently required ventilatory support and dialysis before transplantation. Additionally, a weak positive correlation was observed between preoperative ECMO use and no-TS-affected donors (r = 0.14), while no significant correlations were found between TS and CRP, bilirubin, and renal function (GFR) in the preoperative period. Postoperative variables, including ECMO use, dialysis (CVVH), infections, and mechanical ventilation, showed no strong correlations with TS, suggesting that postoperative conditions were not significantly influenced by donor type. In terms of mortality, the Kaplan-Meier analysis revealed lower mortality rates for patients transplanted with TS-affected donors compared to those transplanted with non-TS donors (p < 0.05).

Conclusions: These findings suggest that, while the use of donors with Takotsubo is feasible, careful selection and strict postoperative monitoring are essential to ensure favorable outcomes. Expanding the donor pool through the inclusion of Takotsubo patients could improve access to cardiac transplantation, especially in emergency situations, thereby contributing to the reduction of waiting lists.

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EP_376 EFFECT OF DECEASED DONOR TYPE ON KIDNEY RECIPIENT POST-TRANSPLANT HEALTH SERVICE UTILIZATION IN AUSTRALIA

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Background: Use of expanded criteria donors (ECDs) has increased availability of deceased donor kidneys; however, evidence is limited regarding the impact of these donors on post-transplant healthcare utilization. We examined post-transplantation health service use for deceased donor kidney recipients by donor type.

Methods: We analyzed all kidney transplant recipients 2006-2019 in New South Wales (NSW, largest state in Australia, population over 8 million). We used data from the Australian and New Zealand Dialysis and Transplant Registry linked to administrative health data in NSW. Donors were classified based on pathway (donation after brain death, DBD; and circulatory death, DCD) and criteria (standard, SCD; and expanded, ECD). Outcomes were post-transplant length of stay (LOS), length of delayed graft function (DGF), and rates of DGF (proportion) and readmission (incidence rate ratio, IRR).

Results: We included 1499 donor-recipient pairs; 597 (40%) DBD SCD, 475 (32%) DBD ECD, 274 (18%) DCD SCD, and 153 (10%) DCD ECD. Of these, DGF occurred in 136 (23%) DBD SCD recipients, 107 (23%) DBD ECD, 139 (51%) DCD SCD, and 75 (49%) DCD ECD. Median days of DGF was 6, 5, 7, and 7, respectively (p=0.05). Median days LOS was 9 for DBD SCD, 9 for DBD ECD, 11 for DCD SCD and 11 for DCD ECD (p<0.001, figure 1). Compared with DBD SCD, first year readmission rates were higher for DBD ECD (IRR 1.24, 95%CI 1.09-1.41, p=0.001), but similar for DCD SCD (IRR 0.98, 95%CI 0.85-1.14, p=0.8) and DCD ECD (IRR 1.17, 95%CI 1.00-1.38, p=0.05).

Conclusions: Recipients of ECD kidneys had higher readmission rates, while DCD had longer LOS and higher rates of DGF. These findings may help improve health service design.

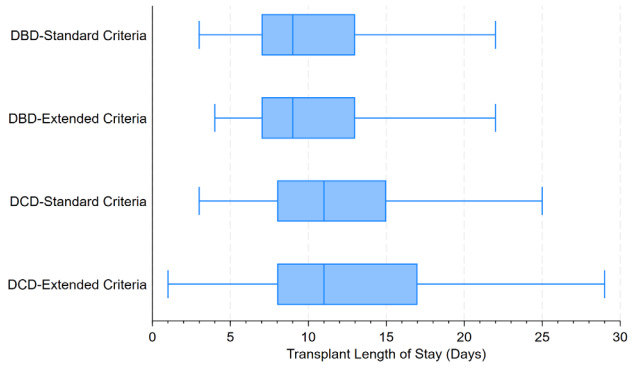

Figure 1: Distribution of post-transplant length of stay by donor pathway and criteria

EP_377 IMPACT OF EXTENDED CRITERIA DONOR ON INFECTIONS IN KIDNEY AND LIVER TRANSPLANTS AND MARGINAL DONOR DEFINITION CRITERIA

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Background: expanded donor criteria (ECD) have become a crucial source of organs, enabling increased access to transplantation as part of a strong effort to increase the donor pool. Marginal graft or ECD refer to an organ with an elevated risk of poor function or failure, which may lead to a higher risk of infections. However, this relationship has been poorly investigated. Additionally, the definition of ECD is variable across studies complicating the interpretation of findings. This systematic review aims to evaluate the impact of ECD versus standard criteria donor (SCD) on infections rates in kidney and liver transplant recipients and to examine the variability in the definitions of ECD.

Methods: PubMed, Scopus and Embase Database were independently searched until June 2024 to retrieve randomized controlled trials or observational studies comparing infections rate in ECD vs. SCD recipients. Quality of included studies was assessed with ROBINS-I tool. Treatment effects were calculated as odds ratio (OR), with a 95% confidence interval (CI) for dichotomous data, using a random effects model. Both viral and bacterial infections were evaluated. Outcome assessment was performed at 30-180 days and 1-3-5 years. A descriptive analysis of marginal donor criteria definitions was provided.

Results: 1233 articles were screened and 138 observational studies met inclusion criteria. At 30 days, the pooled analysis of 15 studies revealed an OR of 1.15 (0.86-1.56; p = 0.35) for bacterial infections (Figure 1). For viral infections, across 10 studies the OR was 1.44 (0.77-2.68; p = 0.25). At 1 year, bacterial infections were reported in 3 studies with an OR of 1.75 (0.72-4.25; p = 0.22). Viral infections were assessed in 5 studies yielding an OR of 1.58 (0.93-2.67; p = 0.09). ECD definitions (Table 1) exhibited significant heterogeneity, particularly in liver transplantation, limiting comparability.

Conclusions: The findings suggest that while ECD organs may be associated with a slightly increased risk of infectious complications compared with those with standard criteria donors. Variability in ECD definitions, particularly for liver transplantation, could be an additional bias. Harmonized and clear-cut criteria for marginal donor definition are necessary to better assess infection's implications of ECD use.

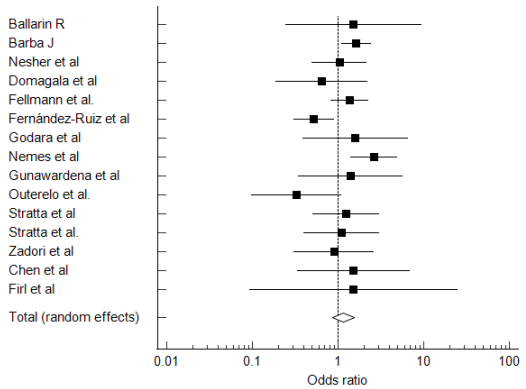

Figure 1.

Table 1

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EP_378 UTILIZING HEALTHCARE CONFERENCES TO PROMOTE ORGAN DONATION AND TRANSPLANTATION INITIATIVES: A NOVEL APPROACH IN THE UAE

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Background: In January 2023, the UAE National Center for Organ Donation and Transplantation (NCDT) initiated its Training section to foster awareness and knowledge regarding organ donation (OD) and transplantation (T) among healthcare professionals. An innovative and cost-effective strategy was adopted, integrating specialized sessions/tracks on OD and T into national and regional (N/R) healthcare conferences (HCC).

Methods: A meticulous assessment of HCC held in the UAE in 2023 was conducted, focusing on events aligning with NCDT objectives and addressing themes related to chronic organ diseases, end-of-life care, OD, and T. Targeting key healthcare professionals such as ICU physicians, neurologists, anesthesiologists, pediatricians, nurses, and transplant physicians was prioritized. Presentation topics were selected based on audits identifying deficiencies in the healthcare system to bolster understanding and interest in organ donation and transplantation. These sessions were strategically dispersed across multiple conferences throughout the year to ensure widespread dissemination of information. Various participation pathways were offered, including a specific track for OD and T, plenary lectures on OD in the main track, OD awareness booths at congress exhibition areas, and local seminars in collaboration with critical care chapters featuring international experts.

Results: In 2023, the National Center actively engaged in ten N/R conferences and local seminars spanning diverse healthcare domains. Through these collaborations, over 5000 healthcare professionals in the UAE and GCC were effectively reached, enhancing knowledge and awareness about OD and T.

Conclusions: Training initiatives are pivotal for enhancing the efficacy and quality of OD and T practices while fostering a culture of organ donation among healthcare professionals. Identifying optimal training strategies tailored to different healthcare settings and specialties is crucial for maximizing intervention success. This innovative approach of participating in N/R conferences enabled broader audience outreach compared to standalone conferences, efficiently delivering our message to a larger demographic in a cost-effective manner.

EP_379 USING THE DIA APPROACH TO LCMS-BASED PROTEOMICS TO EXPLORE THE RESPONSE TO REPERFUSION IN HUMAN KIDNEYS

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Background: Ischaemia reperfusion injury (IRI) remains an unavoidable aspect of deceased donor kidney transplantation and is recognised to impact on long term graft survival. Normothermic machine perfusion offers an opportunity to deliver therapies to target this injury but is also a human model in which to study the mechanisms involved.

Methods: Human kidneys declined for clinical transplantation (n=5) and with cold ischaemic time of at least 12 hours underwent normothermic machine perfusion (NMP) with urine recirculation for 24 hours. Core biopsies collected at the end of cold ischaemia (before perfusion started) and after 24 hours of NMP were snap frozen and subsequently analysed by liquid chromatography mass spectrometry-based proteomics using data independent acquisition (LCMS-DIA). Cytokine release and levels of injury marker NGAL were assessed with immunoassay on perfusate and urine samples respectively. TUNEL stain quantified apoptosis.

Results: The ability of the model to mimic the inflammatory injury following reperfusion was validated by increase in inflammatory cytokine and NGAL levels during perfusion. There was a trend for increased apoptosis at the end of perfusion. Over 4000 proteins were identified and included in analysis. Sparse principal component analysis plots showed samples to cluster by timing relative to perfusion. 400 proteins were differentially expressed between the start and end of perfusion. Assessment of protein markers of different nephron segments and cell types showed consistency in core biopsy sampling. HMOX1 was one of the proteins most upregulated during reperfusion whereas the negative complement regular CFH was one of the most downregulated.

Conclusions: We have conducted a focused analysis using the LCMS-DIA approach to proteomics to explore the response to human kidneys occurring during the reperfusion phase of IRI. Modulation of protein expression could be detected with this bulk method and initial analysis shows consistencies with existing data using alternative techniques or models. Further work will include pathway analysis to predict the key processes being modulated by the identified differential protein expression. The data generated through this unbiased global approach has the potential to identify new therapeutic targets for kidney IRI.

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EP_380 USE OF DONORS WITH EXTENDED CRITERIA IN HEART TRANSPLANT

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Background: Cardiac transplantation is the gold standard for the treatment of advanced heart failure. There is an imbalance between the number of patients waiting for transplantation and the availability of donors. The use of donors with extended criteria is an important resource in cardiac transplantation.

Methods: Retrospective study performed on 160 recipients of standard donor hearts and 60 recipients of extended criteria donors. The preoperative characteristics of the populations were comparable. The incidence of PGD, the use of short mechanical support, the incidence of CVVH, infections and medium-term survival were analyzed.

Results: No statistically significant differences were found between the two groups in terms of: incidence of PGD (p=0.26), short mechanical support (p=0.36), use of CVVH (p=0.36), in-hospital infections (p=1.00) and medium-term survival (0.50).

Conclusions: The use of extended criteria donors represents a valuable resource in cardiac transplantation to address the gap between donor availability and the number of recipients waiting for transplantation.

EP_381 HEALTH-RELATED QUALITY OF LIFE AFTER LIVING KIDNEY DONATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Living donor kidney transplantation (LDKT) is the most effective treatment for end-stage kidney disease, offering better outcomes than deceased donor transplantation or dialysis. However, as LDKT involves healthy individuals undergoing surgery, assessing post-donation health-related quality of life (HRQoL) is essential to understand its impact on their mental and physical well-being. This study evaluates whether donors' HRQoL after LKD is comparable to pre-donation levels and other populations, including potential donors, the general population, and healthy controls, while identifying subgroups at risk of impaired HRQoL.

A comprehensive search was conducted up to December 11, 2024, to identify studies on HRQoL following LKD. Seventy studies involving 13,277 donors met predefined inclusion criteria, focusing on pre- and post-donation HRQoL outcomes. Data extraction followed PRISMA guidelines, with independent reviewers ensuring accuracy. Study quality was assessed, and pooled data were analyzed using a random-effects model. Primary outcomes included SF-36 mental (MCS) and physical (PCS) component scores, comparing post-donation HRQoL to baseline and other populations."

The meta-analysis included 70 studies and 13,277 donors. The MCS showed no significant differences at 3, 6, and 12 or more months post-donation compared to pre-donation levels. However, the PCS was significantly lower at 3 months post-donation (SMD: -0.31; 95% CI: -0.59 to -0.04; p = 0.02) but returned to baseline at 6 and 12 or more months. Donors exhibited significantly higher PCS and MCS scores compared to the general population. HRQoL scores among living kidney donors were comparable to or better than healthy controls, recipients, patients undergoing nephrectomy for non-transplant reasons, and dialysis patients.

We demonstrated that physical HRQoL temporarily declines after living kidney donation but returns to baseline by 6 months post-donation and is maintained at 12 months. Mental HRQoL remains stable throughout the post-donation period. Importantly, living kidney donors have better HRQoL than the general population and healthy controls, underscoring the positive outcomes of donation. These findings suggest that concerns over post-donation HRQoL should not discourage living kidney donation.

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EP_382 EX-SITU REMOVAL OF DAMPS DURING NMP AND FOLLOWING ALLOGENIC WHOLE BLOOD REPERFUSION IN DISCARDED HUMAN ECD LIVERS

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Background: We have previously identified damage associated molecular patterns (DAMPs) in NMP perfusate and demonstrated successful removal of these propagators of injury in an ex-situ porcine DCD liver transplant model. Herein, we describe our experience of DAMP removal using NucleoCapture® technology in extended criteria donor (ECD) discarded human livers declined for transplantation.

Methods: Eight ECD discarded human livers were included in this study. Of these, 5 were historical controls from standard-protocol NMP perfusions. The experimental group comprised of 3 livers that underwent 12h of NMP (using pRBC) and a further 6h of allogenic whole blood reperfusion using the OrganOx *metra* with continuous application/integration of in-line NucleoCapture® hemoperfusion column during both perfusion and reperfusion. In both groups, perfusate measurements of DAMPs were performed on samples collected at 1h, 4h and 12h of perfusion. In the experimental group, additional measurements were performed on samples collected at 1h and 6h of allogenic whole blood reperfusion.

Results: All livers demonstrated satisfactory lactate clearance, **Figure 1A.** Standard-protocol NMP livers demonstrated a sustained increase in perfusate histones by 12h of perfusion compared to the NucleoCapture® treated livers (142.47±133.34µg/ml vs. 69.31±52.13µg/ml, *P*=0.41), **Figure 1B**. Similarly, standard-protocol NMP resulted in an increase in cfDNA during perfusion. Conversely, NucleoCapture® treated livers demonstrated a significant reduction in perfusate cfDNA, most pronounced between 4h to 12h of perfusion (6.31±0.55µg/ml vs. 3.03±1.70µg/ml, *P*=0.048) and a further significant reduction at 1h of allogenic whole blood reperfusion (1.89±1.60µg/ml, *P*=0.0014), **Figure 1C.** Standard-protocol NMP livers demonstrated a significant increase in microclots over 12h perfusion. However, the application of NucleoCapture® resulted in a significant reduction of microclots by the end of perfusion and reperfusion, **Figure 1D.**

Conclusions: NucleoCapture® effectively removes circulating DAMPS from the perfusate demonstrating benefit in both ex-situ perfusion and reperfusion. If translated into clinical practice, this technology may improve outcomes of ECD liver transplantation.

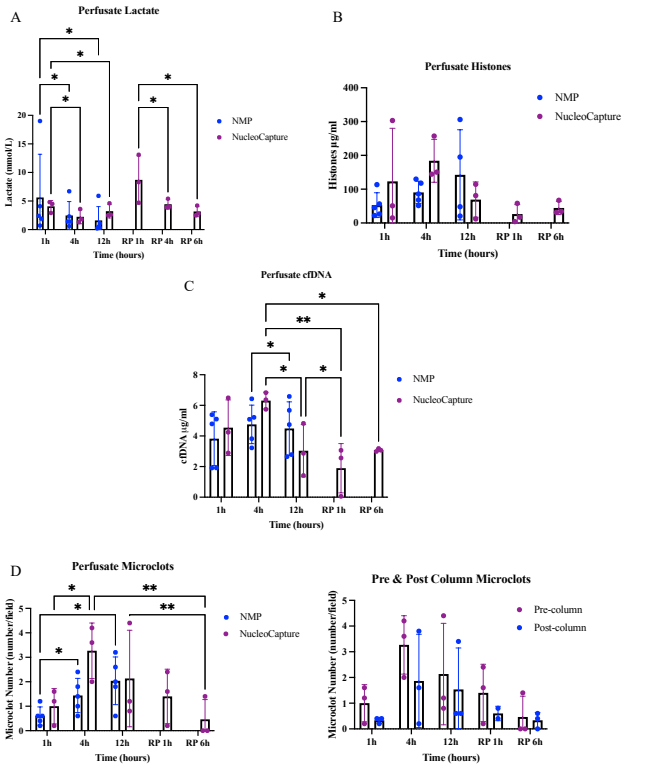

Figure 1A-D. Clearance of lactate during perfusion (in both groups) and during allogenic whole blood reperfusion in NucleoCapture® treated livers **(A).** Reduction in perfusate histones with NucleoCapture® treatment **(B).** Similarly, reduction in perfusate cfDNA with NucleoCapture treatment **(C).** NucleoCapture® results in reduction in microclots by the end of perfusion and allogenic whole blood reperfusion **(D).** The student's t-test was used to compare timepoints

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EP_383 HYPOTHERMIC OXYGENATED PERFUSION IN PEDIATRIC LIVER TRANSPLANTATION: PRELIMINARY RESULTS

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Background: Pediatric liver transplantation (PLT) faces challenges related to donor-recipient size matching and organ availability. Hypothermic oxygenated perfusion (HOPE) has shown promise in adult transplantation but lacks pediatric data. This study evaluates HOPE in a pediatric transplant program.

Methods: A retrospective analysis was conducted on children (1 month-18 years) who received HOPE-treated liver grafts between February and January 2025. Indications for HOPE included prolonged cold ischemia time (>7 hours), atypical or ex situ split reductions during bench surgery, and suboptimal donor conditions, such as donation after circulatory death (DCD).

Results: A total of 14 transplants were performed using HOPE. Total median cold preservation time (static cold storage + HOPE) was 341 minutes (273-415) and total HOPE time was 105 minutes (93-129.5). Three were DCD donors (one pediatric), and 11 brain death donors. In 12 cases, graft reduction was necessary: 6 cases were optimal donors to share the liver with an adult transplant team and an ex-situ split technique was performed (in one case an extra reduction was necessary to get a monosegment for a newborn). In 6 more cases an atypical reduction was performed (resection of segments VI-VII, or V-VIII). One multivisceral graft was converted to a liver graft during the bench surgery. One 18 year-old recipient had been transplanted 15 years earlier. All transplants went well; all patients were alive at the end of follow up except one with leukemia recurrence. Initial primary graft dysfunction was not seen in any patient, with normalization of transaminases on the third postoperative day in all cases, without the need for vasoactive support, immediate surgery or retransplantation. Median transaminase levels at 1st, 7th and 15th postoperative day were 826/1458 (557-2053/448-2152), 44/214 (33-55/110-340) and 29/51 (22-39/51/107) respectively. One hepatic artery thrombosis (11%) and two biliary complications (22%, bile leak) were surgically corrected. There was no ischemic cholangiopathy or admissions for cholangitis during follow-up.

Conclusions: HOPE appears beneficial for PLT, particularly for suboptimal or reduced grafts and complex cases requiring extended bench surgeries. Further studies and long-term data are needed to refine indications.

EP_384 ESTIMATED GLOMERULAR FILTRATION RATE REDUCTION AFTER ROBOTIC-ASSISTED LIVING DONOR NEPHRECTOMY: MONOCENTRIC EXPERIENCE

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Background: In Living Donor Kidney Transplantation, donor safety and renal function preservation represent the critical goal. Robot assisted living donor nephrectomy (RALDN) is a minimally invasive technique that allows a reduction of surgical complications and a shorter hospital stay, while assuring equivalent transplant outcomes when compared to laparoscopic or open nephrectomy.

Methods: We considered RALDN performed in our center from November 2019 to December 2023. Donor's age, gender, clinical history and urinalysis were reported. Pre-operative renal function was estimated by CKD-EPI2021 formula and creatinine-CystatinC combined. Creatinine and eGFR were evaluated before surgery and post operatively (1 week, 1,3,6,12 months). The population was divided in two groups according to the relative eGFR reduction (GroupH>30%;GroupL<=30%). Continuous variables are described in terms of mean±standard deviation, categorical variables in terms of frequency. Groups were compared with Mann-Whitney U test or Chi Square as appropriate.

Results: 35 donors were included (34 Caucasians, 1 African; 24 females, 68.6%). Mean age: 54.66±11.3years (32-76). None had diabetes, microscopic albuminuria never exceeded the 30 mg/mg, 5(14.3%) were on antihypertensive medication. Mean BMI: 23,9±4,2kg/mq. Pre-donation mean serum creatinine was 0,78±0,17mg/dl, mean Cystatin C was 0,85±0,14 mg/L, equivalent to a mean CKD-EPI2021 of 97,6±13,4 (70,2-117,6) ml/min/1.73mq and to a combined Creatinine-CystatinC of 98,8±12,4 (79-124)ml/min/1.73mq. After RALDN, creatinine increased to 1.11 ± 0.28 mg/dl, eGFR decreased to 68.6±16.2 ml/min/1.73m², with a relative variation (RV) of -29.7±13.1%. Creatinine and eGFR remained stable in the first-year post-donation; mean eGFR at 1 year: 63.0±10.3 ml/min/1.73m². There were no significant differences between GroupH(n=17) and GroupL(n=18) in terms of age, gender, preoperative creatinine, or eGFR (p>0.05).

Conclusions: RALDN seems to be a promising resource to enlarge the donor. Our study shows a post-operative eGFR reduction of approximately 30%, which is consistent with previous reports using open or laparoscopic methods. Accurate donor screening ensured stable eGFR in the first-year post-donation. Longer follow-up is needed to evaluate long-term outcomes.

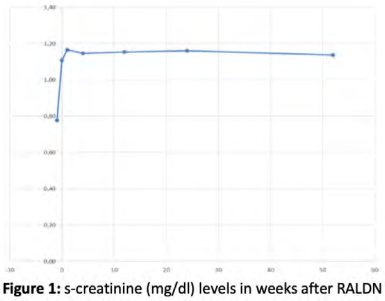

Figure 1: s-creatinine (mg/dl) levels in weeks after RALDN

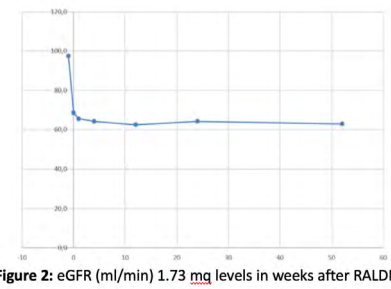

Figure 2: eGFR (ml/min) 1.73 mq levels in weeks after RALDN

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EP_385 CAN THE DONOR'S AND THE RECIPIENT'S LIFESTYLE INFLUENCE THE DEVELOPEMENT OF EARLY CAV IN THE RECIPIENT?

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Background: Cardiac allograft vasculopathy (CAV) is a major cause of advanced graft failure after cardiac transplantation and of limited long-term recipient survival. The aim of this study is to compare the incidence of early CAV (≤ 5 years) considering non-immunological risk factors of donors and recipients, in particular cardiovascular risk factors.

Methods: A retrospective analysis of 109 patients who underwent heart transplantation between 2013 and 2023 was performed. Univariate and multivariate analyses were performed to assess the association between donor variables and the onset of early CAV (≤ 5 years) for adult recipients.

Results: 88 patients [median age 55.8 years] did not develop early CAV while 21 patients [median age 53.7 years] developed CAV within 5 years. In both groups, approximately 70% were men, with a significantly higher BMI [23.5 vs 25.6 (p=0.02)] in the group of patients who developed early CAV. Panel-reactive antibody (PRA) was also evaluated without finding a significant difference between the two groups (p= 0.6). Regarding donor risk factors, no differences were found between the donor groups considering: the presence of coronary artery disease (p= 0.22), alcohol abuse (p=0.39), drug abuse (p=0.11), psychiatric disorders (p=0.65), hypertension (p=0.78), diabetes (p=0.11). The analysis, however, highlighted presence of some independent predictors of CAV in the donor: age (p=0.05), higher BMI (p=0.009), smoking > 20 cigarettes per day (p=0.04), dyslipidemia (p=0.008), peripheral vascular disease (p=0.006). Multivariate analysis confirmed the following as risk factors for the development of early CAV: smoking > 20 cig/day (p=0.048), donor age (p=0.047) and donor BMI (p=0.002). Interestingly donor female sex appeared protective (p=0.038).

Conclusions: Older donor age, higher BMI and tobacco abuse confer a greater risk of early CAV development in the recipient. Moreover, dyslipidemia and peripheral vascular disease are independently associated with recipient CAV. In patients who receive an organ from donors with these characteristics, preventive strategies both to slow the development of CAV and for early identification are warranted.

EP_386 NORMOTHERMIC REGIONAL PERFUSION OUTCOMES IN KIDNEY TRANSPLANTS AT UHB

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Background: Normothermic regional perfusion has been increasingly utilised in non-heart beating cadaveric organ donors with the aim of increasing quality and function of retrieved abdominal organs. We aimed to measure differences in outcomes post DCD renal transplantation in NRP versus non NRP- treated (DCD) kidney donations at the QEH in Birmingham.

Methods: A retrospective single-centre study of DCD renal transplant patients was performed at the QEH in Birmingham. Primary outcome was recipient renal function (serum creatinine) 6 months post transplantation. Secondary outcomes were delayed graft function and primary non-function.

Results: A total of 88 DCD renal transplant patients were identified with at least 6 months follow up. Recipient age range was 25-72. 26 patients were followed up in referring units; blood results at 6 months were not accessible. Of those, 5 were lost to follow-up due to mortality. Cold ischaemic times were not significantly different between the two groups (NRP t=772 min vs DCD t=668 mins (p= 0.25)). The NRP kidney (n=30) group had average creatinine 133 (range 64-258) at 6 months post-operatively, versus average creatinine 147 (range 63-287) at 6 months post operatively in the DCD group (n=58) . This did not reach statistical significance (p=0.29). Primary non-function was observed in 1 (3%) NRP transplant versus 5 (8.6%) of DCD transplants. Chi squared test found no significant difference in DGF rates between the two groups (p=0.6).

Conclusions: Our expectation was of better outcomes in the function of DCD donor kidney transplants that had been retrieved following NRP, as has been observed in previous literature supporting NRP use. It was interesting to observe higher rates of primary non function in the DCD group. However, our data should be interpreted with caution due to sample size and without the use of advanced statistical analysis. Confounding factors were not adjusted for. Outcomes from NRP donors were not inferior to standard DCD donors. Further analysis in the future could consider the duration of normothermic regional perfusion used and in-detail donor and retrieval data. Further study using a larger population would be of use.

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EP_387 OUTCOMES IN HEART TRANSPLANTATION USING DONORS WHO COMMITTED SUICIDE: A RETROSPECTIVE STUDY

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Background: Suicide, a multifactorial and growing public health concern in the Americas, encompasses complex psychosocial factors. Despite its rising incidence, organs from suicidal donors represent a minority in organ donation for transplants. In kidney, liver, and lung transplants, studies have shown no differences in mortality or graft dysfunction when comparing suicidal to non-suicidal donors. However, data on suicidal donor hearts for transplantation remains limited.To evaluate whether heart transplantation using suicidal donor hearts is associated with increased rates of primary graft dysfunction (PGD) and mortality compared to non-suicidal donor hearts.

Methods: Between 2020 and 2021, a total of 105 heart transplants were performed, with 97 patients included in the analysis. Pre-, intra-, and postoperative data were collected for both donors and recipients. Statistical comparisons were conducted using ANOVA, the Mann-Whitney Test, and the Chi-square Test, with significance set at $p < 0.05$ using the R statistical program.

Results: Among the 97 transplants, 6 were from suicidal donors (6.2%), and 91 were from non-suicidal donors (93.8%). Comparing recipients of suicidal donor hearts to non-suicidal donor recipients, intraoperative times showed no statistically significant differences. However, postoperative data revealed increased ECMO use (33.3% vs. 4.4%; $p = 0.036$), a higher incidence of PGD (66.7% vs. 19.8%; $p < 0.05$), and increased 30-day mortality (50% vs. 3.3%; $p < 0.05$) in the suicidal donor heart group.

Conclusion: This study is the first to identify an association between heart transplants from suicidal donors and elevated risks of primary graft dysfunction and 30-day mortality. Given the limited literature on this topic, further research is essential to confirm and explore these findings.

EP_388 NORMOTHERMIC REGIONAL PERFUSION IN LIVER TRANSPLANTATION FOR PRIMARY SCLEROSIS CHOLANGITIS

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Background: Liver transplantation in primary sclerosing cholangitis (PSC) is fraught with peril due to disease recurrence and higher risk of biliary and arterial complications affecting graft survival. This led to apprehension in using donation after circulatory death (DCD) livers in PSC patients. Transplantation outcomes of Normothermic regional perfusion (NRP) livers are excellent and comparable to donation after brain death (DBD). In this study, we share our experience of liver transplant in PSC patients with NRP livers.

Methods: Retrospective analysis of liver transplantation in PSC patients at our institute from January 2015 till August 2023. The liver transplantation outcomes in PSC recipients with NRP livers (NRP-PSC group) were compared to the standard DCD (DCD-PSC group).

Results: There were 171 NRP liver transplants during the study duration. PSC was indication in 27 (16%) of the patients and two of them were for recurrent PSC. During the same period, 12 PSC patients were transplanted with standard DCD livers. The donors in the NRP-PSC group were younger (median age 44 years vs 52 years) with lower donor risk index (median DRI, 2.1 vs 2.6). The warm ischaemia (median 28 mins vs 27 mins) and cold ischaemia times (median 484 mins vs 424 mins) were comparable. Ischaemic cholangiopathy (IC) was significantly higher in the DCD-PSC group (50% vs 20%) with no hepatic artery thrombosis in either of the groups. There were four graft losses in the DCD-PSC group: one primary nonfunction, two IC and one disease recurrence. None of the grafts failed in the NRP-PSC group.

Conclusions: Livers recovered from DCD donors using NRP appear to be an excellent source of livers for PSC patients with favourable outcomes.

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EP_389 CROSS-BORDER ORGAN DONATION AND TRANSPLANTATION: UAE EXPERIENCE IN REGIONAL COLLABORATION WITH SAUDI ARABIA AND KUWAIT

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Background: The Hayat Program, led by the UAE Ministry of Health and Prevention, integrates organ donation and transplantation into the Emirati health system, adhering to strict legal, medical, and ethical standards for both living and deceased donors. With the increasing number of deceased donors, surplus organs not used in the UAE are offered to neighbouring MENA countries like Saudi Arabia through innovative logistics and cross-border agreements. The UAE also collaborates with Kuwait for domestic transplants. This study aims to evaluate the UAE's cross-border donation process, identify gaps, and improve logistics for transporting transplant teams, recipients, and organs.

Methodology: In 2023, the UAE coordinated with Saudi Arabia and Kuwait in order to organize a transnational collaboration program with the following premises:1) Ensure compliance with legal, medical, technical and ethical protocols when using organs for transplantation between these countries; 2) Receive referrals from deceased organ donors from teams regulated by government authorities; 3) Ensure organ matching with recipients in Kuwait transplant centers; 4) Establish logistics for chartered flights to transport transplant teams between UAE, Kuwait and Saudi Arabia.

Results: On 2023, 41 air flights were carried out between the UAE and Kuwait and Saudi Arabia underscoring the UAE's commitment to efficient transplant teams, organs and recipients transportation. The average air transport time per process was 5 hours. In total, including collaboration with Saudi Arabia, 88 organ donors were identified and a further 42 transplants were successful through regional collaboration.

Conclusion: The UAE's Al Hayat Program exemplifies leadership in regional organ donation and transplantation coordination, achieving high success rates through effective collaboration with Saudi Arabia and Kuwait, saving numerous lives by successfully transporting and transplanting organs across borders using surplus valid organs under legal regulations. To enhance its life-saving impact, future efforts should focus on harmonizing regulatory frameworks, investing in advanced preservation technologies, and optimizing logistical workflows.

EP_390 SYNERGISTIC EFFECT OF ISCHEMIC PRECONDITIONING AND COLD CARDIOPLEGIA IN ADVANCING THE DONOR HEART REANIMATION

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Background: Donors after circulatory death (DCD) present significant challenges due to the detrimental effects of warm ischemia on organ viability. Cold cardioplegia perfusion has been the widely used method to reduce the effects of warm ischemia during graft preservation. This study explores the synergistic effects of ischemic preconditioning (IPC) and cold cardioplegia on the initial preservation and subsequent functional recovery of DCD hearts using a slaughterhouse ovine model.

Methods: Ovine hearts (n = 16) were procured from a slaughterhouse after 15 minutes of warm ischemia. Hearts were perfused with a 4°C Krebs-Henseleit-based cardioplegia solution using two approaches; (i) continuous cold cardioplegia perfusion (C_CP), n = 8 and (ii) cold cardioplegia by IPC (IPC_CP: 3 minutes of perfusion followed by 2 minutes of ischemia), n = 8. Following C_CP/IPC_CP, the hearts were transitioned to a normothermic machine perfusion system and perfused for 4 hours. Parameters of myocardial recovery, including functional performance, tissue damage, and injury markers, were evaluated.

Results: IPC-CP protocol yielded superior myocardial preservation compared to C_CP protocol. Hearts treated with IPC_CP exhibited faster recovery of contractile function, as evidenced by early restoration of pulsatile flow and normal ECG patterns. Perfusate analysis showed reduced levels of injury markers, including lactate dehydrogenase (IPC_CP- 279 ± 64 U/L vs C_CP- 635 ± 91 U/L) and troponin I (IPC_CP- 2.37 ± 0.94 µg/L vs C_CP- 5.22 ± 1.7 µg/L), in the IPC_CP group. Histological analysis confirmed the preservation of myocardial architecture and reduced cellular damage in the IPC_CP treated hearts.

Conclusions: The combined approach of IPC and cold cardioplegia offers significant protection against ischemic injury in DCD hearts resuscitated in normothermic machine perfusion system. This strategy improves initial preservation, accelerates functional recovery, and holds promise for advancing heart transplantation outcomes in DCD settings.

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EP_391 THE CLINICAL PROGRESS OF ISLET CELL TRANSPLANTATION IN TYPE I DIABETICS, A SYSTEMATIC REVIEW

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Background: All type one diabetics require exogenous insulin to regulate their blood glucose levels. Where subcutaneous injections are inadequate at achieving glycaemic control, or where there are severe side effects, islet cell transplantation is a therapeutic option. This systematic review aims to address whether islet cell transplantation in adult type one diabetics is able to induce insulin independence, reduce HbA1c levels and eradicate severe hypoglycaemic events.

Methods: This review included all studies published in English from Jan 1, 2014 to Jan 31, 2024. We included articles where adult type one diabetics had at least one islet cell infusion from a human source. We excluded articles that did not record at least one of our three parameters of interest. The final search was conducted on the 4th of February 2024 using the EMBASE, Medline and PubMed databases. The identification of studies, data extraction and analysis was conducted by two independent reviewers (HH and SB). Any discrepancies were resolved through consultation with the senior author (SF).

Results: Twenty studies amounting to a total of 1,655 islet cell recipients, were included in the analysis. 80% of the included studies were able to induce insulin independence, 65% reduced HbA1c levels compared to the pre-transplantation level and 60% of studies reduced severe hypoglycaemic episodes. Not all studies reported all parameters. All of the studies consisted of level IV evidence, except for a single case control study which was of level III evidence.

Conclusions: The general trends indicate islet cell transplantation is a successful therapeutic method. However, the true effect remains to be determined, due to all the articles being of a low level of evidence. Recommendations for the future include introducing a standardised reporting scheme to enable easy comparisons between studies, as well as highlighting the need to collect data on quality of life factors.

EP_392 STREAMLINING TRANSPLANTATION VIA A COMPREHENSIVE AND SECURE DIGITAL TRANSPLANT MANAGEMENT PLATFORM

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Background: In the current fragmented transplantation ecosystem, costly inefficiencies exist as systems operate in silos without seamless sharing of key data. Outdated paper and manual processes lead to errors, compliance issues, time-intensive procedures, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.

Methods: A donation and transplant software company developed a comprehensive, modern, digital interoperative platform to manage the transplantation workflow, working in conjunction with transplant hospitals to design the system specifically curated to the needs of transplant centers. The platform also has the potential to securely interface with external systems such as Organ Donation Organization's (ODO) software systems as well as hospital Electronic Medical Records (EMRs) and laboratory systems.

Results: The platform is a modern web-based system which streamlines the clinical workflow by providing: 1) management of organ offers; 2) tracking of clinical data including tissue typing, medications, labs, and serologies; 3) real-time and retrospective data quality tools to flag potential errors; 4) reporting, data visualization, and compliance tools; and more.

Conclusions: Adoption of a comprehensive clinical workflow platform curated to the processes of transplant centers has the potential to streamline the transplantation workflow and enable increased compliance, patient safety, and transplants.

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EP_393 ADVANCING LIFE THROUGH LOSS: THE IMPACT OF MAASTRICHT II DCD IN PORTUGAL

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Background: Portugal has become a world leader in organ donation and transplantation, with donation after circulatory death (DCD) Maastricht II playing a key role since its implementation in 2016 as a pilot program at an ECMO Reference Center in northern Portugal. Following the publication of the first pilot results in 2018, the program was expanded to three additional national ECMO reference centers.

Methods: Data on DCD Maastricht II donors were retrospectively collected and analyzed to assess the impact on Portuguese organ donation and transplantation rate.

Results: Between 2016 and 2024, the number of DCD Maastricht II donors showed significant growth, peaking at 51 donors in 2024, representing 11.4% of all donors, compared to 2.4% in 2016. Kidney retrievals increased from 56 in 2018 to 92 in 2024, achieving a transplantation rate of 85%. This marked a 31% increase in kidney retrievals and a 77% rise in kidney transplants compared to 2023. Liver retrieval progressed more slowly but still improved in 2024, with 10 livers retrieved and 7 successfully transplanted, yielding a 70% success rate.

Conclusions: The DCD Maastricht II program has significantly advanced organ retrieval and transplantation in Portugal, especially for kidneys, with steady progress in liver transplantation. Despite Portugal's high transplant activity, demand continues to exceed supply. Building on the success of the Maastricht II program in Portugal, the next logical step is to expand efforts to increase the number of transplants. A study in the Northern region suggests that implementing a controlled circulatory determination of death (Maastricht III) program could increase transplant activity by at least 21%. Effectively leveraging the Maastricht II framework not only allows us to gain more organs but also serves as a crucial preparation for the introduction of Maastricht III and Maastricht IV. These advancements have the potential to unequivocally transform organ transplantation in Portugal, saving more lives, honoring donors, and solidifying Portugal's leadership in this critical field.

EP_394 SUCCESSFUL KIDNEY TRANSPLANT FROM A METHANOL INTOXICATED DONOR: A CASE REPORT

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Background: Methanol poisoning is a significant cause of metabolic acidosis and systemic toxicity. Organ transplantation from donors with methanol poisoning presents unique challenges, including concerns about systemic toxicity, organ viability, and recipient outcomes. We report the first successful kidney transplants in Malaysia using organs from a donor with methanol poisoning.

Methods: Clinical case study.

Results: A 35-year-old male presented with status epilepticus and severe metabolic acidosis following methanol ingestion. Despite treatment with fomepizole and hemodialysis, he succumbed to multi-organ failure and declared brain dead. Terminal creatinine was 199 µmol/L, and the Kidney Donor Profile Index (KDPI) score was 31%. Both kidneys were successfully transplanted into two recipients, both receiving induction with intravenous Thymoglobulin. The first recipient, a 45-year-old female on dialysis for 20 years, achieved immediate graft function but developed a basal ganglia bleed due to a hypertensive emergency on day 3. She recovered with stable graft function (creatinine ~105 µmol/L) and was discharged after rehabilitation. The second recipient, a 46-year-old male on dialysis for 16 years, experienced slow graft function, contributed by prolonged cold ischemic time of 22 hours. His creatinine improved from 291 µmol/L on day 5 to 120–130 µmol/L within two weeks. At 12 months of follow-up, both recipients demonstrated stable graft function with no complications or systemic sequelae related to the donor's methanol poisoning.

Conclusions: Transplanting kidneys from methanol-intoxicated donors results in successful short- and long-term outcomes, with no evidence of direct toxicity. These findings support their potential use in transplantation.

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EP_395 EVALUATION OF A PATIENT AND CARER INFORMATION EVENING EVENT PROMOTING LIVE DONOR KIDNEY TRANSPLANTATION

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Background: Leeds Kidney Transplantation Service hosted an information evening for people with chronic kidney disease (CKD) on the deceased donor kidney transplantation waitlist and their family members/carers (November 2024). The event featured presentations by the multi-disciplinary team and aimed to a) support those awaiting transplantation and b) promote live donor kidney transplantation (LDKT) as a treatment option.

Methods: A survey of attendees was conducted before (T1) and after (T2) the session. Measures included: usefulness of talks, views on LDKT, decision-making stage, decisional conflict, and perceived barriers to donation.

Results: Surveys were completed by 29 people with CKD and 22 carers at T1, and by 20 people with CKD (67%) and 17 carers (77%) at T2. Attendees were predominantly white, aged 51–70, married, and educated to degree level. Talks on "why we promote LDKT" and "transplant waiting times" were rated most useful. Attendees reported learning about CKD, living with LDKT, and its psychological aspects. After the session, people with CKD were more likely to believe they would live longer with LDKT [$X^2(1, n=44) = 7.23$, $p = 0.01$], and carers believed the person they cared for would experience fewer complications [$X^2(1, n=39) = 3.40$, $p = 0.07$] and faster recovery [$X^2(1, n=39) = 5.77$, $p = 0.02$]. Barriers to LDKT included difficulties approaching others, guilt, worry, lack of understanding of the procedure, and absence of potential donors. Decision-making stage remained unchanged, though carers reported greater certainty and reduced conflict at T2.

Conclusions: The information evening was valuable to patients and carers. Modifiable barriers to LDKT, such as confidence and knowledge around donation, suggest targeted interventions. Encouragingly, carers felt more supported in decision-making post-session. Four new potential donors came forward, and two previous contacts re-engaged to advance their assessments.

EP_396 MACHINE KIDNEY PRESERVATION BY PLACING TWO KIDNEYS FROM THE SAME DONOR IN A SINGLE PERFUSION KIT: TWO-YEAR RESULTS

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Background: Hypothermic machine perfusion (HMP) is associated with higher cost of supplies, mostly associated with the perfusion kit; even so, studies have shown that economic benefits would justify its use. The reduction in the incidence of delayed graft function (DGF), defined as the need for dialysis within the first week post-kidney transplant (Tx), as well as a higher percentage of graft survival at one year, could reduce the total cost of hospitalization and dialysis. The aim of this study was to evaluate the safety and efficacy of using HMP in the preservation of two kidneys from the same deceased donor (DD) placed together or sequentially in a single perfusion kit.

Methods: This is a retrospective analysis of all kidney transplant (Tx) patients at our center between 01/2021 and 06/2022. Tx patients were allocated into two groups, according to the preservation method used: Group-I, who received Tx from DD placed in HMP together or sequentially in a single kit (n=90); Group-II, recipients of kidneys preserved in HMP using one kit for each kidney (n=230). The post-Tx results were compared, with analysis of the occurrence and duration of DGF episodes, need for dialysis and the length of hospital stay (LHS).

Results: Group-I presented results comparable to Group-II, regarding the DGF rate (28% vs 26%), need for dialysis [3.0 ± 2 vs 3.3 ± 2 (P = 0.258)], LHS [13 ± 9 days vs 15 ± 9 days (p = 0.094)]; Cold ischaemia time [25 ± 6.3 vs 26 ± 7h (P = 0.270)], as well as acute rejection rates (5% vs 3.5%).

Conclusions: The use of HMP for the preservation of two kidneys from the same DD placed together or sequentially in a single kit proved to be safe and effective, with results comparable to those obtained with traditional kidney preservation in HMP, using one kit for each kidney.

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EP_397 DONORS WITH ACCEPTABLE RISK FOR PATIENTS IN CRITICAL CONDITION: PRELIMINARY ANALYSIS OF FOLLOW UP

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Background: Donor organs with transmission risk of severe disease (mainly neoplastic or infectious) can be assigned to patients in critical clinical condition (since the benefit exceeds the concept of risk of infectious or oncological disease trasmission). The Technical Transplant Council has established that patient follow-up should be investigated if organs from donors with increased risk are transplanted

Methods: We used our application (Trapnet and Donor Manager) to extract donors with non-standard risk, acceptable for patients in critical clinical condition, from application onset (August 2022) to June 2024 in the North Italian Transplant (NITp) area; for each patient, we collected follow-up (mortality at 1, 6, 12 months; complications, especially infectious diseases).

Results: In the study period, 50 donors were defined as non-standard but acceptable for patients in critical condition; risk increase concerned infectious disease for 36/50 (72%), cancer 11/50 (22%), hematological disease 1/50 (2%), immunological disease 1/50 (2%), methanol intoxication 1/50 (2%). Sixty-eight patients (44 liver recipients-11 of them in the extra NITp area- 9 heart, 12 kidney) were transplanted with a follow-up of 13 months (median). Infectious complications occurred in 15/68 (22%; 11 liver recipients, 2 hearth recipients, 2 kidney); 6 of them died (5 liver recipients; 1 heart); 3 patients died for sepsis, 3 for cardiovascular disease.

Conclusions: The preliminary data analysis highlights the importance of risk-benefit evaluation made by the clinician (non-life-saving organs from donors with increased risk are not usually allocated in the NITp area). Follow-up of recipients of donors with this type of risk will be further investigated.

EP_398 SEPTIC PATIENTS ACCEPTED AS AN ORGAN DONORS

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Background: According to national as well as the European regulations the basic guiding principle in organ donation and transplantation is “first, do not harm” Considering that almost all of those patients at the ICU are infected or colonised we need to find acceptable risk and balance ratio.

Methods: We evaluated 16 organ DBD donors, which met the criteria for severe sepsis at the admission time. 10 out of them suffered from severe bacterial CNS infection, 3 of them were admitted due to COVID19 pneumonia and 3 with active RSV related pneumonia. Risk/benefit ratio was evaluated according to the type of organ which planned to be harvested, taking into account available literature data.

Results: We accepted all the donors for multi organ procurement with bacterial meningitis or encephalitis, where the etiological agens was known in the time of organ procurement – we excluded microorganisms capable to create septic metastases such as Listeria spp. In the group of patients with an active RSV infection (by PCR from BAL), as well as COVID19 pneumonia, we accepted all the donors for multi organ procurement except the lungs. Together 56 organs were accepted for the transplantation. Recipient hospital was provided by the information related to the susceptibility of bacterias. The average antibiotic treatment time in recipients was 2.5 days. There was no known donor derived infection transmission into recipient.

Conclusions: As there is worldwide huge lack of the organs suitable for transplantation, we suggest to take into account only clinical relevant information and stay aware of “routine” praxis not to accept donor with even severe septic infection. Of course, risk and benefit validation has to be done.

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Donation, preservation & regeneration

EP_399 INDUCTION OF STEATOSIS IN MONKEY LIVER ORGANOIDS AS AN MASLD MODEL

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Background: While several methods for inducing liver steatosis have been well established in rodents, the variability between species limits the applicability of these results to humans. In vivo studies on human livers are limited. Liver organoids derived from monkey tissue offer a genetic background closer to humans, thus addressing the limitations seen in traditional models for researching Metabolic Dysfunction Associated Steatotic Live Disease (MASLD). This research aims to establish a reliable monkey derived model for drugs evaluation in MALSD and liver transplantation in the future.

Methods: Liver organoids were created from monkey liver tissue. After 5 days differentiation, these organoids were treated with 250μM palmitic acid (PA) and oleic acid (OA) for 24 hours to induct steatosis, which was subsequently confirmed by Oil Red O staining and total cholesterol (TC) detection. Supernatant was collected before and after treatment with free fatty acid for LC-MS to perform a metabolomics study.

Results: Oil O Red staining and TC detection confirmed the liver organoids' lipid accumulation and secretion ($p<0.05$). Metabolomics analysis revealed significant upregulation of Lysophosphatidylcholines (LPS)(17:1), LPS(18:3), phosphatidylcholine (PC)(18:0/14:0) and sphingomyelin (SM)(d18:1/18:0) ($p<0.05$), indicating of cellular membrane reconstruction? and inflammation-promoting pathways; Conversely, HexCer 8:1;2O/4:0 and Cys-His were significantly downregulated ($p<0.05$), suggesting disturbance in amino acid metabolism and a status of oxidative stress.

Conclusions: FFA-treated monkey liver organoids showed significant features of metabolism disorders, oxidative stress, and inflammation. Preliminary results suggested that monkey liver organoids have the potential to serve as a research model for MASLD, on which we will test anti-steatosis compounds as preclinical evaluations, to reduce the fat content of donated livers to enlarge the donor pool.

Infectious diseases, malignancies & long term challenges

EP_400 OUTCOME OF ABO-INCOMPATIBLE LDLT WITH HEPTATOCELLULAR CARCINOMA BEYOND MILAN CRITERIA

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Background: Given the organ scarcity, ABO incompatible (ABOi) living donor liver transplantation (LDLT) emerged as a treatment option for hepatocellular carcinoma (HCC) and underlying liver disease. Milan criteria became standard criteria but expansion beyond the Milan criteria have resulted in similar post-transplant outcomes, thus suggesting LT is a viable treatment option for HCC presenting beyond the Milan Criteria. However, there was few reports the outcome of the patients receiving ABOi LDLT in beyond the Milan Criteria. The aim of our study was to review the HCC-related survival outcomes in the ABOi and ABO compatible (ABOc) groups in the beyond Milan Criteria.

Methods: We retrospectively reviewed the medical records of patients undergoing LDLT for HCC from January 2000 to July 2021 at two tertiary centers in Korea. In total of 114 patients underwent ABOc and 25 patients underwent ABOi LDLT for HCC presenting beyond the Milan Criteria. The eligibility of the beyond Milan Criteria was assessed using preoperative findings by imaging study.

Results: There was no significant difference in pre-transplantation tumor staging, recipient and donor demographics between groups. In terms of operative outcomes and pathologic outcomes, there was no significant difference in both groups. The overall patient survival at 1-,3-, and 5-year was 88.4%, 72.0% and 69.9% after ABOc LDLT and 58.9%, 58,9% and 58.9% after ABOi LDLT, respectively (P=0.139). The recurrence free survival at 1-,3-, and 5-year was 94.7%, 86.6% and 82.7% after ABOc LDLT and 87.5%, 60.0% and 48.5% after ABOi LDLT (P<0.001). Recurrence type (intrahepatic versus extrahepatic) was no significant difference in both groups.

Conclusions: Although, recurrence free survival was significant poor in ABOi LDLT for patients with HCC presenting the beyond Milan Criteria than ABOc LDLT, overall survival was comparable between groups. ABOi LDLT may be an option for HCC with beyond Milan Criteria.

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EP_401 AUTOMATED INSULIN DELIVERY AFTER BETA-CELL REPLACEMENT FAILURE IN PEOPLE LIVING WITH TYPE 1 DIABETES

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Background: Patients living with highly unstable type 1 diabetes (T1D) are eligible to beta-cell replacement (βCR) therapy (islet or pancreas transplantation). This study aimed to evaluate glycaemic control in patients treated with automated insulin delivery (AID) following βCR dysfunction, defined as secondary graft failure or marginal function.

Methods: A national, multicentre, retrospective study was conducted on 23 patients with βCR dysfunction treated with AID for at least three months. The primary outcome was the proportion of patients achieving recommended glucose targets (time in 70-180mg/dl range [TIR]>70%, time below range [TBR]<4% and HbA1c < 7%). Secondary outcomes included TIR, glycaemia risk index [GRI], HbA1c, coefficient of variation [CV], body weight, insulin doses, severe hypoglycaemia and AID discontinuation.

Results: The proportion of patients achieving recommended glucose targets under AID increased from 5.0% to 60.0% after 12 months (p=0.02). TIR increased from 54.2±18.0% to 75.4±9.8% after 12-month AID (p<0.001), while GRI decreased from 45.8±22.2% to 25.9±10.5% (p=0.001). HbA1c levels decreased from 7.5±0.9% to 7.0±1.1% after 12-month AID (p=0.006). CV, body weight and insulin doses did not change. All patients were free from severe hypoglycaemia under AID, including those who had experienced severe hypoglycaemia after βCR dysfunction. No patient discontinued the AID.

Conclusions: This study highlights the effectiveness of AID in achieving glucose control targets and preventing severe hypoglycaemia in patients with T1D following βCR dysfunction. AID may serve as a valuable therapeutic option to improve glucose control when graft function declines.

EP_402 PLASMA TRIMETHYLAMINE N-OXIDE CONCENTRATION AND ALL-CAUSE MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Trimethylamine N-oxide (TMAO) is a pro-atherosclerotic molecule produced by intestinal microbiome. TMAO has been linked to increased mortality risk in chronic kidney disease, but its effect in kidney transplant recipients (KTR) is unclear. We investigated the pre-post-transplantation plasma TMAO change, and the association of post-transplantation plasma TMAO with all-cause mortality in KTR.

Methods: This prospective study included two cohorts. Cohort A comprised 623 KTR from the TransplantLines Cohort and Biobank Study (ClinicalTrials.gov: NCT03272841), assessed pre-transplantation and at 3, 6, 12, and 24 months post-transplantation. Cohort B included 544 KTR with a functioning graft for ≥1 year (median 7.4 [3.9-13.0] years post-transplantation) to study late associations. Potential kidney donors (n=315) served as healthy controls. Plasma TMAO was measured by proton nuclear magnetic resonance. Time-dependent coefficient Cox regression analyses were performed to assess TMAO association with all-cause mortality.

Results: Plasma TMAO concentration significantly declined after transplantation (from 29.0 [IQR 20.6-48.5] µmol/L to 4.5 [IQR 2.7-8.6] mol/L at 3-months post-transplantation, P<0.001). Afterwards it remained stable (β=-0.4 (95% CI -2.2-1.34) µmol/L per post-transplantation year, P=0.63), remaining consistently higher than that of healthy control (2.6 [IQR 1.8-4.3] µmol/L). In cohort A, during a median follow-up of 2.2 years, 41 KTR (7%) died. In cohort B, over a median follow-up of 4.1 years, 78 KTR (14%) died. A 1-standard deviation higher plasma TMAO concentration was independently associated with an increased risk of all-cause mortality in both cohorts (HR 1.35 [95% CI 1.19–1.53]; P<0.001, and HR 1.34 [95% CI 1.23–1.47]; P<0.001; respectively).

Conclusions: Plasma TMAO decreases sharply after kidney transplantation, without reaching healthy controls levels. A higher plasma TMAO concentration was independently associated with an increased mortality risk in KTR. Further research is warranted to assess whether accounting for gut dysbiosis and TMAO could improve clinical outcomes in KTR.

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Infectious diseases, malignancies & long term challenges

EP_403 ARE KIDNEY AND LIVER TRANSPLANTS AN OBSTACLE TO BECOMING A MOTHER?

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Background: Many female patients who underwent liver and kidney transplants during childhood express a desire to become pregnant once they reach reproductive age. Among these patients, concerns about the potential adverse effects of immunosuppression on the fetus and the impact of pregnancy on allograft function are significant sources of anxiety. We conducted a retrospective analysis of pregnancy outcomes following liver and kidney transplantation at our transplant center.

Methods: We performed a total of 3589 kidney transplantations (KT) and 767 liver transplantations (LT) since 1975. In total, 42 kidney and liver transplant recipients experienced pregnancies. During pregnancy, recipient patients received immunosuppressive medications such as tacrolimus or cyclosporine, in addition to prednisone.

Results: Among these patients, 20 were LT recipients, and 22 were KT recipients. The average age at which these patients gave birth was 31 years (ranging from 24 to 38 years). The average time between organ transplantation and delivery was 9.9 years (ranging from 1 to 22 years). The average gestational age at delivery for the babies was 35.5 weeks (ranging from 24 to 39 weeks). While one patient delivered vaginally, the other patients underwent cesarean sections. Remarkably, all babies except one were born healthy. One baby died at 24 weeks due to placenta previa. A mother who underwent liver transplantation due to autoimmune hepatitis had a second liver transplant in the early period due to de novo autoimmune hepatitis. Unlike other mothers, she did not experience any significant complications or organ rejection during or after childbirth.

Conclusions: Female recipients of liver and kidney transplants can experience a safe pregnancy and give birth to healthy children if they receive follow-up care and treatment at experienced medical centers.

EP_404 THE BRIDGE TO A LONG, HAPPY AND SUCCESSFUL LIFE: LIVER TRANSPLANTATION

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Background: Chronic disorders may negatively affect people's learning status, marital status, occupational life, and social life. Liver transplant is the only curative treatment for chronic liver diseases. This study was undertaken to evaluate the psychosocial effects of liver transplant in adult patients who had undergone liver transplant during the pediatric period compared with psychosocial facts in the general population.

Methods: We retrospectively reviewed adult patients (>18 years of age) who had received liver transplant as children. We compared sex, age at the time of transplant, current age, donors, graft survival status, marital status, age at first delivery, number of children, educational status, and occupational status in the study population versus the normal population. To compare the liver transplant patients included in the study with the normal population correctly, we used Turkish Statistical Institute (TSI) data.

Results: Among 77 liver transplant patients included in our study, the mean age at transplant was 10.9 years (range, 0.5-16) and the mean age at the time of the study was 25.2 years (range, 18-42). Of the patients, 61 (79.2%) were single and 16 (20.8%) were married. Patients in the study population married at a younger age than the general population (25.5 vs 28.1 years for men, 24.3 vs 25.4 years for women). Of 16 married patients, 9 (56.2%) had healthy child/children. The percentage of patients who graduated from higher education or were continuing their higher education process was higher in our study population than in the general population (22.8% vs 36.3%). Among our study population, 37 patients (48%) were workers.

Conclusions: Our study shows that liver transplant had no negative effects on the social, educational, and professional lives of adults who received transplants in the pediatric period.

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EP_405 BENEFITS OF PHYSICAL ACTIVITY FOR ORGAN TRANSPLANT RECIPIENTS: REVIEW OF MEDICAL PUBLICATIONS

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Background: Physical activity (PA) is recognized as essential for enhancing the health and quality of life of organ transplant recipients (OTR). This systematic review aims to consolidate the findings from various published studies, highlighting the multiple benefits that physical activity confers on this population.

Methods: A comprehensive systematic review was conducted using PubMed/Medline and the Cochrane Central Register of Controlled Trials, focusing on studies published between 2000 and 2024 that discuss the benefits of PA for OTR. Only studies that assessed the impact of PA during the post-transplant period were included in the final analysis, which encompassed 65 studies among 138 from 19 countries.

Results: The analysis revealed that the majority of studies reported positive outcomes associated with PA in OTR, underscoring its necessity as a vital therapeutic intervention. Only four studies indicated adverse impacts or a lack of significant improvement. There is a demonstrated need for early rehabilitation programs, structured programs, including supervised and tailored exercise, coaching, and educational workshops, to maximize the benefits of PA. It is crucial to raise awareness among transplant professionals and healthcare providers about the importance of PA, including the need for exercise prescriptions and collaboration with sports medicine centers.

Conclusions: The most frequently observed benefits of PA for OTR are: Reduction of Cardiovascular Risk Factors, Improvement in Strength and Body Composition, Enhanced Quality of Life and Well-being The review emphasizes the importance of conducting further research specifically on pediatric and adolescent populations. Additionally, long-term studies on recipients under 40 years old, as well as the development of standardized key performance indicators (KPIs) to assess the benefits of PA, would provide valuable insights and guidelines for clinical practice.

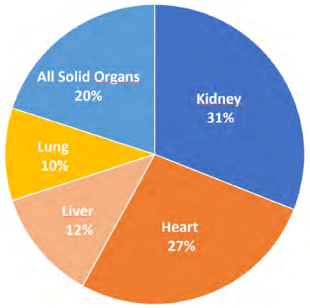

Figure: Frequency of reported benefits of Physical Activity across analyzed studies

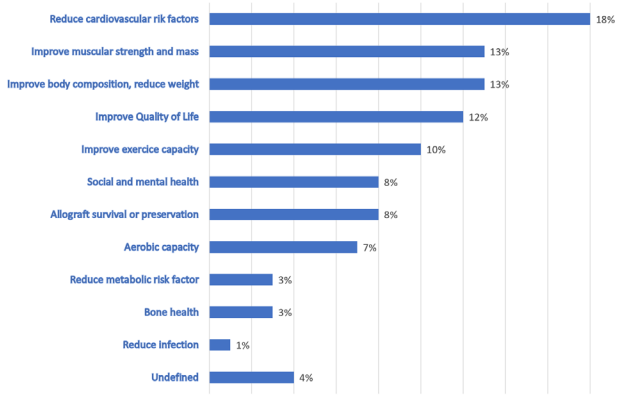

Figure: Distribution of Studies Across Different Types of Solid Organ Transplants

EP_406 RECIPIENT DONOR SEX COMBINATION DIFFERENCES OF INFECTIONS AFTER TRANSPLANTATION - A SWISS TRANSPLANT COHORT STUDY

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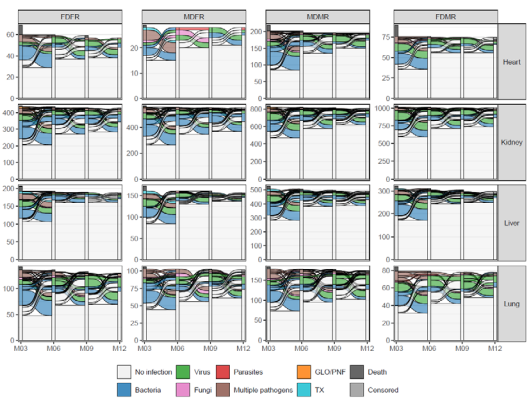
Background: Infections contribute significantly to morbidity and mortality after solid organ transplantation (SOT). While recipient sex interacts through multifactorial effects with infections, the importance of higher granularity regarding recipient and donor sex combination (RDSC) in risk-stratification for these events remains largely unknown.

Methods: Adult (≥ 18 years) single organ kidney, liver, lung, or heart recipients (May 2008 - December 2021) were retrieved from the Swiss Transplant Cohort Study. Follow-up was considered until December 2022. Patients were categorized into four RDSC groups. Primary endpoint was the incidence of clinically significant infections ≤ 365 days post-transplant. Competing risk analysis was performed (competing events: graft-loss & death) and visualized with Sankey plots.

Results: The 5 033 patients received 408 heart, 2 886 kidney, 1 224 liver, and 515 lung grafts. The cohort was categorized into 860 female-donor-female-recipients, 876 male-donor-female-recipients, 1 528 female-donor-male-recipients, and 1 769 male-donor-male-recipients. In a crude time-to-event analysis for the first infectious event, a significant difference between RDSC was seen in kidney (Gray test = 37.21; $p < 0.01$), with no difference in heart (Gray test = 4.00; p-value = 0.26), in liver (Gray test = 0.54; p-value = 0.91), and lung (Gray test = 1.31; p-value = 0.73) recipients. 1 796 patients (35.7%) suffered from an infectious episode within the first three months (Figure 1), with pathogens being in 944 (52.6%) events bacterial, 481 (26.8%) viral, 42 (2.3%) fungal, 9 (0.5%) parasitic, and in 112 (6.2%) multiple pathogens. RDSC was associated with differences in heart recipients for deaths and occurrences of multiple pathogens. In kidney recipients, variations were noted in repeated bacterial infections. For liver recipients, differences were identified in re-transplantation rates and multiple pathogen events ≤ 3 months. In lung recipients, differences were observed in the distribution of infectious events > 3 months.

Conclusions: An organ-dependent crude association was observed between RDSC and competing infectious events. A better understanding of how RDSC effects early post-operative outcome may allow for a risk-stratified management of potential infectious events.



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Infectious diseases, malignancies & long term challenges

EP_407 CHRONIC NOROVIRUS INFECTION IN KIDNEY TRANSPLANTATION

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Background: Noroviruses cause a fifth of diarrhoeal illnesses worldwide. Kidney transplant recipients (KTR) suffer severe, protracted symptoms that can lead to graft dysfunction and inferior long-term outcomes. Data is limited to case reports, series and a few retrospective studies that describe heterogenous cohorts, making it difficult to ascertain true incidence and outcomes. We sought to establish the incidence of norovirus infections, including chronic infections amongst KTR over a ten-year period.

Methods: This was a retrospective, single-centre study looking at KTR with Norovirus infections diagnosed between 1st June 2013 and 30th June 2023. Patients above the age of 18 at the time of diagnosis with a history of KT were included in the study. Data was collected using electronic patient records on demographics, graft function and outcomes.

Results: We identified a total of 63 kidney transplant recipients with norovirus infection over a ten-year period with a median follow-up of 62.5 months (IQR 44.3-84.8). Out of the patients who were exclusively transplanted during the study period, 3.4% of patients developed norovirus infection during the same timeframe. Chronic infection, defined by symptoms lasting more than 4 weeks, was identified in 56.9% of patients. A third of patients with chronic symptoms had delays in diagnosis and underwent multiple investigations prior to diagnosis. There was a trend for patients with chronic NoV infection towards inferior graft outcomes, although there are limitations due to sample size.

Conclusions: Our analysis adds to the growing body of literature supporting the significance of norovirus infections in KTR. Chronic norovirus causes morbidity and may be associated with inferior transplant outcomes. Delays in diagnosing chronic infection highlights the need to improve awareness amongst medical professionals.

EP_408 CLINICAL CHARACTERISTICS AND OUTCOMES OF KIDNEY TRANSPLANTATION IN ADPKD PATIENTS

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Background: Kidney transplantation (KT) is the best treatment for autosomal dominant polycystic kidney disease (ADPKD). We aimed to investigate clinical characteristics and outcomes of KT in ADPKD patients compared to those in non-ADPKD patients.

Methods: We retrospectively analyzed KT recipients in two Korean transplantation centers from 2005 to 2020. A propensity score-matching and Cox regression analysis were used to assess the clinical outcomes of ADPKD compared to non-ADPKD and prognostic factors influencing outcomes in ADPKD.

Results: Among a total of 4,452 KT patients, 189 (4.2%) were ADPKD patients. Median age at transplantation were 53.0 and 47.0 in ADPKD and non-ADPKD patients, respectively. In both groups, living-donor KT were more common than deceased-donor KT. The ADPKD group had a 4.09-fold higher risk of post-transplant diabetes mellitus and a 1.65-fold higher risk of post-transplant infection compared to the non-ADPKD group; however, it had similar risk of rejection, graft failure, and mortality. In the ADPKD group, kidney volume decreased after KT irrespective of kidney volume status (Mayo classification), while size of hepatic cyst increased. Either kidney volume or nephrectomy of native kidneys was not associated with risk of infection, graft failure, or mortality in the ADPKD group.

Conclusions: ADPKD patients have a higher risk of post-transplant diabetes mellitus and infection than non-ADPKD patients without a significant impact of kidney volume or nephrectomy on post-transplant outcomes.

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EP_409 MANAGEMENT OF EBV ASSOCIATED LYMPHOPROLIFERATIVE DISORDER AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: Post-transplant lymphoproliferative disorders (PTLD), though being the one of the most common de-novo malignancies following liver transplantation (LT) in children with attendant high morbidity and mortality rates, still does not have standard treatment protocols for its management in view of its rarity.

Methods: We hereby report 2 pediatric cases with EBV-associated PTLD that were successfully managed by chemotherapy protocols.

Results:

Case	Age at LT	Age at PTLD diagnosis	Symptoms of PTLD	EBV levels at diagnosis of PTLD	PET-CT report	Biopsy	Regimen used	Outcomes
1	1.5 years	4.5 years	Progressively increasing right cheek swelling, bleeding from gums, recurrent fever, and weight loss for last 6 weeks.	2.2 x 10^6 copies/ml	Metabolically active irregular mass involving the right maxillary sinus and retro-orbital region, along with multiple lesions in right kidney and ileal loops(figure 1-A2).	High-grade large B-cell lymphoma; Double-hit lymphoma). I	4 cycles of 3 weekly Rituximab-CHOP with intrathecal methotrexate followed by 4 x three weekly Rituximab	Repeat PET CT- No evidence of abnormal metabolic activity (figure 1-A2).
2	4.5 years	8 years	Abdominal pain with palpable right hypochondrial and right lumbar abdominal mass, loss of appetite, and weight loss for last 8 weeks	3.1 x 10^5 copies/ml	Metabolically active heterogeneously enhancing lobulated mass measuring 11 x 12 x 8 cm in the right side of the abdomen in close relation to jejunal loops (figure 1-B)	Monomorphic PTLD-Burkitt lymphoma and was positive for CD20, CD3, Bcl-6 with patchy positivity of CD 10 and Ki67 nearly 90%	Same as above	Repeat PET CT showing no evidence of abnormal metabolic activity (figure 1-C)

Conclusions: In conclusion, we report two cases of EBV-associated PTLD in the pediatric population managed promptly by immunosuppression reduction, and aggressive chemotherapy. These cases also emphasize the importance of developing institution specific EBV load monitoring protocols in for regular surveillance and early diagnosis of PTLD.

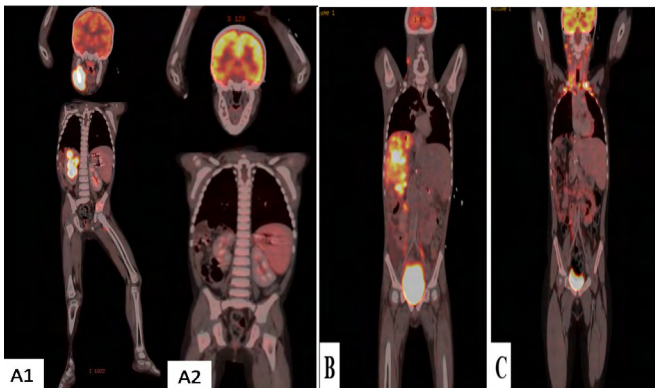

Figure 1: Pre- and post-chemotherapy PET CT images [case 1 (A1 & A2), and case 2 (B & C)]

EP_410 ASSOCIATION OF QUANTITATIVE AND PHENOTYPICAL CHARACTERISTICS OF BKPYV-SPECIFIC CD4 T CELLS AND VIRUS REPLICATION

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Background: Uncontrolled replication of BK polyomavirus (BKPyV) is one of the most common infectious complications after renal transplantation, which may lead to polyomavirus-associated nephropathy (PyVAN).

Methods: To identify immunological correlates for protection from PyVAN in patients with active BKPyV replication, we performed cross-sectional and longitudinal analyses of BKPyV-specific CD4 T-cell characteristics in the first 6 months after renal transplantation. BKPyV-specific CD4 T cells were quantified and characterised using flow cytometry based on expression of cytokines (IFNγ, IL-2, and TNF) and markers for activation (CD69) and regulation (CTLA-4).

Results: Among 37 patients, 14 had no detectable BKPyV DNA in urine and/or plasma, 12 had low-level DNA, and 11 developed clinically relevant DNAuria/DNAemia. BKPyV-specific CD4 T-cell levels were low and showed strong inter-individual variability. Stratification according to DNA load revealed significantly higher T-cell levels in patients with high-level DNAuria/DNAemia (median 0.08%, IQR 0.12%) when compared to patients without (median 0.02%, IQR 0.03%) or with low-level DNA (median 0.02%, IQR 0.03%; p=0.006). Percentages of multifunctional BKPyV-specific T cells co-expressing all three cytokines were lower in patients with detectable BKPyV DNA, independent of its level (p=0.042). Expression of CTLA-4 was clearly elevated in patients with high-level DNAuria/DNAemia (p=0.0005). Longitudinal analyses revealed an increase in percentages and CTLA-4 expression and a decrease in triple-cytokine-expression of BKPyV-specific CD4 T cells in temporal association to onset of DNAuria/DNAemia.

Conclusions: There is an association between BKPyV-specific CD4 T-cell characteristics and high-level BKPyV replication. However, the use of BKPyV-specific CD4 T-cell monitoring for individual identification of patients at risk for PyVAN remains challenging due to low T-cell levels with strong inter-individual variations.

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EP_411 DESMOID TUMOR POST KIDNEY TRANSPLANTATION: A TALE OF TWO CASES WITH DIVERGENT OUTCOMES

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Background: Desmoid tumors (DTs), or aggressive fibromatosis, are rare, benign, yet locally invasive fibroblastic neoplasms. They have a higher incidence in kidney transplant recipients due to immunosuppressive therapy, compared to the general population. Despite being non-metastatic, these tumors can pose significant challenges due to their infiltrative growth and high recurrence rates. This study presents two cases of post-transplant desmoid tumors with differing outcomes, highlighting clinical management strategies and their implications.

Methods: Two kidney transplant recipients who developed DTs were evaluated. Clinical presentations, diagnostic workups, and management strategies were analyzed. Both patients were monitored through imaging, biopsy, and multidisciplinary consultations. Treatment approaches included surgical intervention and immunosuppressive regimen adjustments, with a focus on preserving graft function where feasible.• **Results**: **Case 1:** A 23-year-old male developed a 7.5 cm DT four years post-transplantation, arising from the graft and infiltrating surrounding tissues. Surgical excision necessitated graft nephrectomy. The patient resumed chronic hemodialysis with cessation of immunosuppression. • **Case 2:** A 17-year-old female presented with a 17 cm DT five years post-transplantation. Surgical excision successfully preserved graft integrity. At follow-up, the patient maintained stable graft function (serum creatinine: 1.4 mg/dL).

Conclusions: Desmoid tumors, though rare, should be considered in the differential diagnosis of post-transplant masses. Timely diagnosis and a tailored therapeutic approach can significantly influence outcomes, balancing tumor control with graft preservation. Regular follow-up and imaging are critical for early detection and intervention.

EP_413 DIABETES AFTER RENAL TRANSPLANTATION: EPIDEMIOLOGICAL AND CLINICAL BIOLOGICAL ASPECTS

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Background: Diabetes after kidney transplantation was first described in 1964 by Starzl et al. and since then this pathology has been the subject of several studies to specify its clinical-biological and therapeutic epidemiological aspects.

Methods: This is a descriptive study of 39 patients kidney transplant who developed diabetes after kidney transplantation in the nephrology department of university Hospital of sahloul .

Results: our series was composed of 33 men and 6 women with a sex ratio of 5.5. The average age was 43 years ± 10 with extremes ranging from 20 to 69 years. Pre-graft obesity was noted in 11 patients (28.2%). The underlying nephropathy was mainly of interstitial origin (53.8%). Diabetes was discovered during a systematic control biological examination in all patients. Its median of occurrence was 6 months with a minimum of 15 days and a maximum of 6 years. The mean blood glucose at the time of discovery of diabetes was 8.48 mmol/l with a minimum of 7 and a maximum of 14 mmol/l. The mean HbA1C level at the time of diagnosis was 6.18% with extremes ranging from 5.1 to 7.4%. Arterial hypertension was noted in 29 patients or 74.4% of the cases of which 25 patients (78.1%) were already known to have pre-graft hypertensive. Dyslipidemia was noted in 25 patients (64.1%) of which 21 patients (63.6%) were already known in pre-transplant. Biologically, creatinine nadir was observed at a median of 30 days post-renal transplantation. Its average value was 118 ± 82.35 umol/l with a DFG= 65.52 ± 20.80 ml/min. Hypomagnesemia was retained in 17 patients (43.6%) and vitamin D deficiency in 9 patients (23.1%).

Conclusions: Diabetes after kidney transplantation remains a common metabolic complication in post-transplant whose clinico-biological and epidemiological aspects are close to those related to type 2 diabetes.

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EP_414 INFLUENCE OF AGE ON SPORT PREFERENCES IN TRANSPLANT RECIPIENTS: A COMPARATIVE STUDY

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[1]Association Trans-Forme; Patient Care Association, [2]Association Trans-Forme, [3]University Hospital Caen; Transplantation

Background: Physical activity plays a crucial role in post-transplant rehabilitation. However, sport preferences may vary with age, a factor that remains underexplored within the transplant population. This study analyzes sport the age and preferences among active transplant recipients, comparing trends in France, Europe, and Worldwide over a ten-year period.

Methods: Data were collected from participants in transplant-specific sports games for the periods 2023/2024 and 2014/2015. Analysis includes an age and region-based distribution of sports, cross-sectional comparisons of sport preferences by age group and geographic area, as well as a ten-year longitudinal analysis.

Results: In France, transplant recipients participating in the games events are on average 8 years younger than the general transplant population. Comparing sport intensity reveals that the median age for low-intensity sports is 53 years, 50 years for intermediate-intensity sports, and 43 years for high-intensity sports. Worldwide and European transplant recipients are on average 3 to 4 years older than those in France. The median age of transplant recipients increases by 1 year in France, 4 years in Europe, and 5 years worldwide between 2014 and 2024.

Conclusions: This study reveals age-related variations in sport preferences among transplant recipients. The median age of transplant recipients participating in games is progressively increasing compared to the general transplant population, indicating a low participation rate among those under 30. These findings underscore the importance of age-specific rehabilitation programs, particularly to encourage younger transplant recipients under 30 to engage in physical activity. The study's limitations, including sample size in France and the absence of variables such as recipient age when transplanted or gender, point to the need for future research with more diverse samples and additional variables to better understand the sport dynamics in this population.

Number of transplant recipients participating in the transplant games	Region	Number of countries	Summer	Winter
	France	1	70	20
	Europe	25	500	N/A
	World	45	1300	250

Table 1 (period 2023/2024)

Median Age in Years	2024	2014
All transplant recipients in French games	45	43
All French transplant recipients	53	51
The entire French population	42	40

Table 2 (France)

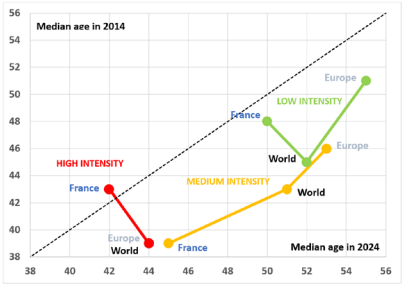

Figure 1: Comparison of sport intensity level by age among transplant recipients in France, Europe, and worldwide (2014 vs 2024)

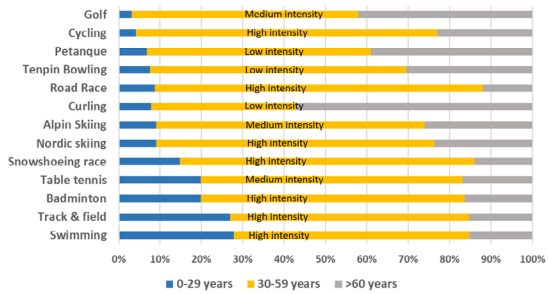

Figure 2: Distribution of sport preferences by intensity level and age group among transplant recipients

EP_415 ASSOCIATION OF HLA IN IGA NEPHROPATHY RECURRENCE AFTER KIDNEY TRANSPLANTATION

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Background: IgA nephropathy (IgAN) is the leading cause of primary glomerulopathy globally, presenting a high lifetime risk of kidney failure, with up to 50% of patients requiring kidney function replacement by age 51. Kidney transplantation (KT) is the preferred treatment method. The recurrence of IgAN post-transplantation is a significant factor leading to graft failure, occurring in 9-61% of cases based on various studies. Younger age and aggressive disease are associated with higher recurrence risk. The predisposition to IgAN may be linked to specific HLA-DR and -DQ alleles. This analysis sought to identify risk and protective HLA alleles.

Methods: his retrospective monocentric analysis included patients with biopsy-verified IgAN who underwent KT at the Transplant-Nephrology Department of the University Hospital Martin. Patients were monitored for IgAN recurrence through histological confirmation in graft biopsies. HLA typing was conducted before placing patients on the KT waiting list. The analysis included a comparison to a control group of 10,000 healthy donors from the Eurotransplant registry, capturing demographic and clinical characteristics of the patients.

Results: Out of 470 patients screened post-KT, 7.2% (n = 48) were found to have biopsy-verified IgAN, primarily affecting men (77%). The allele DRB1*11 was found in 47.92% of IgAN patients, indicating a significant risk for IgAN (OR 2.09), while DRB1*03 appeared in 4.17% and was protective against IgAN (OR 0.2). Recurrence of IgAN post-KT was confirmed histologically in 10% of patients (n = 5), all of whom were men, with an average time of 51.4 months to recurrence. All patients with confirmed recurrence had the risky allele DRB1*11, and 80% also had DRB1*03. Notably, one patient exhibited early recurrence after a secondary KT and carried both risk alleles.

Conclusions: The study found a 7.2% incidence of biopsy-confirmed IgAN and a 10% recurrence rate in grafts following KT. The allele DRB1*11 was identified as a risk factor, while DRB1*03 was protective against the development of IgAN and recurrent disease post-transplantation.

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EP_416 KIDNEY TRANSPLANTATION IN PATIENTS WITH ADULT CONGENITAL HEART DISEASE

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Background: Congenital heart disease (CHD) is the most common congenital anomaly. Due to advances in medical care 85-90% of these patients survive into adulthood resulting in an increasing number of adults with CHD (ACHD). Nearly 50% of ACHD patients have reduced kidney function with chronic kidney disease prevalence 6.4 times higher than in the general population. While kidney transplantation is preferred treatment for end stage renal disease (ESRD), data for ACHD patients is lacking. This study aims to explore the outcomes of kidney transplantation in ACHD patients.

Methods: We retrospectively analyzed medical records of kidney transplant recipients (KTRs) who received kidney allograft between August 2007 and December 2022 in our center. Characteristics and outcomes of KTRs with ACHD were investigated.

Results: Of 1242 KTRs, 8 (0.64%) had ACHD, 4 women and 4 men. Two patients had aortic coarctation, one bicuspid aortic valve, two ventricular septal defect and three atrial septal defect. The causes of kidney failure varied: three patients had congenital conditions with urinary tract involvement, three biopsy proven primary kidney disease, one Wilms tumor and one adult polycystic kidney disease. The median dialysis vintage prior kidney transplantation was 3.3 years (0.7-9.7 years). Two patients received kidney from living and 6 from deceased donors. The median donor age was 46.5 years (22-63 years) and the median recipient age at transplant was 24.6 years (16.2-54.3 years). All patients received basiliximab induction followed by standard triple immunosuppression. After a median follow up of 6.4 years (1.1-14.2 years) all patients were alive. One patient experienced kidney allograft failure 2.4 years after transplantation while the rest had functioning grafts with a median eGFR of 68 ml/min/1.74 m^2 (39-72 ml/min/1.74 m^2) at the time of last follow up. Two patients had indication biopsy during follow up, one of them was treated for rejection. No cardiovascular complications were reported during follow up.

Conclusions: Kidney transplantation in ACHD patients and ESRD should be considered and encouraged. It could offer favorable outcomes, though long-term monitoring is essential. Further research with larger cohorts is needed to better understand the outcomes and challenges in this specific group of patients.

EP_417 A LONG-TERM RESULT OF RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: We experienced one case of diaphragmatic metastasis of hepatocellular carcinoma (HCC) that occurred 12 years after living donor liver transplant (LDLT) even though there was no evidence of HCC at that time. Many studies have concluded that cancer patients may have better outcomes on the side of morbidity, mortality, and survival rate when their surgery is performed in high-volume rather than low-volume centers. As we are a low volume center and had an unusual recurrence of HCC after LT, we reviewed our long-term outcomes on recurrence of HCC after LT and evaluated the overall outcomes of LT with HCC in our center.

Methods: We did 56 LTs since June 2006 and the last LT was done in 2018. Among then, 17 liver recipients had diagnosed with HCC, 12 associated with hepatitis B virus (HBV), 3 associated with hepatitis C virus (HCV), and 2 associated with alcoholic cirrhosis. We analyzed 16 patients because one died on operative 15th day after LDLT with Model for End-Stage Liver Disease (MELD) score 40 but no deceased donor appeared at that time.

Results: Mean follow up time was 194.8 ± 14.2 (45 ~ 216) months. Mean level of preoperative AFP was 34.3 ± 79.8 (1.30 ~ 318) ng/ml. Mean MELD score was 15.4 ± 5.7 (7 ~ 27). Survivals at 1,5, and 10 years were 100%, 87.1%, and 87.1% and disease-free survivals, 87.5%, 87.5%, and 87.5%. The disease-free survivals went down to 80.2% after 12 years. Recurrence was developed in 3 cases (18.8 %) and death was detected in 2 cases (12.5 %). There was one risk factor for HCC recurrence and it was microvascular invasion at pathologic reports ($P < 0.01$).

Conclusions: We have had acceptable outcomes on HCC after liver transplantation in a low volume transplant center.

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EP_418 IMMUNOSUPPRESSION MODULATION IN KTR WITH CUTANEOUS SQUAMOUS CELL CARCINOMA: A DELPHI CONSENSUS STUDY

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Background: Post-transplant cutaneous squamous cell carcinoma (CSCC) is a significant cause of morbidity and mortality. Increased aggression is due to the off-target effect of transplant immunosuppression (IS). Studies suggest that prompt IS modification after CSCC may reduce further CSCC burden (secondary prevention). There are currently no guidelines for the management of IS after CSCC. This study aimed to establish consensus recommendations for the secondary prevention of CSCC in kidney transplant recipients (KTR) from the transplant nephrology perspective.

Methods: The Delphi method was chosen to present expert transplant nephrologists with CSCC-related scenarios across rounds of questioning by online survey to reach consensus. Scenarios used actinic damage and skin cancer index (AD-SCI) stages 4-6 (Figure 1) across a variety of IS regimens. The peer-esteem snowball technique was used to identify 'experts', defined as English-speaking nephrologists with >5 years experience and ongoing responsibility for long-term management of KTR. Near-consensus and consensus thresholds of 70% and 80% agreement were predefined, respectively, corresponding to previous standards.

Results: 46 experts responded to the first round of the survey, with 31 completing all three rounds. Amongst first-round respondents, there was diverse geographical representation from North America, Europe and Australasia. 95% were members of a national/international professional transplantation society. Over half had >15 years' experience in practice. Recommendations are summarized in Figure 1. Liaison with transplant dermatology to optimize dermatological care was recommended at all AD-SCI stages. Consideration of IS change was recommended at stages 5/6, depending on the existing IS regimen and patient factors, typically involving change from azathioprine (if present) or commencement of MTOR inhibitor (if not on azathioprine).

Conclusions: We provide the first consensus recommendations for IS management in the setting of CSCC to reduce secondary disease burden in KTR. Prospective studies are urgently needed to validate these recommendations.

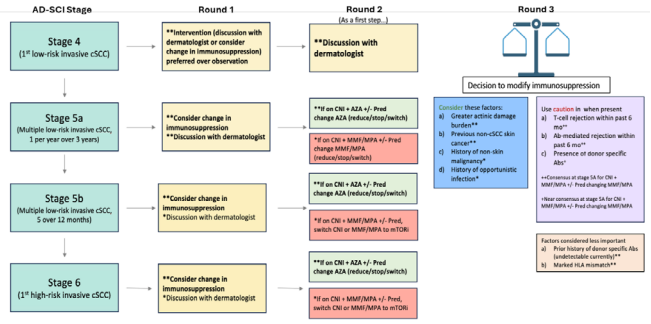

Figure 1: Flow chart for IS management after cutaneous squamous cell carcinoma (CSCC) in kidney transplant recipients. *near-consensus; **consensus

EP_419 TORQUE TENO VIRUS BASED LONG TERM MONITORING FOR THE DETECTION OF INFECTIONS IN KIDNEY TRANSPLANTATION

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Background: Personalized balance of immunosuppression is crucial to prevent organ rejection and infections in kidney transplant recipients. Plasma load of the non-pathogenic and highly prevalent torque teno virus (TTV) has been suggested to assess the state of immunosuppression. A cut-off value for risk prediction of infections in the first year post-transplant has been defined and is currently tested in an interventional randomized clinical trial (TTVguideIT). Defining cut-off values beyond year one post-transplant are crucial for the design of follow-up trials (e.g. TAOIST) and long term routine clinical care.

Methods: For this secondary analysis of the prospective single-center AdTorque study, all 268 consecutive adult patients who underwent a kidney transplantation between January 1st, 2018 and December 31st, 2019 at the Medical University of Vienna were included and followed up for a maximum of 4 years. Over this time, all infectious events with respective treatments, hospitalizations and changes of immunosuppression were recorded. Infectious disease work up included syndromic PCR panel testing including SARS-CoV-2 PCR. Additionally, immunologic monitoring via TTV PCR from plasma was performed.

Results: In a preliminary analysis including 150 patients (37,2% female; median age 52.7 years) 621 infectious events were recorded, with 24 patients not experiencing an infection. Of all events the majority were urinary tract infections (204; 32.9%), 178 of all events led to hospitalization. The most commonly identified pathogens were cytomegalovirus (n=97), Escherichia coli (n=71) and SARS-CoV-2 (n=53). The overall event rate declined over the first three years post-transplant, with a rise in the fourth year (year 1: 94.9%; year 2: 48.0%; year 3: 44.7%; year 4: 78.4%).

Conclusions: This interim analysis gives valuable insight on the epidemiology of infectious disease in the current post-transplant era. The strength of the study is the long term follow-up, the overlap with the height of the COVID-19 pandemic and the inclusion of multiplex PCR panels for routine work-up. The full data set including associations with TTV load on and respective cutoffs are currently being assessed, and will be presented at the ESOT congress 2025 in case of acceptance.

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EP_420 2D PHASE CONTRAST MAGNETIC RESONANCE ANGIOGRAPHY AND KIDNEY TRANSPLANT ARTERY FLOW: FACTORS AND OUTCOMES

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[1]Imperial College Healthcare NHS Trust; Renal; Renal, [2]Imperial College Healthcare nhs Trust, [3]Hammersmith Hospital / Imperial College Healthcare NHS Trust; Imperial College Healthcare nhs Trust, [4]Imperial College London Faculty of Medicine; Imperial College London; Department of Immunology and Inflammation

Background: Cardiovascular health and kidney transplant health are interconnected. 2D phase contrast magnetic resonance angiography (PC MRA) is a non invasive means of quantifying blood flow, but its utility for assessing flow in transplant arteries has not been explored. This study set out to: • Establish the normal range of transplant artery flow measured by 2D PC MRA. • Assess 2D PC MRA flow measurements as a screening test for transplant renal artery stenosis (TRAS). • Determine if transplant artery flow is influenced by donor or recipient factors, and/or influences clinical outcomes.

Methods: 218 PC MRA were performed on 203 patients with suspected TRAS. Arterial flow data were generated using CVI42 software. Baseline and outcome data were collected for all participants.

Results: Demographic data are in Table 1. Median follow up was 49 (IQR 40-54) months. Mean transplant artery flow for the cohort was 0.41, 95%CI (0.39-0.45) L/min. ROC analysis revealed poor sensitivity (57.9) and specificity (67.1) of PC MRA flow as diagnostic test for TRAS. There was a negative correlation between transplant artery flow L/min and donor age ((r = -0.25 95% CI(-0.37 - 0.12) p=0.0002)) and recipient age at time of PC-MRA ((r = -0.38 95% CI (0.48 - -0.25) p<0.0001)). There was a positive relationship between flow L/min and contemporaneous eGFR p<0.0001 (Fig1a) Overall, 30 (14.8%) recipients experienced allograft failure and 33 (16.3%) died with a functioning allograft. There was no difference in allograft survival between recipients categorised according to transplant artery flow L/min, logrank P=0.3854. However, subjects in the lowest flow quartile were at greater risk of death compared with subjects in the highest flow quartile, HR 17.23, 95% CI (6.11–48.60) logrank P=0.0004 (Fig1b). On multivariate analysis, flow was independently associated with death with a functioning allograft b=-0.003, exp(b) 0.997, 95% CI (0.994 – 0.999), P=0.009

Conclusions: PC-MRA flow cannot be used to diagnose TRAS. However, this study found significant associations between transplant artery flow, donor factors and recipient outcomes. Although neither cause not effect of low flow have been elucidated, improving flow by optimising cardiovascular health may have a positive impact on outcomes for kidney transplant recipients and warrants further study.

Table One – Demographic data of study participants

	MRA negative for TRAS	MRA positive for TRAS	P value
Total Participants • 13 had >1 MRA. Data at index MRA reported here	160	43	
Age, years – median (IQR)	54 (45.5 - 62)	59 (49.3 – 69)	P = 0.03
Male – total (%)	110 (68.8)	33 (76.7)	P = 0.31
Ethnicity – Total (%) - Non –white - White	 103 (64.4) 57 (35.6)	 35 (81.4) 8 (18.6)	P = 0.03
Diabetes – total (%)	75 (46.9)	26 (60.5)	P = 0.11
Months at ESKD prior to transplant – median (IQR)	23.5 (8 – 50.5)	34 (14.8 – 60.8)	P = 0.08
Days from transplant to MRA – median (IQR)	629 (79.5 – 2080)	183 (63.6 – 485.3)	P = 0.03
Living donor – total (%)	51 (31.9)	8 (18.6)	P = 0.09
Cause ESKD – Total (%) - ADPKD - DKD - GN - Other	 15 (9.4) 42 (26.3) 55 (34.3) 48 (30)	 3 (7.0) 22 (51.2) 8 (18.6) 10 (23.2)	P = 0.47

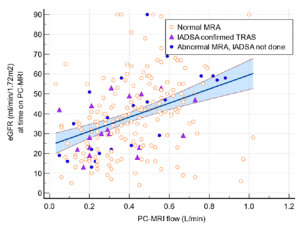

Fig 1a. Regression analysis – PC-MRA transplant artery flow (L/min) and eGFR (ml/min/1.72m2) R2 0.14 DF regression 1 DF residual 214 F ratio 34.72 p<0.0001

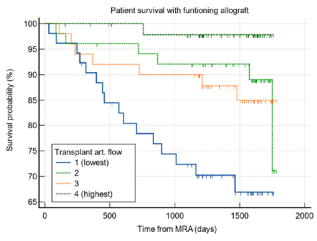

Fig 1b. Recipient survival with functioning allograft categorized according to transplant artery flow volume (L/min) logrank test p= 0.0004

EP_421 UNMASKING SARCOMATOID RENAL CELL CARCINOMA IN A REJECTED ALLOGRAFT: A CASE REPORT OF AN UNCOMMON POST TRANSPLANT CANCER

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Background: Kidney transplantation is the preferred treatment for end-stage renal disease (ESRD) due to its ability to enhance quality of life and survival compared to dialysis. However, post-transplant malignancy is a significant complication, with transplant recipients at an increased risk of cancers, including skin, hematologic, and genitourinary malignancies. Renal cell carcinoma (RCC), the most prevalent genitourinary malignancy, commonly arises in native kidneys and accounts for 5–16% of post-transplant malignancies. RCC in transplanted allografts is rare (0.1–0.5%) but carries a risk of metastasis, largely due to chronic immunosuppression. This case report details an RCC with sarcomatoid features in a rejected allograft kidney with metastases.

Methods: A 53-year-old male with a rejected kidney transplant presented with lower abdominal pain, nausea, and vomiting. Imaging revealed a suspicious renal mass in the allograft, along with features of xanthogranulomatous inflammation and adhesions to calcified iliac vessels. A retroperitoneal nephrectomy was performed, and histopathology confirmed RCC with sarcomatoid differentiation. Postoperatively, the patient developed a hematoma managed with drainage and antibiotics. Due to advanced disease and extensive comorbidities, palliative care with adjuvant radiotherapy was recommended.

Results: The case underscores the rarity and complexity of RCC in renal allografts, influenced by prolonged immunosuppression, recipient comorbidities, and environmental factors. Sarcomatoid differentiation, associated with poor prognosis, further complicates management

Conclusions: This case highlights the importance of early recognition and multidisciplinary management of RCC in transplant recipients. Standardized guidelines for diagnosis and treatment are essential to improve outcomes in these complex cases.

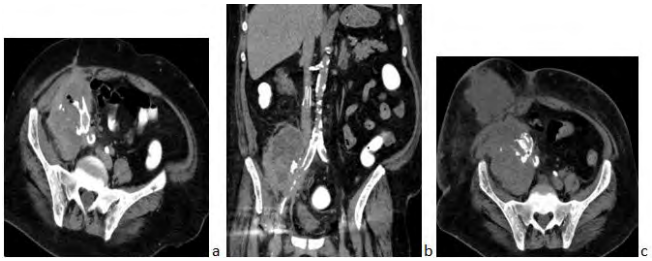

Figure 1

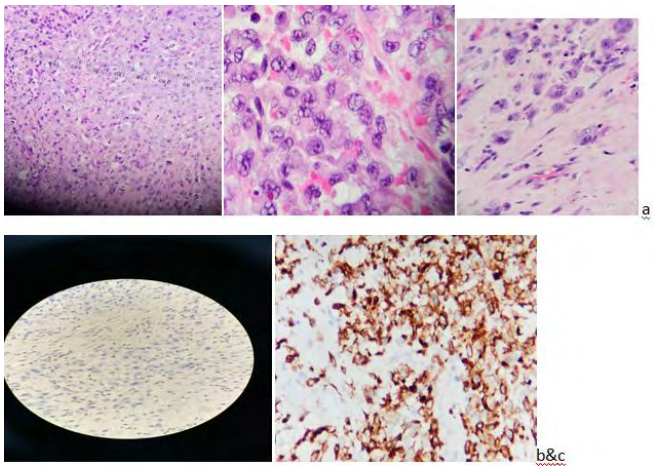

Figure 2

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EP_422 TORQUE TENO VIRUS (TTV) IN PATIENTS AFTER HEART TRANSPLANTATION - PRELIMINARY STUDY

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[1]Slaski Uniwersytet Medyczny W Katowicach; Faculty of Medical Sciences in Zabrze; Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, [2]Faculty of Public Health in Bytom, Medical University of Silesia; Department of Biostatistics, [3]Silesian Park of Medical Technology Kardio-Med Silesia, [4]Silesian Center for Heart Diseases, [5]Medical University of Vienna; Department of Cardiac Surgery, [6]Medical University of Vienna; Department of Cardiac Surgery; Dept of Cardiac Surgery, [7]Faculty of Medical Sciences in Zabrze, Medical University of Silesia; Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, [8]Medical University of Silesia; Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia; Department of Cardiac, Vascular and Endovascular Surgery and Transplantology

Background: To evaluate the prevalence and kinetics of TTV virus in heart transplant recipients

Methods: We analyzed a cohort of 39 heart transplant recipients, including 18 females, based on their TTV infection status. The TTV viral load was quantified using RT-PCR kit following the manufacturer's protocol. TTV levels were measured at three different time points: immediately before heart transplantation (HTx),one month post-HTx, and three months post-HTx. Data collection occurred between March 2023 and December 2023 at a high-volume heart transplant center.

Results: The median age of the patients at the time of transplantation was 52 [43–62] years. The median BMI was 24.4, with 31% of patients diagnosed with diabetes. The predominant etiologies of heart failure were ischemic cardiomyopathy (36%) and dilated cardiomyopathy (39%). Patients received induction therapy with basiliximab. For maintenance immunosuppression, tacrolimus, mycophenolate, and steroids were prescribed. During the observation period, 8 patients died. TTV was present in 92.3% of recipients at baseline and in 100% at the subsequent two time points. By the 1st month, 10 patients experienced infections, and between the 1st and 3rd months, 5 patients had infections. By the 1st month, 8 patients (20.5%) had acute cellular rejection (ACR) graded ≥ 2R according to the ISHLT 2004 criteria, and between the 1st and 3rd months, 3 patients (9.7%) met this threshold. The mean acute cellular rejection index (ACRI) was 0.086 ± 0.2 by the 1st month and 0.041 ± 0.069 by the 3rd month. In the analyzed cohort, TTV levels significantly increased over time, with the highest values observed at the 3rd month: median (IQR) copies/mL: baseline 510 (201, 4,425), 1st month: 464,500 (108,025, 6,942,500),.3rd month: 18,550,000 (7,797,500, 50,425,000); P<0.001. The ACRI was not significantly correlated with TTV load: -0.28, p = 0.199 at the 1st month, and -0.23, p = 0.269 at the 3rd month. Mean tacrolimus levels were 13.4 ± 3.9 vs. 13.95 ± 4.1 µg/mL; P=0.4, mycophenolate mofetil dosage was 2 (2.0, 2.5) vs. 1.50 (1.13, 2) g/d; P= 0.015, prednisone dosage was 7.5/d.

Conclusions: TTV is a frequent pathogen among heart transplant recipients. The number of viral copies significantly increases during the first three months post-transplantation. Further investigations are required.

EP_423 CANDIDA ARTERITIS IN KIDNEY TRANSPLANT RECIPIENT

Filip Hudik[1], Michaela Matyskova Kubisova[2], Igor Gunka[3], Lenka Ryskova[4], Eva Hovorkova[5], Michal Lesko[6], Roman Safranek[7]

[1]University Hospital in Hradec Kralove; Department of Nephrology; Department of Nephrology, [2]University Hospital in Hradec Kralove and Faculty of Medicine in Hradec Kralove; Department of Nephrology; Department of Nephrology, [3]University Hospital in Hradec Kralove; Department of Surgery; Department of Surgery, University Hospital in Hradec Kralove, [4]University Hospital in Hradec Kralove and Faculty of Medicine in Hradec Kralove; Department of Clinical Microbiology; Department of Clinical Microbiology, [5]University Hospital in Hradec Kralove and Faculty of Medicine in Hradec Kralove; Department of Pathology; Department of Pathology, [6]University Hospital in Hradec Kralove, Czechia and Faculty of Medicine in Hradec Kralove; Department of Surgery; Department of Surgery, [7]University Hospital Hradec Kralove; Department of Nephrology; Department of Nephrology

Background: Graft site candidiasis is a rare but life - threatening complication of renal transplant. Due to limited data, there are no specific guidelines for its diagnosis and treatment.

Methods: A 50 year old man with end stage renal failure secondary to polycystic kidney disease underwent a preemptive kidney transplant. The cold ischemia time was six hours thirty-four minutes. Good perfusion of the transplant kidney was noted with immediate graft function. Basiliximab was given at induction and maintenance immunosuppression was achieved using tacrolimus, mycophenolate mofetil, and prednisolone. Our patient was discharged on postoperative day 8, his serum creatinine was 109 µmol/l and level of hemoglobin was 10.1 g/dl. He is readmitted the same day and he complained of diffuse abdominal pain. Severe bleeding from renal graft anastomosis was confirmed on computed tomography (CT). This led to urgent surgery and graftectomy was necessary. Directed biopsy of the affected area was performed, histopathological examination revealed the infiltration of renal artery with budding yeast forming pseudohyphae. *Candida* etiology was confirmed by T2Candida panel, *Candida albicans/tropicalis* was detected. Other centers in which other organs from multi-organ harvesting were transplanted did not report any complications.

Results: The antimicrobial therapy with intravenous anidulafungin was immediately commenced. Seventeen days after surgery, a computed tomography scan was performed due to a decrease in the blood count. Examination confirmed the presence of a pseudoaneurysm of the external iliac artery and active bleeding, which was treated with an endovascular stent graft. Oral flucytosin was added to the antimycotic therapy. Our patient is currently undergoing hemodialysis for the third month and antifungal treatment continues.

Conclusions: Candida graft infection remains a rare complication of renal transplant; however, it can have catastrophic results resulting in death or graft loss. Contamination of the renal allograft or preservation fluid at organ retrieval is the most likely source of arterial candidiasis. Life-long antifungal therapy should be considered if complete resection of the infected tissue cannot be confirmed.

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EP_424 SEROLOGICAL PROFILE OF HEPATITIS B AND C IN LIVER TRANSPLANT PATIENTS FROM A TRANSPLANT CENTER IN BRAZIL

Luize Kremer Gamba[1], João Nicoluzzi[2], Paolla Hampel Pires[3], Felipe Caron[2], David Serra Hayne[2], Mauro Duarte Monteiro[2]

[1]Pontifícia Universidade Católica Do Paraná, [2]Hospital Angelina Caron, [3]Hospital Angelina Caron; Hospital Angelina Caron

Background: Viral hepatitis (HEP) represents a serious public health problem and is the leading cause of chronic liver disease in the world. Despite the campaigns for vaccination against HEP B and the recent national plan for the elimination of HEP C, hepatitis viruses remain the main cause of indication for liver transplantation (TX) in Brazil.

Methods: The aim of this study was to describe the serological profile of HEP B and C in liver transplant patients and to analyze the influence of serology on waiting time for the organ and survival. To this end, a retrospective analysis was performed with a sample of 148 patients who underwent hepatic TX in 2016 and 2017 at a transplant service in the metropolitan region of Curitiba.

Results: HEP B and C were the second and third highest indications for TX, respectively, behind only alcoholic cirrhosis. 12.8% of the sample has HBSag reagent, 16.9% antiHBS reagent and 9.5% anti-HCV reagent. Patients immunized for HEP B spent, on average, 45 days less on the waiting list (p=0.081), while those who were reactive for anti-HCV spent 61 days longer on the waiting list than those who were not reactive (p=0.063). A percentage of death (PD) of 33% was described in the 18 patients diagnosed with HEP B (p=0.390), with a hazard ratio (HR) of 0.69 (0.29 – 1.61) and PD of 43% in the 14 patients diagnosed with HEP C (p=0.837), with HR 0.92 (0.39 – 2.13), a measure of association HR with a 95% confidence interval.

Conclusions: It is concluded that there is a need to expand national campaigns for immunization and early diagnosis of hepatitis in the general population. In addition, non-immunized patients on the waiting list for hepatic TX should be strongly encouraged to vaccinate for HEP B, seeking shorter times on the list.

EP_425 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER AFTER ALEMTUZUMAB INDUCTION: SEROSTATUS, HISTOLOGY AND OUTCOMES

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Background: Post-Transplant Lymphoproliferative Disorder (PTLD) is a common malignancy with poor long-term outcomes. It is associated with two key factors; burden of immunosuppression over time and the effect of infection with Epstein Barr Virus (EBV). Studies have suggested an increased risk of PTLD in patients receiving alemtuzumab and ATG induction. Here we report on the serological, histological classification and outcomes in PTLD following Alemtuzumab induction.

Methods: Transplant patients were identified from a local haemoncology registry (2017-2024) and included in the analysis if they had a diagnosis of PTLD and had received Alemtuzumab induction. Data on EBV status and clinical outcomes were retrospectively collected and analysed.

Results: 47 patients with PTLD post-Alemtuzumab were included for analysis. The mean time from first transplantation to diagnosis 8.8 years (range 0-16.75 years) with 2/47 (4.3%%) presenting within 1 year. 19/47 40.4%) were female, 21/47 (44.6%) were Caucasian and the mean age at presentation was 55 years. 27/47 (57.4%) received a deceased donor and 5/47 (10.6%%) had received >2 transplants. 23/47 (48.9%) had EBV+ disease. Histology showed 25/47 (52/2%) monomorphic (MM), 6/47 (12.8%) polymorphic (PM), 5/47 (10.6%) classical Hodgkin's Lymphoma(cHL), 2/47 (4.3%) Marginal zone (MZ), 1/47 (2.1%) T-cell lymphoma and 2/47 (4.3%) plasma-cell hyperplasia and 6/47 (12.8%) MM/MZ. Overall 25/47 died (53.2%) and a further 3/47 (6.4%) experienced allograft failure after a median follow up of 1.4 years.

Conclusions: PTLD has a poor prognosis, there is high mortality within 1 year of diagnosis. Monomorphic, T Cell and classical Hodgkin's type PTLD confer the highest risk of death. However, we report lower mortality than in ATG induction (up to 80% in MM PTLD). In those receiving alemtuzumab there is an even split between EBV positive and negative disease and few present <1 year from transplantation.

	Total number	Overall mortality	Mortality at 1 year	Graft Failure without death
All	47	25/47 (53%)	15/47 (32%)	3/47 (6%)
EBV+VE	23	14/23 (61%)	8/23 (35%)	1/23 (4%)
EBV-ve	24	11/24 (46%)	7/24 (29%)	2/24 (8%)
MM PTLD	25	16/25 (64%)	10/25 (40%)	1/25 (4%)
PM PTLD	6	0/6 (0%)	0/6 (0%)	1/6 (17%)
cHL	5	3/5 (60%)	3/5 (60%)	1/5 (20)
T - Cell	1	1/1 100%	1/1 (100%)	0 (0%)
Other	10	5/10 (55%)	1/10 (10%)	0 (0%)

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EP_426 A QUALITATIVE STUDY OF CYTOMEGALOVIRUS AWARENESS AND EXPERIENCE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Infection with cytomegalovirus (CMV) is a prevalent and significant complication in kidney transplant recipients, increasing the risk of graft rejection, premature graft failure and mortality. Despite its ubiquity and potentially severe consequences, there is currently no data exploring the kidney transplant patient experience of CMV. This study aimed to address this gap in the literature, by exploring patient knowledge and awareness of CMV and its management, as well as determining the extent to which CMV infection impacts quality of life.

Methods: We performed semi-structured interviews with 50 adult recipients who had undergone kidney transplantation within the last two years. Participants were divided into two groups: those who had experienced CMV (n=25) and those who hadn't (n=25). The interviews were recorded and transcribed for analysis. Data was analysed using quantitative and qualitative methods.

Results: Awareness of CMV was low, particularly among those who had not experienced the virus. 32% of the non-CMV group were aware of CMV, compared to 88% in the CMV group ($p<0.001$). Knowledge of CMV symptoms and complications was sparse, contributing to minimal concern about the virus. Most CMV-affected participants (78%) reported no symptoms and treatments were rated highly effective, with a preference for pre-emptive management. There was a strong consensus on the need for better patient education about CMV, with suggestions for more direct communication through healthcare professionals.

Conclusions: This study is the first to provide a comprehensive evaluation of CMV awareness and management from the perspective of kidney transplant recipients in the UK. We highlight a significant gap in CMV awareness among kidney transplant recipients. Enhanced patient education, particularly through multimedia patient educational tools, could help bridge the knowledge gap and ensure better management of CMV in this population. These insights are vital for shaping future patient care strategies and could significantly impact clinical practice.

EP_427 IS HEPATO-RENAL POLYCYSTIC DISEASE A RISK FACTOR TO DEVELOP COMPLICATIONS FOLLOWING KIDNEY TRANSPLANTATION?

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Background: The hepato-renal polycystic (HRPD) disease is one of the leading causes of kidney transplantation globally. Observational studies suggest graft survival is higher compared to other etiologies of chronic kidney disease (CKD). However, there are no large registries that systematically assess whether the incidence of surgical or medical complications is higher in these patients.

Methods: This is a retrospective, single-center case-control study including patients who received a kidney transplant at Hospital Universitario La Paz between January 2018 and December 2021, where CKD etiology was HRPD (cases). For each case, a matched control was selected—a patient with CKD of a different etiology who received a graft from the same donor or underwent transplantation immediately after the case. Patients were followed until December 31, 2023. Data were analyzed using SPSS, with Cox regression employed for multivariable analysis.

Results: A total of 30 kidney transplants were performed on polycystic patients, with 30 respective controls. Renal function, proteinuria, and medical complications (stroke, thrombosis…) did not show significant differences in their evolution. However, a markedly higher incidence of obstructive uropathy related to compressive lymphocele was observed in HRPD patients (40% vs. 3.3%, $p < 0.05$). This variable was associated with significant risk factors ($p < 0.05$) identified in the sample through Cox regression analysis, confirming a hazard ratio (HR) of an 11-fold higher risk of lymphocele development in polycystic patients and a three-fold higher risk when induction therapy included mTOR inhibitors.

Conclusions: Our study highlights a significant difference in the incidence of obstructive uropathy due to compressive lymphocele in polycystic patients compared to those with other CKD etiologies. This complication was confirmed by Cox regression analysis and was also associated with mTOR inhibitor-based induction therapy. We conclude that, despite the need for larger studies to validate our findings, lymphocele is a frequent cause of obstructive acute kidney injury (AKI) in the post-transplant period for polycystic patients. Preventive measures should be considered during and after surgery, such as avoiding mTOR inhibitor-based induction therapy when possible.

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EP_428 DE NOVO ATYPICAL HEMOLYTIC UREMIC SYNDROME AFTER LIVER TRANSPLANTATION

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening disease characterized by thrombotic microangiopathy and multi-organ failure. Liver or combined liver-kidney transplantation has been proposed as a potential curative treatment. Nonetheless, de novo aHUS after liver transplantation (LT) presents complex challenges, requiring further study of optimal management strategies.

Methods: From February 2016 to February 2024, we retrospectively analyzed 33 aHUS cases, including 4 de novo aHUS after LT. Collected data encompassed demographics, donor types, diagnosis timing, clinical features, genetics, treatment strategies, and outcomes.

Results: Among the four cases of de novo aHUS after LT, three patients were men and one was a woman, aged 52, 59, 61, and 69 years. Three received grafts from living donors, and one from a deceased donor. One case was diagnosed 11 months post-LT, while the other three were diagnosed 2–2.5 years. All patients presented with extra-renal manifestations. Three exhibited poor response to plasma exchange (PE) combined with calcineurin inhibitor (CNI) and mechanistic target of rapamycin (mTOR) inhibitor withdrawal; two of these cases responded well to eculizumab, while one succumbed to liver failure and sepsis due to lack of financial access to eculizumab. The fourth patient responded well to PE and tacrolimus withdrawal. None of them demonstrated CFI or CFH mutations.

Conclusions: In Taiwan, CFH and CFI mutations are uncommon in adult aHUS patients, and none were identified in the four de novo aHUS cases after LT. This suggests that liver or combined liver-kidney transplantation may not be an optimal treatment for aHUS in Taiwan, especially since CNI and mTOR withdrawal does not consistently improve outcomes and may increase liver rejection risk. After reducing CNI and mTOR inhibitor doses, performing PE, and excluding secondary TMA causes, anti-complement therapy remains a critical rescue strategy.

EP_429 HIGH SERUM PHOSPHATE INCREASES MORTALITY RISK AND GRAFT LOSS AFTER KIDNEY TRANSPLANTATION

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Background: Graft loss in renal transplant may be related to non-traditional cardiovascular risk factors such as calcium and phosphate dysregulation, but prior studies have reached conflicting findings. We aimed to assess the impact of calcium and phosphate derangements in the first six months post-transplant on long-term patient and graft survival.

Methods: We studied 358 patients who received a first kidney allograft in Sheffield, UK, between January 2007 and December 2014. We obtained baseline demographics and laboratory investigations, with outcome data censored on June 30, 2020. We studied the association of serum phosphate and calcium concentrations at six months post-transplantation with long-term mortality and allograft survival.

Results: Over a median follow-up of 8 years, x participants died, and y lost their graft. Higher serum phosphate was independently associated with increased all-cause mortality (adjusted HR: 6.53; 95% CI 2.19 - 19.47, P = 0.001) and death-censored graft loss (..) and graft loss (HR: 8.12; 95% CI 2.59 - 25.43, P = 0.001). However, no association was found between serum calcium and patient or graft loss.

Conclusions: Higher serum phosphate, but not higher serum calcium, at six months post-transplantation is independently associated with increased mortality and excess graft loss.

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Infectious diseases, malignancies & long term challenges

EP_431 FOUR YEARS OF CLINICAL EXPERIENCE WITH COVID-19 OUTCOMES IN HEART TRANSPLANT RECIPIENTS

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Background: COVID-19 has had a significant impact on patient outcomes, particularly among individuals with comorbidities, including solid organ transplant recipients. This study aimed to evaluate the incidence and mortality of COVID-19 and to identify independent risk factors associated with COVID-19-related mortality in patients undergoing orthotopic heart transplantation (OHT).

Methods: This retrospective cohort study included 556 adult heart transplant recipients from a high-volume transplant center, monitored between March 2020 and March 2024. Patients were classified as infected based on positive RT-PCR or antigen test results.

Results: The mean age of the study cohort was 58 years (IQR: 44–66), with 24% being female, 23% classified as obese, 51% having diabetes, and 77% diagnosed with hypertension. The median creatinine level was 114 mg/dL (IQR: 91–146). The primary indications for heart transplantation were advanced heart failure due to dilated cardiomyopathy (48%) and ischemic cardiomyopathy (35%). The COVID-19 vaccination rate in the cohort was 80.1%. Among the cohort, 189 patients (34%) were diagnosed with COVID-19 following OHT. The median time from OHT to COVID-19 diagnosis was 1,478 days (IQR: 509–4,421). Recurrent SARS-CoV-2 infections were reported in 15 patients (8%), including one individual with three documented infections. A total of 33 patients (6%) required hospitalization for COVID-19. Of the 75 deaths recorded in the cohort (13.5%), 18 (24%) were directly attributable to COVID-19. Multivariable analysis revealed that COVID-19 vaccination was a protective factor against COVID-19-related mortality (OR = 0.15, 95% CI: 0.05–0.51, p = 0.002), while advanced age was associated with an increased risk of mortality (OR = 1.09, 95% CI: 1.02–1.17, p = 0.008).

Conclusions: Advanced age and lack of COVID-19 vaccination were significant risk factors for COVID-19-related mortality among heart transplant recipients. These findings underscore the critical importance of vaccination in this high-risk population.

EP_432 RADICAL PROSTATECTOMY IN KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE MULTICENTER EXPERIENCE

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Background: Kidney transplant recipients have an increased risk of developing genitourinary cancers. Prostate cancer is expected to become more prevalent due to an aging kidney transplant recipient population. Thus, enhancing the knowledge of surgical outcomes, including treatment of prostate cancer, appears crucial.

Methods: Data of 62 kidney transplant recipients undergoing radical prostatectomy from 2006-2023 at nine urologic transplant centers were retrospectively analyzed. The perioperative outcome was assessed including complications according to Clavien-Dindo. Overall survival (OS), biochemical recurrence-free survival (BRFS), and death-censored graft survival were determined via the Kaplan-Meier method and log-rank testing.

Results: Overall, 50 open radical retropubic (ORRP) and 12 robot-assisted radical prostatectomies (RARP) were included. The median patient age at prostatectomy was 64 years (range 32-77), the median time from transplantation to prostatectomy was 71 months (4-309). Unilateral Lymphadenectomy was performed in 61% cases. The intraoperative blood loss was lower after RARP, but operative time was longer. 50% of patients experienced no postoperative complication, and ≥ grade 3 complications were observed in 14.5%. There was no graft loss related to radical prostatectomy. Histopathologic analysis revealed pN1 in 8.1%, and positive surgical margins in 25.8% of the cases. At a median follow-up of 49 months, median OS was 128 (95%CI 71-185), BRFS was 106 (95%CI 56-156), and graft survival was 127 (95%CI 67-187) months. There were 27% biochemical recurrences, at median 35 months post radical prostatectomy.

Conclusions: Our findings support radical prostatectomy as a feasible and safe treatment option for localized prostate cancer in kidney transplant recipients with acceptable oncologic outcome. Special care in screening and awareness for the risk of understaging is required.

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EP_433 KIDNEY OUTCOMES IN LUPUS NEPHRITIS: AFTER TRANSPLANTATION VS. CONSERVATIVE CARE DURING COVID-19

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Background: Lupus nephritis is a severe complication of systemic lupus erythematosus requiring diverse management strategies, including kidney transplantation (KTX) and conservative care. This study examines kidney function changes, measured by serum creatinine (sCr) and eGFR, in these patient groups before and during the COVID-19 pandemic.

Methods: This study analyzed 28 matched pairs of lupus nephritis patients treated from 2019 to 2023. Transplanted patients (LN-KTX, n=11) were matched to conservatively managed patients (LN-CT) by age, gender, and baseline kidney function. Data on kidney function (sCr, eGFR), hematological parameters, inflammation markers, and treatments were collected annually and analyzed at four time points (baseline, 2020, 2021, and 2023). The severity of COVID-19 infections, including hospitalizations and systemic complications, was recorded and considered as a potential confounder.

Results: At baseline, kidney function was comparable between groups (sCr: 1.30mg/dL [LN-KTX] vs. 1.47mg/dL [LN-CT], p=0.25; eGFR: 49mL/min/1.73m2 vs. 46mL/min/1.73m2, p=0.44). By 2023, the LN-KTX group demonstrated better kidney outcomes (sCr: 1.38 mg/dL vs. 2.01 mg/dL, p=0.002; eGFR: 44mL/min/1.73m2 vs. 31mL/min/1.73m2, p=0.01). Hematological parameters in the LN-CT group showed significant variability in Hb, PLT, and WBC, often linked to disease flares. This variability may be attributed to disease activity and the absence of stable immunosuppressive treatment in LN-CT patients. Inflammatory markers, such as CRP, fluctuated more in LN-CT, reflecting higher systemic activity and burden.

Conclusions: Kidney transplant recipients with lupus nephritis had better kidney function than conservatively managed patients during the COVID-19 pandemic. Intensive immunosuppression in LN-KTX protected against over-reactive immune responses (cytokine storm) and lupus flares, ensuring more stable kidney function. These findings highlight the importance of personalized immunosuppressive regimens to balance immediate and long-term outcomes, even under systemic challenges like COVID-19.

Funding: This work was supported by the Polpharma Scientific Foundation, grant no. 1/XX/2021 “The immune system of patients with lupus nephritis post SARS-CoV-2 infection”(awarded to A.W.).

EP_434 THE EVOLUTION AND PROGNOSTIC VALUE OF PHYSICAL FITNESS IN LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is a life-saving treatment for end-stage liver disease (ESLD), yet long-term mortality remains suboptimal due to cardiovascular complications, with low physical fitness as a modifiable risk factor. While ESLD patients often exhibit poor physical fitness, longitudinal data on post-LT changes and survival impact are scarce. This study assessed changes in VO_2peak, 6-minute walk distance (6MWD), and handgrip strength (HGS) pre- and post-LT, and their association with survival and length of ICU and hospital stay.

Methods: This single-centre retrospective cohort study included 81 ESLD patients transplanted between 2009-2015. Physical fitness parameters were measured pre-LT at the time of activation on the waitlist and at 0, 3, and 12 months post-LT. Longitudinal changes were analysed using multivariate linear models, and associations between pre-LT fitness parameters and clinical outcomes were evaluated using Cox survival models and Spearman correlations.

Results: VO_2peak declined from 20.5mL/kg/min (66% of predicted value) pre-LT to 18 mL/kg/min (59%; p=0.055) immediately post-LT and recovered to 22.5 mL/kg/min at 1 year (75%; p=0.545) (*Figure 1*). 6MWD decreased from 458 m (61%) pre-LT to 399 m post-LT (53%; p=0.001), but improved to 534 m at 1 year (77%; p<0.0001) (*Figure 2*). HGS dropped from 28.9 kg pre-LT (74%) to 23.4 kg post-LT (58%; p<0.0001), recovering to 29 kg at 1 year (76%; p=0.999) (*Figure 3*). Pre-LT VO_2peak was significantly associated with survival (p=0.037, HR 0.894, 95% CI 0.804–0.993) and ICU stay (p=0.027). Similarly, the 6MWD was significantly associated with survival (p=0.012, HR 0.997, 95% CI 0.994–0.999) and ICU stay (p=0.005). HGS was also significantly associated with ICU stay (p=0.009).

Conclusions: Physical fitness, already severely impaired pre-LT, declines further immediately post-LT but improves within a year, though remaining below normative values. Pre-LT physical fitness parameter, such as 6MWD, VO_2peak, and HGS, are strong predictors of long-term survival and ICU duration, underscoring the need for targeted (p)rehabilitation to enhance recovery and outcomes.

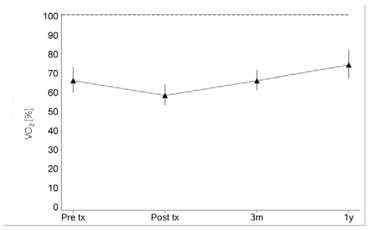

Figure 1: Longitudinal changes in VO_2peak (% of predicted value) pre- and post-LT. The dashed line at 100% represents the average VO_2peak of the normal population.

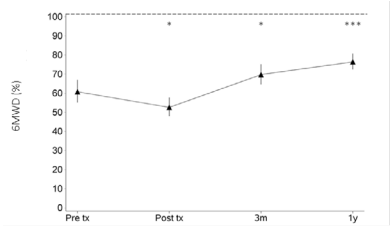

Figure 2: Longitudinal changes in 6MWD (% of predicted value) pre- and post-LT. The dashed line at 100% represents the average 6MWD of the normal population.

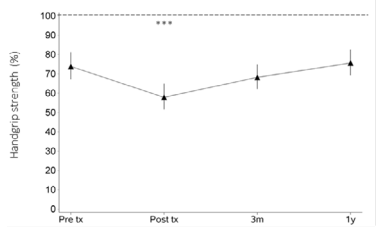

Figure 3: Longitudinal changes in HGS (% of predicted value) pre- and post-LT. The dashed line at 100% represents the average HGS of the normal population.

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EP_435 OPTIMIZING URINE CULTURE TESTING IN RENAL TRANSPLANT RECIPIENTS: COST-SAVING PERFORMANCE INITIATIVE

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Background: Asymptomatic bacteriuria (ASB) is common among renal transplant recipients, yet treatment is not recommended after three months post-transplantation, except in specific situations such as ureteric stents, urologic procedures, or pregnancy, according to Infectious Diseases Society of America (IDSA) guidelines. Our renal transplant program, one of the largest worldwide with over 500 transplants annually and 4,500 active recipients, historically performed routine urine culture testing at every clinic visit, regardless of clinical indication. This practice incurred significant costs, wasted laboratory and physician time, and did not improve patient outcomes.

Methods: In April 2022, we initiated a performance improvement (PI) project to reduce unnecessary urine culture testing. The goal was to decrease monthly testing costs by 50% within one year and sustain the reduction. The intervention involved educating transplant nephrologists on IDSA guidelines, training nursing staff to remove routine urine culture orders from lab care sets, and restricting testing to specific indications: ureteric stents, urologic procedures, pregnant patients, and symptomatic urinary tract infection cases. Weekly monitoring ensured compliance and sustainability through 2024.

Results: In 2023, 4,571 unnecessary urine cultures were eliminated without a significant increase in missed urinary tract infections (42 cases vs. 48 previous year, p=0.2). Cost savings in the first year totaled 3,598,140 Saudi Riyals. Additionally, annual time savings included 2,500 hours for nursing staff, 1,456 hours for physicians, and 240 hours for pharmacists. The project was recognized with a PI Award by King Faisal Hospital in December 2024.

Conclusions: This initiative demonstrates that routine urine culture testing beyond three months post-transplantation is unnecessary and resource-intensive. Limiting testing to guideline-based indications effectively reduces costs and workload without compromising patient care. These findings underscore the importance of evidence-based practices in renal transplant programs to enhance efficiency and optimize outcomes.

EP_436 REVIEW OF PUBLICATIONS ON FRAILTY IN KIDNEY TRANSPLANT RECIPIENTS IN THE WEB OF SCIENCES DATABASE

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Background: Frailty is associated with difficulty performing activities of daily living, weight loss, weakness, prolonged hospitalization, and increased complications. This study analyzed studies on frailty in kidney transplant recipients between 2014-2024.

Methods: This literature review used the Web of Science electronic database, which was searched between 2014 and 2024 using the keywords «kidney transplantation» OR «kidney transplant» and «frailty» OR «fragility.» All articles published between these dates were included in the study.

Results: The review yielded a total of 116 documents. 72 were meeting abstracts, 5 were review articles, 2 were early access, 2 were editorial material, 1 correction and 1 proceeding paper. 35 articles were included and analyzed. When analyzed by study type, 2 were reviews, 13 were prospective, 8 were multi-center, 5 were cohort studies. 21 studies were conducted with kidney transplant recipients, 11 with waiting list and 1 with both KTR and candidates. When analyzing the research fields, 48.57% (n=17) were surgery, 45.71% were transplantation, 34.28% (n=12) were urology/nephrology. The three countries with the highest number of regions were the United States of America (n=19), Japan (n=4), and Spain (n=4). Frailty is a common condition in kidney transplant patients and transplant recipients. This condition can lead to decreased quality of life, increased dependency, graft loss, and risk of death. However, frailty is reversible in many post-transplant patients. Particularly when combined with depressive symptoms, the negative impact of frailty becomes even more pronounced. Furthermore, polypharmacy is strongly associated with frailty, and medication management is important to reduce these effects.

Conclusions: Physical rehabilitation, multidisciplinary approaches, and individualized interventions are crucial for mitigating the effects of frailty and improving patients' health status.

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EP_437 DURATION OF BACTRIM PROPHYLAXIS AND INFECTION RATE AFTER KIDNEY TRANSPLANT: A TARGET TRIAL EMULATION

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Background: Trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis effectively prevents opportunistic and non-opportunistic infections in kidney transplant recipients (KTRs), but optimal duration remains uncertain. This study investigated whether extending TMP-SMX prophylaxis is associated with lower infection rates.

Methods: This target trial emulation using observational data from the Swiss Transplant Cohort Study compared short (<7 months) vs. long (>7 months) TMP-SMX prophylaxis. The primary outcome was bacterial infection potentially susceptible to TMP-SMX up to 12-months post-transplant. Inverse probability weighting (IPW) adjusted for confounders including age, living donation, lymphocyte counts, use of antithymocyte globulin (ATG), acute rejection and transplant centre. All bacterial and opportunistic infections, kidney function, and patient and allograft survival were summarized descriptively.

Results: 1700 KTRs fulfilled inclusion criteria; 1325 (78%) participants received a short prophylaxis and 375 (22%) received a long prophylaxis. Median TMP-SMX duration was 179 days in the short group and 280 days in the long group. At 12-month post-transplant, the primary outcome was observed in 120/1325 (9.1%) in the short group and 43/375 (11.5%) in the long group. IPW analysis estimated an adjusted risk difference of 2.11% (95% CI -0.47 to 5.27%). Center, rejection, and use of ATG were variables associated with longer TMP-SMX duration, but risk difference of the primary outcome was similar before and after weighting. Urinary tract infection caused by Enterobacterales was the most common bacterial infection. Opportunistic and overall infection rates, kidney function, patient and graft survival were similar among groups.

Conclusions: In this target trial emulation study, we did not find differences in bacterial infection rates at 12-month post-transplant between a short and a long duration of TMP-SMX prophylaxis.

EP_438 KIDNEY TRANSPLANTATION IN A PATIENT WITH LECITHIN:CHOLESTEROL ACYLTRANSFERASE (LCAT) DEFICIENCY

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Background: Familial lecithin:cholesterol acyltransferase (LCAT) deficiency (FLD) is a rare autosomal recessive disease that impacts lipid metabolism, caused by a missense mutation in the LCAT gene. Renal complications can manifest as proteinuria early in life, progressing to renal insufficiency and eventual renal failure. Disease may recur after kidney transplantation.

Methods: We present a case of successful kidney transplantation in young patients with LCAT deficiency.

Results: The patient is a 39-year-old man diagnosed with LCAT deficiency in 2016. The examination revealed corneal opacities, elevated blood pressure, hepatosplenomegaly, pleural effusions, edema in the lower extremities, and anemia. An eye examination revealed characteristic changes described as “fish eye.” Haemodialysis began in January 2019 until the transplantation, in June 2021. Since the transplant, he has been having regular check-ups, and no warning signs have been observed. His blood pressure is within normal limits, his cardiopulmonary status is stable, and the graft is functioning normally.

Conclusions: Currently, there is no effective treatment for FLD; however, an HDL mimetic and several LCAT activators and recombinant LCAT options are undergoing testing. A combined liver-kidney transplant may be considered, as LCAT is produced in the liver. Our experience demonstrates that kidney transplantation present excellent solution.

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EP_439 INCREASE OF EPICARDIAL FAT OVER TIME AFTER HEART OR LUNG TRANSPLANTATION

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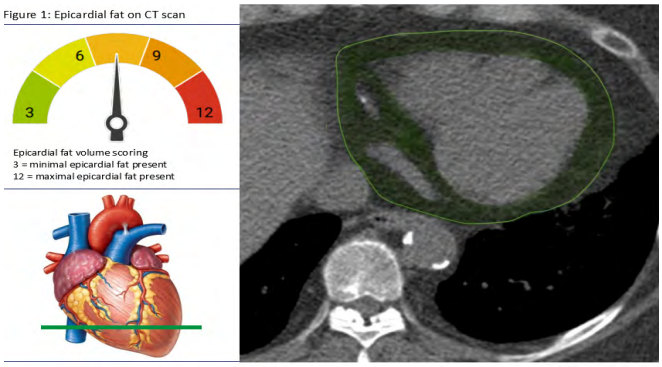
Background: Post-transplantation, steroids may increase rates of obesity and diabetes, while calcineurin inhibitors can cause hypertension and diabetes. All are known cardiometabolic risk factors, while an increase in epicardial fat (EF) is linked to metabolic syndrome. We performed a pilot study to measure EF over time.

Methods: We included heart (HT) or lung (LT) transplantation patients with CT scans shortly after transplantation and 1 year later. Anonymized and randomized scans were assessed for EF by two independent observers at three pre-defined spots. A semi-quantitative scoring system was used, ranging from 1 (minimal EF present) to 4 (maximum EF present) per spot. Total EF per scan ranged from 3-12; Figure 1. EF differences were calculated. Data on body mass index (BMI), steroid usage and rejection was extracted from the patient database.

Results: We included 19 HT patients (median age at transplant: 54 [IQR 39-61] years; 3 (16%) female) and 120 LT patients (median age at transplant: 60 [IQR53-64]; 52 (43%) female). Baseline characteristics are found in Table 1. In HT patients, EF increased in 11 (58%) patients from 3 [IQR 3-4] at baseline to 5 [IQR 4-6] at follow-up (p=0.002), remained stable at 4 [IQR 3-4] in 7 (37%) and decreased in 1 (5%) from 5 to 3. In LT patients, EF increased in 48 (40%) patients from 5 [IQR 4-6] at baseline to 7 [IQR 6-8] at follow-up (p<0.001), remained stable at 5 [IQR4-6] in 57 (48%) and decreased in 15 (12%) from 6 [IQR 5-7] to 4 [IQR 4-6] (p<0.001). Baseline BMI is significantly associated with EF increase (OR 1.1, 95% CI 1.02 – 1.3, p = 0.017), while BMI at 1 year was not.

Conclusion: This pilot shows EF increased among thoracic transplant patients over one year and that this was associated with baseline BMI. As EF is linked with metabolic syndrome, further research is needed to assess the influence of immunosuppression and rejection on EF over time and if this influences graft function.

Figure 1: Epicardial fat on CT scan



	HT (n=19)			LT (n=120)		
CT	Baseline	Follow-up	p	Baseline	Follow-up	p
Days post-Tx	35 [15-50]	411 (374-448)		19 [14-32]	388 [345-437]	
BMI kg/m²	24 (22-26)	24 (22-26)	0.56	24 [21-27]	25 [22-28]	**<0.001**
Steroid mg/day	10 [10-15]	9 [5-10]	**0.001**	15 [15-15]	10 [10-15]	**<0.001**
Rejection n, %	3 (16%)	4 (21%) Episodes/pt: 1 ep: 3 (75%) 2 ep: 1 (25%)		10 (8%)	55 (46%) Episodes/pt: 1 ep: 28 (51%) 2 ep: 19 (35%) 3 ep: 6 (11%) 4 ep: 2 (3%)	

Table 1

[]=IQR, ()=95%CI

EP_440 EFFICACY AND SAFETY OF ROSUVASTATIN COMPARED TO OTHER STATINS POST-HEART-TRANSPLANTATION

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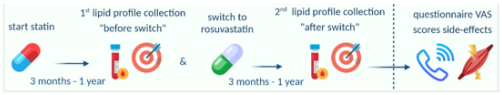
Background: The International Society of Heart and Lung Transplantation (ISHLT) 2022 guideline recommends statin therapy in heart transplantation (HT) patients, with the therapeutic low-density lipoprotein (LDL) target being <2.5 mmol/L. Particularly pravastatin is recommended, given the proven beneficial effects on long-term clinical outcome and the low prevalence of side effects. In the general population, rosuvastatin has been shown to be even more potent. We investigated the lipid-lowering effect and severity of side-effects of rosuvastatin compared to less potent statins in HT patients.

Methods: In this before-after study, we included all adult (≥18 years) HT recipients whom were prescribed a change from the statin they were using to rosuvastatin, for better cardiovascular risk management and/or because of side-effects, between January 2004 and October 2024. Data on lipid profiles and kidney function (CKD-EPI eGFR) was collected during annual checkup. Side-effects (including myalgia, cramps, stiffness and weakness) were measured in a visual analogue scale (VAS) ranging from 0-10. A visual timeline of the data collection is shown in Figure 1. We compared the differences using a Wilcoxon signed rank test.

Results: We included 94 patients (median age at transplant: 51 [IQR 45-58] years ; 26 (28%) female). Median time since HT was 9 [IQR 5-15] years. The distribution and dosage of prescribed statins can be found in Table 1. Compared to statins used prior to therapy change, rosuvastatin was associated with lower total cholesterol, LDL- and triglyceride levels, with high density lipoprotein (HDL) levels remaining the same and no difference in CKD-EPI eGFR was found (Table 1). Before switch, 39 (41%) patients achieved the LDL-target of <2.5 mmol/L. After switch, 71 (76%) patients achieved the target. The severity of myalgia and cramps decreased significantly after switch (Table 1).

Conclusions: In HT patients that were prescribed a change of statin due to better cardiovascular risk management and/or complaints of side-effects, rosuvastatin is related to a more favorable lipid profile, without additional side-effects, compared to other statins. Furthermore, more patients achieve the guideline recommended LDL-target. Ongoing research should determine whether this translates to a better clinical outcome.

Figure 1: Visual timeline of data collection in heart transplant patients



VAS = visual analogue scale

Table 1: Statin efficacy and safety before and after switch to rosuvastatin in HT patients

	Before switch to rosuvastatin	After switch to rosuvastatin	p-value
Statin distribution, *n (%)*	94 (100)		
Rosuvastatin	0 (0)	94 (100)	-
Pravastatin	75 (80)	0 (0)	-
Atorvastatin	15 (16)	0 (0)	-
Simvastatin	4 (4)	0 (0)	-
Statin dosage, *(mg per day)*			
Rosuvastatin	n.a.	10 [5-10]	-
Pravastatin	20 [10-40]	n.a.	-
Atorvastatin	40 [40-40]	n.a.	-
Simvastatin	1x10, 2x20, 1x40	n.a.	-
Lab values, *n (%)*	94 (100)		
Total cholesterol (mmol/L)	4.7 [IQR 4.2-5.5]	4.0 [IQR 3.3-4.7]	**<0.001**
LDL-C (mmol/L)	2.7 [IQR 2.3-3.3]	2.0 [IQR 1.6-2.5]	**<0.001**
HDL-C (mmol/L)	1.4 [IQR 1.2-1.7]	1.4 [IQR 1.1-1.8]	0.992
Triglycerides (mmol/L)	1.8 [IQR 1.4-2.4]	1.6 [IQR 1.1-2.2]	**0.035**
CKD-EPI eGFR (ml/minx1.73m2)	56 [44-71]	56 [45-72]	0.247
LDL-target <2.5 mmol/L reached, *n (%)*	39 (41)	71 (76)	**<0.001**
VAS scores of side-effects, *n (%)*	56 (60)		
Myalgia	5 [IQR 0-8]	0 [IQR 0-5]	**<0.001**
Cramps	5 [IQR 0-8]	2 [IQR 0-7]	**0.002**
Weakness	0 [IQR 0-5]	0 [IQR 0-5]	0.394
Stiffness	3 [IQR 0-7]	2 [IQR 0-7]	0.745

CKD-EPI eGFR = Chronic Kidney Disease Epidemiology Collaboration Estimated Glomerular Filtration Rate, HDL-C = high-density lipoprotein, IQR = interquartile range, LDL-C = low-density lipoprotein, n = number, , mg = milligram, n = number, n.a. = not applicable, VAS = visual analogue scale

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EP_441 LATE ONSET TMA IN KIDNEY TRANSPLANTS; POOR OUTCOME DESPITE ECULIZUMAB TREATMENT

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Background: Atypical haemolytic uraemic syndrome (aHUS) is a rare cause of end stage kidney disease (ESKD) associated with a high rate of recurrence in kidney transplants, where it presents with a post-transplant thrombotic microangiopathy (TMA). Prophylactic eculizumab can prevent disease recurrence in select patients. Treating at the time of post-transplant TMA occurrence is the only option if the diagnosis of aHUS is not established pre-transplant. We report our approach in using eculizumab at the point of post-transplant TMA occurrence in those with a diagnosis or suspicion of aHUS.

Methods: We conducted a case note review of 26 patients treated with eculizumab for post-transplant TMA. Baseline data on recipients and native kidney disease, onset of post-transplant TMA, transplant biopsy results, graft survival, cause of graft failure, duration of eculizumab treatment and reason for treatment cessation were recorded. Cases were reviewed for any concurrent evidence of rejection. Screening for complement pathway defects included testing for variants in genes of the complement pathway and anti-factor H antibodies.

Results: Median age at transplantation was 41 years and 73% of recipients were female. Six recipients had a diagnosis of aHUS or HUS as the cause of ESKD. 35% of recipients had an identified complement pathway defect. Median time to presentation with post-transplant TMA was 8 months. Death-censored graft survival 12 months after starting eculizumab was 68% for the cohort. In those presenting within 12 months of transplantation this figure was 78%, compared to 43% for those presenting >12 months post-transplant.

Conclusions: Graft outcome after eculizumab treatment of post-transplant TMA due to suspected aHUS appears better in those presenting earlier post-transplant. In patients presenting >12 months after transplantation the outcome is poor despite eculizumab treatment reflecting either delayed diagnosis or non-complement mediated TMA.

EP_442 A PROSPECTIVE ASSESMENT OF HEALTH RELATED QUALITY OF LIFE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Organ transplantation is the ideal approach for patients with chronic end-stage kidney disease. A qualitative indicator of the effectiveness of a therapeutic intervention in the field of health is the assessment of Health-Related Quality of Life (HRQoL). The study aimed to prospectively assess the HRQoL in a cohort of kidney transplant recipients (KTRs), estimate its potential changes and identify factors that may influence these changes.

Methods: Kidney Transplant Questionnaire 25 (KTQ-25) (after being adapted to Greek KTR) and SF-36 were administered twice (study entry and after one year). Sociodemographic, clinical-lab data were collected at both time points. Inclusion criteria were, age≥18y old, time since transplant≥1 year, functioning graft.

Results: 84 KTRs included in the study. Mean age was 53.5 years (59 males), mean e-GFR 47.7±15ml/min/1.73m^2 and average time since transplant 56±48 months. The majority of KTRs were married (73.8%), non-smokers (81.6%), retired (60.7%), on hemodialysis before transplantation (62%) and had a deceased graft (59.52%). KTRs were receiving steroids in 84.3%, Tacrolimus 54.2%, Cyclosporine 40.9% and MMF 91.8%. The observed KTQ-25 and SF-36 scores in all dimensions both time-points were similar without significant changes. A multivariate regression analysis for the 5 KTQ-25 dimensions at study end showed that variables significantly associated with Physical Symptoms dimension were age (p=0.02) directly and osteoporosis (p=0.02) inversely. Significant variables for Fatigue dimension were, female sex (p=0.04) and higher serum cholesterol (p=0.01). Uncertainty/Fear dimension was significantly worse in KTRs with cardiovascular disease (CVD) (p=0.03). Appearance dimension was positively correlated with female sex and negatively with age and CVD (p=0.02, p=0.04 and p=0.04, respectively). Total KTQ-25 score was significantly correlated with female sex (p=0.02), while history of CVD had a negative impact on the score (p=0.01).

Conclusions: In this prospective study of HRQoL in a Greek cohort of stable KTRs, no significant changes were found in the scores of KTQ-25 and SF-36 instruments, over one year of FU. Age, sex, osteoporosis, serum cholesterols' levels and history of CVD are among factors that might affect HRQoL of KTRs.

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EP_443 PRE-TRANSPLANT T LYMPHOCYTE SUBSETS ASSOCIATED WITH POOR VIRAL OUTCOMES IN ELDERLY TRANSPLANT RECIPIENTS: A KTOP STUDY

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Background: Older patients with end stage kidney disease (ESKD) are vulnerable to post transplantation complications, including infectious complications. Post transplantation absolute lymphocyte count (ALC) has been used as a risk predictor for viral complications. However, the association between pre-transplantation lymphocyte subset counts, and post transplantation infectious complications has not been investigated.

Methods: The Kidney Transplantation in Older People (KTOP) Study is a single centre, prospective, mixed methods, observational study which recruited potential kidney transplant recipients aged ≥60years. At enrolment of this study, participants were consented for lymphocyte subset studies prior to transplantation. Using this cohort of patients, data was collected retrospectively including pre-transplantation lymphocyte counts, episodes of post transplantation cytomegalovirus (CMV), polyoma (BK) virus and Epstein-Barr virus (EBV), as well as episodes of rejection, graft loss or death.

Results: 130 participants were included in the final analysis. The demographic details of the cohort is described in Table 1. 28 participants (22%) had post transplantation CMV viraemia, 25 (20%) had BK viraemia and 26 (20%) had EBV viraemia. In the CMV viraemic cohort, the median pre-transplant ALC was 1266 cells/microL (IQR 900-1570) compared to 1465 cells/microL (IQR 1100-1800) in the non-CMV viraemic participants (p value 0.037). CD8+ T cell were also lower in the CMV viraemic group, with a median CD8+ count of 247 cells/microL (IQR 91-364) compared to 398.5 cells/microL (IQR 218-582) (p value 0.028). CD4+ cell count were similar between groups (Figure 1).

Conclusions: This analysis of the KTOP study cohort revealed an association between pre-transplantation ALC and CD8+ T lymphocyte counts and episodes of post transplantation CMV viraemia. Further studies assessing the role of pre-transplantation lymphocytes in guiding post-transplant viral surveillance are warranted.

EP_444 INTERNAL ILIAC ARTERY CALCIFICATION PREDICTS CARDIOVASCULAR DISEASE AND MORTALITY

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Background: Cardiovascular disease remains a significant cause of death in kidney transplant recipients. While several studies have demonstrated the association of aortoiliac calcification with cardiovascular disease and mortality, few have reported the association between segmental (especially internal iliac artery) aortoiliac calcification and prognosis. This study aimed to evaluate the association between segmental aortoiliac calcification scores and cardiovascular disease incidence and mortality after kidney transplantation.

Methods: This retrospective study included 104 primary living donor kidney transplant recipients at our hospital between 2009 and 2023 who underwent preoperative computed tomography. The aortoiliac calcification quantification was performed on non-contrast computed tomography using the Agatston score. The aortoiliac artery was divided into four segments: distal aorta, common iliac artery, external iliac artery, and internal iliac artery.

Results: The median follow-up period was 61 months; 15 recipients died and 28 experienced cardiovascular disease. The ability to distinguish cardiovascular disease was the best for the internal iliac artery, followed by the common iliac artery (area under the curve: 0.75 and 0.73, respectively). The high calcification group, classified by the internal iliac artery and common iliac artery calcification scores, was associated with a poorer prognosis for cardiovascular disease-free and patient survival. Multivariate analysis revealed that internal iliac artery calcification and age were independent risk factors for cardiovascular disease (hazard ratio: 5.08 and 5.74, respectively) and patient survival (hazard ratio: 4.67 and 7.61, respectively).

Conclusions: The internal iliac artery calcification score was more closely associated with cardiovascular disease onset and mortality than other segment calcification scores.

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EP_445 EFFICACY AND SAFETY OF BELATACEPT IN KIDNEY TRANSPLANT RECIPIENTS: A TARGET-TRIAL EMULATION

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Background: Belatacept is used as a maintenance regimen in kidney transplant recipients (KTRs), but most studies focus on surrogate endpoints or lack comparators. We conducted a comparative study to assess its efficacy and safety using clinically relevant outcomes.

Methods: We emulated a target trial using data from a single-center retrospective cohort. The "intervention" group included all KTRs exposed to belatacept between 2013 and 2022, regardless of initiation type (de novo or switch). Patients were matched to up to 3 calcineurin inhibitors-exposed controls based on age (±5 years), time from transplant to inclusion (±3 years), donor type, and early graft function (delayed/immediate). Outcomes were compared using further propensity score weighting (i.e., double adjustment), accounting for eGFR, uPCR, DSA, and Banff scores (cv, ah, ifta).

Results: We included 45 KTRs in the intervention group (switch: 78%) and 124 in the control group. The median age was 51 years (IQR: 37–60), and the median time from transplant to inclusion was 0.8 years (IQR: 0–3.6). Over a median follow-up of 3.8 years (IQR: 2.3–6.1, cumulative: 724 person-years), 85/169 patients (51%) experienced at least one serious non-opportunistic infection (181 events), 17 (10%) a serious opportunistic infection (22 events), 15 (9%) a non-skin cancer (15 events), 20 (12%) a serious cardiovascular event (24 events), and 16 (9%) a diabetes-related hospitalization (18 events, all in the control group). After propensity-score adjustment, the hazard ratio for death during follow-up was 0.83 (95% CI: 0.15–4.48, p = 0.83, 17 events), for death-censored graft loss was 0.30 (95% CI: 0.07–1.29, p = 0.09, 21 events), and for the composite of death or graft loss was 0.52 (95% CI: 0.16–1.7, p = 0.28, 38 events). Incidence rates per 100 patient-years in the intervention versus control groups were: 25.4 versus 24.8 (p = 0.70) for non-opportunistic infections, 3.9 versus 2.7 (p = 0.34) for opportunistic infections, 26.9 versus 26.8 (p = 0.75) for any infection, 2.4 versus 3.7 (p = 0.05) for cardiovascular events, and 2.9 versus 1.7 (p = 0.74) for non-skin cancers.

Conclusions: In this emulation of a target trial, we found no significant difference in the incidence of serious infections between belatacept-based and calcineurin inhibitor-based regimens.

EP_446 BACTERIOPHAGE THERAPY IN TWO LUNG TRANSPLANT RECIPIENTS: EARLY CLINICAL EXPERIENCE FROM INDIA

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Background: Bacteriophage therapy(BT)uses bacteriophages to treat bacterial infection and is an emerging tool in the treatment of multi-drug resistant (MDR) pathogens. Experience of BT in lung transplant recipients (LTR) is limited. Here are two case reports which describes role of BT in treatment of MDR Pseudomonas aeruginosa in LTR, not responding to antibiotic therapy with persistent bronchial wash culture positivity and airway complications.

Methods: BT protocol-15days course of twice a day oral and nebulized phage cocktail with 2 ml of phage solution for nebulization and 8 ml of phage solution for oral consumption as per Eliava phage therapy center recommendations. Case 1: A 46yr old male with ILD underwent bilateral lung transplantation in 2024. His bronchoscopies done periodically to assess airway healing showed right airway narrowing with bronchial wash culture showing MDR Pseudomonas. It was treated with culture appropriate systemic and inhaled antibiotics for 4 weeks and airway dilatation. However, his bronchial wash cultures were persistently positive for MDR Pseudomonas. In view of persistent culture positivity and airway narrowing he was started on BT after institutional ethics committee clearance on compassionate grounds. He was continued on adjunctive systemic and inhaled antibiotic treatment. Case 2: A 28yr old female with paraquat induced lung fibrosis on VV ECMO underwent successful bilateral lung transplantation in 2024 with uneventful intro op and immediate post op period. Later she developed antibody mediated rejection which was treated as per protocol, she developed bilateral airway malacia and underwent bilateral airway stenting. Subsequently repeated bronchial wash cultures grown MDR Pseudomonas not responding to 4 weeks of inhaled and systemic antibiotics. Decision to try BT was made on compassionate grounds and started after ethical clearance and consent.

Results: After 2 weeks, repeat bronchial wash cultures were sterile in both cases with reduced airway secretions and complications

Conclusions: BT was safe, associated with reduced airway complications and microbiological clearance when used as an adjunct to existing systemic and inhaled antibiotics in LTR with MDR pseudomonas infection. BT deserves further evaluation in well-designed large clinical trials.

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EP_447 THE PERFORMANCE OF THE FUNCTIONAL IBOX IN PREDICTING ALLOGRAFT OUTCOMES IN A UK COHORT

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Background: The iBox is a kidney allograft survival prediction system that has been validated in international cohorts and been approved by the European Medicines Agency as a surrogate endpoint for clinical trials. Its development is based on a regression analysis of clinical variables associated with allograft loss. Its performance to predict allograft survival in UK kidney transplants is unknown.

Methods: We undertook a retrospective study to analyse the performance of the functional iBox to predict allograft survival in kidney transplants undertaken between 2012 and 2020 at a single UK centre where 70% of patients are managed steroid free. The functional iBox includes creatinine and proteinuria determined at 1 year post transplant within the model. We determined the discrimination performance of iBox (i.e. the ability of the model to separate patients who are going to lose their allografts from those who aren't) by calculating c-statistics for allograft survival prediction at 3-, 5-, and 7-years post evaluation.

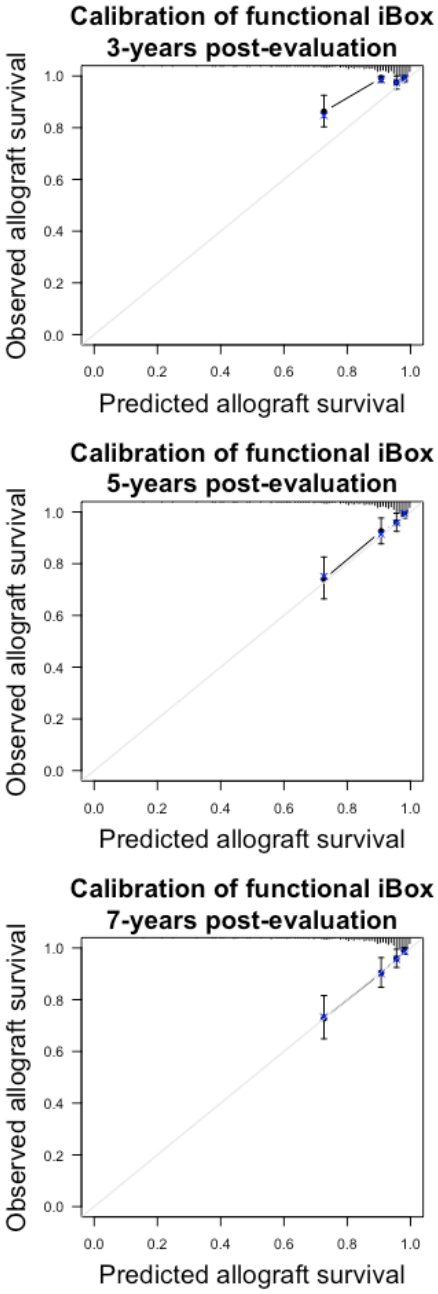
Results: 501 kidney transplant recipients (KTRs), mean age 50?14.3 years and 172 (34.5%) female, were included. Median creatinine and proteinuria were 132 (IQR 108-173) µmol/L and 24 (IQR 12-53) mg/mmol respectively determined at a median of 1.04 (IQR 1.01-1.09) years post-transplant. 47 (9.4%) graft losses were observed during a median follow-up time of 6.2 (IQR 4.4-7.8) years. The iBox predicted graft survival up to 7 years post evaluation is outlined in **Table 1**. C-statistics for the functional iBox to predict survival were 0.8, 0.79. and 0.79 at 3-, 5-, and 7-years post evaluation respectively. Calibration between predicted and observed allograft survival was good at all timepoints (**Figure 1**).

Conclusions: The functional iBox was effective in predicting kidney allograft survival in a UK cohort. Whether the functional iBox can be used prospectively to highlight deviations from the predicted allograft trajectory and change clinical care should be investigated.

Table 1: iBox predicted graft survival

Time post risk evaluation	1 year	2 years	3 years	4 years	5 years	6 years	7 years
iBox projected allograft survival	**98.4%**	**97.0%**	**95.8%**	**94.7%**	**93.5%**	**92.0%**	**90.4%**

Figure 1: The agreement between the predicted allograft survival and the observed allograft survival at 3-, 5-, and 7-years post evaluation



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EP_448 SYSTEMATIC EVALUATION AND PREDICTION OF SERIOUS INFECTIOUS EVENTS AFTER KIDNEY TRANSPLANTATION

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Background: The immunosuppressive treatment required for long-term kidney allograft survival induces a delicate balance between under- and over-immunosuppression. In this study, we evaluated the frequency of infectious events leading to hospitalization in the first-year post-transplantation and focused on simple immunological predictors of these infectious events.

Methods: We included all patients who received a kidney transplant between 2016 and 2018 at Grenoble University Hospital with a M3 post-transplantation biological evaluation, including a lymphocyte profile (CD3, CD4, CD8, CD19 positive cells). We systematically reviewed hospital charts to identify infection-related hospital stays. Classical transplantation parameters were included in the analysis (patient's age, CMV status, induction strategy, maintenance immunosuppressive regimen) and lymphocytes count and subpopulations. Patients received mainly thymoglobulin induction (89.6%) or basiliximab (10.4%), and a maintenance immunosuppression with tacrolimus (trough levels target 5-8 µg/l), mycophenolate and prednisone (5mg/day).

Results: A total of 428 patients were transplanted between 2016 and 2018 included. Among them, 341 had a kidney allograft survival > 6 months and available biological results at M3 post-transplantation. A total of 55 (16.1%) patients were hospitalized for an infectious event over the first year (38 were hospitalized only once, 17 twice or more), amounting to a total number of 84 hospital stays. The median time between transplantation and the first infectious event was 185 days (IQR: 76-261 days). Among all investigated predictors of hospitalization for an infectious complication, the absolute number of total lymphocytes was lower in the infection group that in the no-infection group (median 0.4 VS 0.7 G/L, p=0.004), as well as the percentage of CD8 cells among CD3 cells (median 20.5% VS 29%, p=0.006), but not CD4 cells. In a multivariate logistic regression, both predictors remained significantly associated with the outcome.

Conclusions: In a setting of modern immunosuppression, with a reduced-tacrolimus exposure, even with a depleting induction, the 16% incidence of hospitalization for infectious events was associated with total lymphocytes and the percentage of CD8 T cells, not CD4 T cells.

EP_449 HUMAN HERPESVIRUS 8 IN SOLID ORGAN TRANSPLANTATION: CLINICAL OUTCOMES AND THE NEED FOR IMPROVED DIAGNOSIS

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Background: Human herpesvirus 8 (HHV-8) is an oncogenic herpesvirus primarily affecting immunocompromised individuals. The clinical manifestations of HHV-8 infection in solid organ transplantation (SOT) recipients can range from asymptomatic cases to severe diseases affecting both graft and patient survival. The incidence of HHV-8 infections in SOT patients is not well-defined, which may lead to an underestimation of its prevalence.

Methods: We report four cases of donor-derived HHV-8 primary infections in SOT recipients from Catalonia and the Balearic Islands over the past five years. Serological assays conducted with stored serum from the day of transplantation confirmed primary infection in all cases.

Results: Two of the primary infections were fatal, originating from two different donors. The first donor was a native of Sub-Saharan Africa who passed away in 2019. His heart transplant recipient developed Kaposi's sarcoma four months post-transplantation. Despite a reduction in immunosuppression and a switch to mTOR inhibitors, the patient died within the first year after the transplant from Kaposi-associated inflammatory cytokine syndrome. The kidney transplant recipient from the same donor also developed Kaposi's sarcoma; however, this case partially responded to conversion to mTOR inhibitors and chemotherapy, and the patient is still alive today. The second donor was from Eastern Europe. One of his kidney recipients was admitted three months after transplantation due to a fever of unknown origin, leading to a late diagnosis of multicentric Castleman's disease through a bone marrow biopsy. A delayed treatment with rituximab proved futile, and the patient died shortly after. The other kidney recipient seroconverted but remains asymptomatic.

Conclusions: HHV-8 infection is a significant challenge in SOT recipients due to high morbidity, mortality, and lack of standardized diagnostic tools. Its underdiagnosis can lead to severe complications. Improved prevention, diagnosis, and treatment strategies, along with more research and better screening, are essential for better managing HHV-8 in transplant patients.

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Infectious diseases, malignancies & long term challenges

EP_450 CHIMERIC VACCINAL ANTIGEN T-CELLS: "OPTIMIZING TRANSPLANT PATIENTS'VACCINATION ON IMMUNOSUPPRESSION"

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Background: Because, in solid organ transplantation, the donor is genetically distinct from the recipient, the latter need to be maintained on immunosuppressive drugs that block T cell activation (calcineurin inhibitor, CNI) to prevent graft rejection. One major problem of this approach is that CNI, which act regardless of T-cell receptor specificity, also inhibit T cell response against pathogens and vaccines, making transplant patients vulnerable to infectious complications, as illustrated during the recent SARS-CoV-2 pandemic.

Elaborating on the recent success of CAR-T cells, we aimed at developing an innovative cell-based approach to optimize the vaccinal responses of transplant recipients without increasing their risk of rejection

Methods and results: Lentivector have been designed to induce the expression on the surface of purified CD4+ T cells of a chimeric receptor made of the vaccinal antigen on the extracellular side and signaling domains in the intracellular side. In vitro experiments suggested that when contacting antigen specific B cells, Vaccinal Antigen chimeric Receptor (VAR)-T cells simultaneously deliver BCR dependent- and receive VAR- dependent signal 1 of activation. As a result, VAR-T cells upregulate the surface expression of costimulatory molecules, the second mandatory signal triggering the differentiation of cognate B cells into Ab-producing plasma cells. In vivo experiments demonstrated that CD3?KO mice (devoid of T cells) transferred with SARS-CoV-2 Spike-VAR-T cells efficiently generated detectable levels of anti-Spike antibodies. Additional experiments are under way to optimize VAR-induced antibody-response and promote resistance of VAR T cells to CNI.

Conclusions: VAR-T cells represent a promising innovative cell-based platform to optimize the response of transplanted patients on therapeutic immunosuppression to vaccination.

EP_451 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN KIDNEY TRANSPLANT RECIPIENTS: A NATIONWIDE CASE-SERIES

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Background: Progressive multifocal leukoencephalopathy (PML) is an opportunistic infectious disease affecting the central nervous system caused by JC virus. While extensively studied in patients with HIV infection or undergoing immunotherapies, there is a lack of data concerning kidney transplant recipients (KTRs).

Methods: We performed a retrospective, multicentric, nationwide study. We contacted all kidney transplantation centres in France to gather all cases of PML. We obtained the count of KTRs using the registry of the French regulatory agency.

Results: We collected 24 cases of PML. The estimated minimal nationwide incidence of PML was 4.7/100,000 patient-years. Median duration from kidney transplantation to PML was 88 months (interquartile range: 9 to 355), and 8/24 patients (33%) had been exposed to belatacept. Almost all patients underwent reduction or withdrawal of immunosuppression, and 13 (54%) received a specific treatment. Fifteen patients (63%) died within one year after diagnosis and had higher exposure to belatacept compared to those who survived.

Conclusions: In this nationwide study, the PML incidence rate in KTRs was at least 4.7/100,000 patient-years, resulting in a 63% mortality rate within a year. Further investigations are warranted to confirm a potential association between belatacept exposure and PML occurrence, as suggested by our study.

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EP_452 ANTIFUNGAL MANAGEMENT OF INVASIVE ASPERGILLUS MEDIASTINITIS POST CARDIAC TRANSPLANTATION

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Aspergillus mediastinitis is a rare, life-threatening complication following cardiac transplantation; with greater risk in transplantation involving mechanical circulatory support. We describe a previously fit 49-year-old woman who developed myocarditis due to SARS-CoV-2. She was treated with corticosteroids, extracorporeal membrane oxygenation and a biventricular assist device before receiving an orthotopic heart transplant as a super-urgent case. Induction therapy included anti-thymocyte globulin, mycophenolate mofetil, prednisolone, and tacrolimus. She was discharged after one month.

Two months post-transplant, she complained of worsening chest discomfort and malaise. PET-CT and cardiac MRI revealed mediastinal abscesses and sternal osteomyelitis. Treatment was initiated with liposomal amphotericin B 3mg/kg and caspofungin. After extensive surgical debridement, cultures identified *Aspergillus fumigatus*, and voriconazole was initiated once susceptibilities were available. Immunosuppression was reduced to tacrolimus monotherapy.

She developed bacterial superadded infection and secondary diabetes mellitus. Hypoalbuminemia and malnutrition were also addressed. After multiple debridements, vacuum-assisted closure dressings, and topical treatment with applications of Spongostan® mixed with amphotericin, successful source control was achieved with negative bacterial and fungal margins. She had voriconazole-induced phototoxicity so was switched to posaconazole and remains well on this.

Maintaining good debridement alongside adequate levels of antifungal within the mediastinum is key. A multidisciplinary approach is needed to ensure optimal management of nutrition, interactions, adverse effects of drugs and immune suppression to avoid organ rejection. Antifungal choice, tolerance and tissue penetration is complex and requires careful drug monitoring.

EP_453 RETREAT SCORE ACCURATELY PREDICTS HCC RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) for HCC is still burdened by a considerable risk of tumor recurrence. The RETREAT-score is a validated predictive score for HCC recurrence. To compare RETREAT-score to Milan and Up-To-Seven histological criteria as predictors of HCC recurrence.

Methods: All adult patients who consecutively underwent LT for HCC from January 2000 to July 2022 were retrospectively enrolled and followed-up until September 2024. Demographic, biochemical and histological HCC features were considered at LT.

Results: 308 patients [87% male, 58 years, 71% viral-etiology, 85% with previous HCC treatment, AFP 9 (1-10,507) ng/mL, CPT A 46%, B 37%, C 17%, MELD 12 (6-46] underwent LT after 4 (0-54) months of waiting-list. At explant HCC were multi-nodular in 55% [n=3(2-8)], 21% with vascular invasion; G1:19%, G2:42%, G3:39% with the median higher tumor diameter of 2.5 (0.5-12) cm. Overall, 55%, 36%, 9% had RETREAT-score 0/1 (low), 2/3 (medium) and 4-6 (high), whereas 70% and 87% were Milan-IN and Up-To-Seven-IN, respectively. Fiftythree patients (18%) had HCC recurrence (53% extra-hepatic) 25 (2-202) months after LT, with 1- and 5-year-cumulative risk of 4% (95%CI 2-7) and 16% (95%CI 12-22), respectively; 32 (60%) died due to HCC-progression after 17 (0-196) months. The 5-yr-cumulative risk of HCC recurrence was 10%, 21%, 44% in low, medium and high RETREAT-score (p<0.001); 12% vs 25% in Milan IN and OUT (p=0.033), 14% vs 32% in Up-to-Seven-IN and OUT (p=0.054), respectively. At multivariable analysis, RETREAT-score was the only significant predictor for HCC recurrence (p<0.001), with an HR of 1.55 (95%1.30-1.86; p<0.001). Time to HCC-recurrence and time-to-death after recurrence were shorter in high RETREAT-score vs low [16 *vs* 26 (p=0.07) and 10 *vs* 23 months (p=0.054)]. Overall, 110 (37%) patients died during 64 (1-244) months of follow-up.

Conclusions: The RETREAT score is a usefull score to identify patients at high-risk of post-LT HCC recurrence needing closer HCC surveillance.

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EP_454 VISCERAL ARTERY ANEURYSMS AFTER PAEDIATRIC LIVER TRANSPLANTATION

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Background: The late onset of visceral artery aneurysms (VAA) in paediatric liver transplantation (LT) is a rare complication of portal hypertension, often associated to portal thrombosis with no standardized therapeutic approach. The aim of our study was to identify risk factors for their development and to assess long term outcomes.

Methods: All consecutive paediatric age patients who developed PVT after LT performed between January 1998 to December 2017 at AAST Papa Giovanni XXIII Transplant Centre were retrospectively enrolled and followed-up until November 2023. Clinical, intraoperative and early post-operative data were collected and analysed.

Results: A total of 65 patients, median age at LT of 0.8 years (IQR 0.6–1.6), 36 male (55.4%) were followed up for a median time of 17 years (IQR 6.6-20.2), with portal vein thrombosis (PVT) occurring after a median of 25 months (IQR 0.1-36.7). Fifteen patients (23.1%) developed VAA after a median interval of 15.9 years (11.6-18.3) from LT. VAA occurrence was higher in females (p = 0.048), in those who underwent intraoperative strategies to increase the portal flow at LT (p = 0.01) and in those requiring operative post-LT treatment for complications of portal hypertension (PH) (p = 0.031). We also observed a significantly longer time to PVT development in the VAA group with a median of 36.7 months (1.65-79) compared to the non-VAA group (median 0.6 months, IQR 0.1-21.8; p = 0.011). Operative treatment of VAA (splenic artery embolization and splenectomy) was required for 5 patients (33.3%). The patient and graft survival was similar for VAA and non-VAA group, respectively 92.9% vs 82.8% (p = 0.124) and 92.9% vs 68.1% (p = 0.06) at 10 years.

Conclusions: VAA developed in nearly a quarter of paediatric LT recipients with PVT. However, this complication did not influence patient's outcome and rarely required treatment.

EP_455 BK VIRUS NEPHRITIS IN KIDENEY TRANSPLANT RECIPIENTS, EXPERIENCE FROM SAHLOUL NEPHROLOGY DEPARTMENT

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Background: After an asymptomatic primary infection, the BK virus remains latent in healthy individuals, and reactivates in situations of immunosuppression. This reactivation primarily occurs in kidney transplant recipients, where it can cause acute tubulointerstitial nephropathy, potentially resulting in graft loss in some cases.

Methods: This is a retrospective descriptive study including kidney transplant recipients ,at the nephrology departlent in the Sahloul University Hospital of Sousse , who developed BK virus nephritis, documented by renal biopsy, during their follow-up period. The study covers the period from November 2007 to December 2024.

Results: The study involved 5 patients with a median age of 32 years. The average duration between transplantation and the onset of BK virus infection was 17.4 months, ranging from 4 months to 3 years. All patients were receiving maintenance immunosuppressive therapy, including cortancyl, prograf, and MMF. The clinical presentation was mild in all cases, with only one patient exhibiting microscopic hematuria. The primary diagnostic concern was a decline in graft function. Urinary and serum PCR tests were strongly positive for all patients, and renal biopsy confirmed the diagnosis, revealing histological findings such as a predominantly mononuclear inflammatory infiltrate in 4 patients, intranuclear viral inclusions in all patients, and SV40 positivity by immunohistochemistry in 4 patients. Acute rejection was noted in one patient. The initial treatment approach included reducing immunosuppressive doses, switching from prograf to rapamune, and administering immunoglobulins in one case. The outcome revealed chronic graft dysfunction in 4 patients, with graft loss occurring in one patient after one year.

Conclusions: BK virus infection is an increasingly frequent cause of renal dysfunction. Its incidence rises with the use of high-dose immunosuppression

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Infectious diseases, malignancies & long term challenges

EP_456 PROGRAMME FOR TRANSPLANTATION WITH DONATION AFTER CARDIAC DEATH AT THE SALAMANCA UNIVERSITY HOSPITAL

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Background: Kidney transplantation (KT) is the best option for patients with End-Stage Renal Disease (ESRD). One opportunity to increase the pool of donors is to use donors after cardiac death (DCD). Using this pool of donors must provide our patients the same guarantees and survival (graft and patient) as if they were transplanted with a donor after brain death (DBD). We present the results of this programme in our hospital.

Methods: This study includes all KT from DCD performed at our hospital, from 15th August 2017 to 29th November 2023 (n=75 patients). Of the donors only age was collected. The following data was collected from the recipients: age, sex, number of previous KT, cause of ESRD, time on dialysis, type of immunosuppression, days of hospitalization, cold and warm ischemia time, presence of delayed graft function (DGF-need for haemodialysis in the first week), acute rejection and its type, treatment, complications, number of HLA mismatches, survival of the graft and the recipient. In addition, we collected the following analytical parameters: creatinine, glomerular filtration rate (GFR) and tacrolimus levels at discharge, 6 months and annually thereafter.

Results: The recipients were 55 men and 20 women. The causes of ESRD were different, the most frequent being polycystic renal disease and diabetic nephropathy. 69 patients received their first KT and 6 received their second KT. All patients received immunosuppression with thymoglobulin, delayed introduction of calcineurin inhibitors plus corticosteroids and mycophenolate mofetil. 35 of the 75 patients (46%) had DGF and only 4 patients (5%) presented rejection. 2 transplantectomies were performed due to venous thrombosis. The remainder of the complications were: retroperitoneal hematoma (9), Seroma (2), *Clostridium Difficile* infection (1). Development of Diabetes Mellitus (2). At the end of the study 100% of the patients are alive and only 2 have lost the graft so the survival rate of this is 97.3%.

Conclusions: Although DCD are not considered as good as other kind of donors, and 46% of patients in our group had DGF, this type of transplant in our centre offers excellent graft survival (97.3%), patient survival (100%) and a GFR at 1, 3 and 4 years of 50%, so we should consider this type of donor as being very suitable for kidney transplantation.

EP_457 LONG TERM EVALUATION OF CORONARY CALCIFICATIONS IN KIDNEY TRANSPLANTATION A FOLLOW UP OF 15 YEARS

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Background: Chronic kidney disease (CKD) patients are at high cardiovascular (CV) risk, with coronary artery calcifications (CAC) contributing to CV mortality. Long-term data on CAC progression in kidney transplant (KTx) recipients is limited. This study follows up on a previous investigation of CAC prevalence and progression in 64 KTx patients over 5 years, now presenting preliminary findings from a 15-year follow-up.

Methods: In 2007, 67 kidney transplant patients (KTxps) were studied. At present, 19 were lost to follow-up (8 deaths, 4 due to major cardiovascular events, 11 graft losses, and 20 non-adherence). For this study, 28 KTxps (60±9 yrs) were analyzed. Clinical, blood, and urinary parameters were recorded over 15 years, focusing on the year prior to coronary artery calcification (CAC) evaluation using Agatson scores. Patients were categorized into four CAC groups at baseline and after 15 years (1) 0-10; 2) 10-100; 3) 100-400; 4) >400), and progression was assessed via changes in categories and Sevrukov's formula.

Results: At baseline and at 15 yrs after KTx, 46% and 18 % of pts were in the 1st grp, 14% and 25 % in the 2nd, 29% and 18% in the 3rd and 11 % and 39% in 4th, respectively. CAC at 15yrs were significantly higher than baseline (156 +- 50 vs 334 +-71 p<0.0001). Both at baseline and after 15yrs CAC correlated directly with age and with each other. In the 79% Cat-Prog+T15 was found, in the 10,7% of more than 1 class of CAC. Prog+ was discovered in the 71% of KTxps. They were characterized to have higher systolic blood pressure levels (P=0.05, with no difference in specific therapy), lower mean Hb and Ca levels (p=0.02; p=0.07 resp). In a logistic model, mean Ca Levels resulted the only independent factor inversely related with CAC15prog+ (p=0.04). During the 15 years of KTx a MACE was experienced by the 25% of KTxps, just older than the others. Apparently, no impact for CACs was found in MACE.

Conclusions: This study is the first to assess coronary artery calcifications (CAC) in a kidney transplant (KTx) cohort over 15 years. Preliminary findings indicate a high prevalence of CAC, linked to age and calcium levels. CAC progression was observed in many patients. Larger studies are needed to better understand these findings and the long-term relationship between CAC and major adverse cardiovascular events (MACE).

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EP_458 MORTALITY-GRAFT LOSS IN SIMULTANEOUS PANCREAS KIDNEY BY DONOR RECIPIENT CYTOMEGALOVIRUS SEROSTATUS

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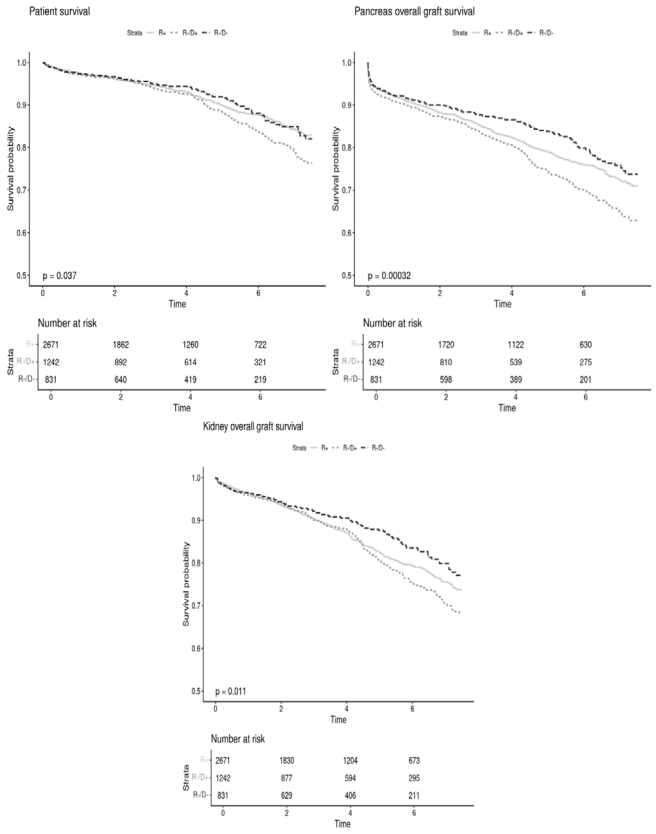
Background: Cytomegalovirus (CMV) primary infection is challenging in Simultaneous Pancreas-Kidney (SPK) transplant recipients, often requiring reduced immunosuppression. This study analyzes recipient and graft outcomes based on CMV serostatus.

Methods: We utilized data from the Scientific Registry of Transplant Recipients (SRTR). All SPK recipients from 2014 to 2024 were analyzed, excluding those with missing or combined induction, immunosuppression other than tacrolimus and mycophenolate, crossmatch positive transplants, and those with missing recipient or donor CMV status (N=4744). Recipients were grouped by CMV status: Recipient positive (R+) (n=2671), recipient negative with a negative donor (D-/R-) (n=831), and recipient negative with a positive donor (D+/R-) (n=1242). Recipient, pancreas and kidney graft survival through 7.5 years were compared using log-rank test. Cox regression models examined the association between high-risk CMV discordance and outcomes, adjusting for relevant donor and recipient characteristics.

Results: The CMV D-/R- had the lowest rates of rejection and hospitalization, while the high-risk D+/R- group had significantly higher combined rejection (16.6%, p=0.02) and one-year hospitalization rates (67.2%, p<0.01) compared to other groups. In the Kaplan-Meier analysis, the D+/R- group had the worst recipient survival, and overall pancreas and kidney graft survival (log-rank p< 0.05 for all) (Figure). In the multivariable models, compared to the R+ group, the D+/R- group had a 30% higher mortality risk [HR 1.30, 95% CI (1.03-1.65), P=0.03], and higher overall risk of pancreas [HR 1.25, 95% CI (1.06-1.48), P<0.01] and kidney graft loss [HR 1.21, 95% CI (1.0-1.47), P=0.046]. Conversely, CMV D-/R- group had a 26% lower risk of death-censored pancreas graft loss [HR 0.74, 95% CI (0.56-0.98), P=0.036] and a 33% lower risk of death-censored kidney graft loss [HR 0.67, 95% CI (0.46-0.97), P=0.035].

Conclusions: High-risk CMV D+/R- serostatus is associated with reduced overall graft and patient survival, while D-/R- serostatus is associated with better death-censored graft outcomes. Testing and developing pragmatic approaches to match CMV status need to be urgently considered.



EP_459 CHOLECYSTOLITHIASIS IN RENAL TRANSPLANT PATIENTS AT THE NATIONAL KIDNEY AND TRANSPLANT INSTITUTE

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Background: Cholecystolithiasis poses increased risks for renal transplant patients, due to metabolic changes and immunosuppressant use. Complications such as cholecystitis, cholangitis, and sepsis can adversely affect transplant outcomes. Data on its prevalence, clinical attributes, and outcomes remain limited. This study investigates the prevalence, management, and complications of cholecystolithiasis among renal transplant recipients at the National Kidney and Transplant Institute (2013–2018).

Methods: A retrospective study analyzed 1,537 renal transplant recipients' records. Inclusion criteria were adult patients with documented cholecystolithiasis pre- or post-transplant and complete follow-up data. Data on demographics, cause of renal replacement therapy, and immunosuppressants were collected. Descriptive statistics summarized characteristics, while chi-square tests analyzed relationships between variables and outcomes, including gallstone development, complications, and adverse events.

Results: The prevalence of cholecystolithiasis was 9.9% pre-transplant and 5.5% post-transplant. Older age (>41 years) significantly predicted gallstone formation ($\chi^2 = 23.818$, $p < 0.001$), while diabetic nephropathy was the leading cause of renal failure in affected patients ($\chi^2 = 23.853$, $p < 0.001$). Post-transplant complications, primarily cholecystitis, affected 10.5% of recipients with gallstones. Pre-existing gallstones significantly increased the risk of complications, including sepsis and cholangitis ($\chi^2 = 1068.839$, $p < 0.001$). Immunosuppressant and steroid use showed no significant correlation with gallstone development ($p > 0.05$).

Conclusions: Elective cholecystectomy is advised for symptomatic and high-risk patients, such as older or diabetic recipients, to prevent complications. For asymptomatic, low-risk patients, conservative management with monitoring is suitable. Individualized assessments and multidisciplinary care are critical to improving post-transplant outcomes.

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Infectious diseases, malignancies & long term challenges

EP_460 FLASH SURVEYS FOR DECISION MAKING FOR KIDNEY TRANSPLANT RECIPIENTS USING HOME MONITORING TOOLS

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Background: The use of home monitoring (HM) in the context of kidney transplantation (KT) is in the process of rapid development and is financially supported by the French Ministry for Health. As a team, we wondered whether we could use HM to promote the participation of patients in our decision-making process at an institutional level.

Methods: In August 2024, we conducted an online survey to assess whether patients would consent to flash surveys intended to help us in decision-making processes. To discuss the results, a roundtable discussion was convened, comprising nephrologists, advanced practice nurse, a professor of ethics, two KT recipients (KTRs), one expert on HM and one on qualitative studies. The study was approved by our institutional ethics committee (IRB00012437).

Results: A total of 103 KTRs (i.e., 29% of our HM cohort) completed the flash survey over a period of 14.5 hours. Fifty-four KTRs (60%) were male, mean age was 59 years (± standard deviation [SD]=14) and time since transplantation was 9 years (±8). Eighty-nine KTRs (86.4%) responded positively to the following question "Would you like to be contacted on NW by your transplant center regarding strategic issues for decision making in the field of kidney transplantation?". The main motivations were: 1) the desire to improve medical practice according to the need of patients (77.5%), 2) the desire to be actively involved in decision making regarding the management of KTRs (53.7%) and 3) have better personal control over the course of their disease (50%). The most discussed themes during the roundtable were the need of a specialized platform and data protection, patient consent, co-construction with patients and tool selection, patient information, methods, the need of distinction between clinical research and clinical practice, trust, the patient-researcher channel, legal framework, the enhanced scientific value of patients' word, frequency of queries, taboos, feedback, patient experience and a need of representativeness of answers.

Conclusions: Flash studies can provide a rapid response to an important question. Provided that hospitals respect important methodological and ethical considerations, KTRs are generally supportive of this approach.

EP_461 WHEN GLOMERULAR FILTRATION RATES IMPROVES IN DONOR AFTER CARDIAC DEATH TRANSPLANTATION IF DELAYED GRAFT FUNCTION?

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Background: The transplant programme using donors after cardiac death (DCD) is a good option of treatment for patients on the waiting list. However, those who suffer delayed graft function (DGF) could have worse renal function in the short or medium term.

Methods: We studied 75 renal transplants from DCD performed in our hospital from 15th August 2017, to 29th November 2023. The age of the donor and recipients were recorded, as well as sex, transplant number, cause of ESRD, time on dialysis, type of immunosuppression, days of admission, cold ischemia time, warm ischemia time, presence or absence of DGF, acute rejection (type and treatment), complications, number of HLA mismatches and graft and patient survival. In addition, creatinine, glomerular filtration rate (GFR), and tacrolimus levels were recorded at discharge, at 6 months, and annually thereafter.

Results: see attached table. GFR was 48.29 (7-85) ml/min at 6 months, 49.9 in the 1st year (15-85), 53.75 (25-79) in the 2nd year, 48 (15-75) in the 3rd year, 52 (16-79) in the 4th year, and in the 5th year there were only 3 patients with follow-up. When comparing patients who had had DGF (46%) versus those who did not (54%), a statistically significant difference was observed in GFR at 6 months and at 1 year, which stopped being statistically significant after the second year.

Conclusions: The presence of DGF may be a risk factor for having a worse glomerular filtration rate, at least during the first year in patients transplanted with a DCD.

Statistics

	DGF[(b)]	N	Average	Standard Deviation	Standard error of the mean
GFR 6 months	0	33	52.42	13.477	2.346
	1	32	44.03	18.138	3.206
GFR 12 months	0	26	54.42	13.073	2.564
	1	18	43.44	15.252	3.595
GFR 2 years	0	18	56.89	12.829	3.024
	1	10	48.10	18.187	5.751
GFR 3 years	0	9	52.89	13.670	4.557
	1	6	40.74	19.616	8.008
GFR 4 years	0	4	57.00	29.246	14.623
	1	7	50.57	13.501	5.103
GFR 5 years	0	3	60.67	8.145	4.702
	1	0[(a)]			

(a) T cannot be calculated because one of the groups is empty

(b) NTA: 0 = No / 1 = Yes

Test for independent samples

		Levene test for equality of variances		T test for equality of means						
		F	Sig.	t	gl	Sig. (bilateral)	Difference of mean values	Typical error of difference	95% confidence interval for the difference	
									Lower	Upper
GFR 6M	Assuming equal variances	3.547	0.064	2.122	63	0.038	8.393	3.955	0.489	16.297
	Not assuming equal variances			2.112	57.196	0.039	8.393	3.973	0.438	16.348
GFR 12M	Assuming equal variances	0.359	0.552	2.558	42	0.014	10.979	4.291	2.318	19.639
	Not assuming equal variances			2.486	32.903	0.018	10.979	4.415	1.994	19.963
GFR 2Y	Assuming equal variances	2.074	0.162	1.495	26	0.147	8.789	5.878	-3.293	20.871
	Not assuming equal variances			1.353	14.093	0.197	8.789	6.498	-5.139	22.716
GFR 3Y	Assuming equal variances	0.102	0.754	1.422	13	0.179	12.152	8.547	-6.312	30.617
	Not assuming equal variances			1.319	8.223	0.223	12.152	9.214	-8.995	33.299
GFR 4Y	Assuming equal variances	2.265	0.167	0.509	9	0.623	6.429	12.639	-22.163	35.020
	Not assuming equal variances			0.415	3.747	0.701	6.429	15.488	-37.740	50.597

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EP_462 FOCAL NECROTIZING GLOMERULONEPHRITIS ANCA-NEGATIVE IN A KIDNEY TRANSPLANT PATIENT

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Background: Pauci-immune crescentic glomerulonephritis (PICGN) is a progressive form of GN that is commonly associated with antineutrophil cytoplasmic antibodies (ANCA) vasculitis. Patients with negative ANCA constitute a minority with PICGN

Methods: We present a case of 65 years old man, diagnosed with chronic kidney disease (CKD) secondary to nephrolithiasis. He started hemodialysis on 11/13/201 . Received a kidney transplant from a cadaveric donor on 01/04/2020. At that moment, the induction was thymoglobulin and maintenance with tacrolimus, , and mycophenolate . He developed Cytomegalovirus infection 2 months after transplant and after that he prresented an episode of acute cellular rejection 1A, treated with 3 pulses of steroids. The patient developed a crusted, nodular lesion on the left cheek diagnosed as moderately differentiated, invasive squamous cell carcinoma, G2.At 18 months post-transplant, renal function decline with microhematuria and non-nephrotic proteinuria. A renal biopsy was performed-

Results: The renal biopsy showed no evidence of rejection or viral infection. Cytomegalovirus presence was ruled out through immunohistochemistry. The sample was representative and included 12 glomeruli, 2 of which showed alteration of their usual architecture. Foci of fibrinoid necrosis associated with karyorrhexis were observed in both glomeruli, affecting between 25% and 50% of the glomerular circumference. The remaining glomeruli showed no lesions. Interstitial fibrosis and tubular atrophy was 30%. Arteries show moderate myointimal proliferation, and arterioles show mild hyalinosis. C4d negative.

Conclusions: In patients with malignancy presenting with acute deterioration of kidney function, although infrequent, one of the conceivable pathological conditions to consider is ANCA-negative PICGN associated with malignancy.

EP_463 THE ANALYSIS OF CV RISK IN RENAL TRANSPLANT: IMPACT OF IMMUNOSUPPRESSIVE DRUGS ON ARTERIAL STIFFNESS

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Background: Kidney transplantation is the best treatment for patients with chronic renal failure, being able to improve life expectancy and the risk of death, which, however, remains higher than in the general population. The leading cause of death in transplant patients is represented by cardiovascular (CV) events.The study aimed to analyze the impact of the immunosuppressive regimens on arterial stiffness, a proxy of CV risk.

Methods: we selected 58 transplant patients treated with tacrolimus, mTOR inhibitors (with or without tacrolimus low dose), and ciclosporin A; these patients underwent regular clinical follow-up and underwent carotid-femoral tonometry to evaluate arterial stiffness parameters as a CV risk factor.

Results: This study did not highlight statistically significant differences in terms of pulse pressure (PP), vascular age, and Pulse Wave Velocity (PWV)between the three groups; the Augmentation Index (Aix) values, however, were suggestively lower in patients receiving tacrolimus, though not statistically significant. It is interesting to note that the linear regression models performed to study the relationship between immunosuppressive regimens and the indices of arterial stiffness demonstrated a statistically significant positive correlation between exposure to tacrolimus and Aix (p= 0.05). This suggests that Aix values progressively worsen in FK506 patients. Patients with higher serum calcium levels had lower PP (p= 0.033); patients with lower phosphorus levels and CaxP product had lower PWV than the median values (p= 0.04 and 0.019).

Conclusions: our study did not disclose differences in arterial stiffness parameters in transplanted patients, with a substantial overlap in CV risk of the different immunosuppressive regimens. The correlation between increased stiffness indices and calcium-phosphorus homeostasis highlights the importance of vascular calcifications as a CV risk factor in patients suffering from chronic kidney disease. Other standard risk factors, such as blood pressure control and vascular calcifications, have been confirmed to be among the main CV risk factors in renal transplant patients.

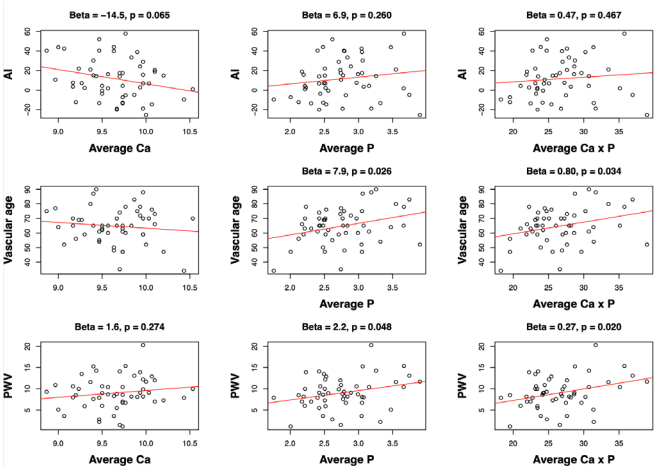

Figure: correlation between calcium, phosphorus and calcium-phosphorus product and Augmentation Index (AI), Vascular age and carotid-femoral Pulse Wave Velocity

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Infectious diseases, malignancies & long term challenges

EP_464 COMPREHENSIVE CARE STRATEGIES FOR POST-TRANSPLANT PATIENTS

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Background: With the recent advances in immunosuppressive agents, transplant is the only effective treatment modality for patients suffering with end stage organ failure. d. Long-term survivors have an increased morbidity and mortality risks, including graft dysfunction, rejection, recurrence of primary disease, and metabolic complications. Long term post-transplant management is complex and requires close follow up to recognize, manage, and to prevent medical complications and comorbidities.

In addition, patients who hope to receive a donor organ typically try to increase their medical knowledge before the transplant process takes place. With the availability of information on the internet& support groups the transplant recipients become well informed. With this knowledge, however, they get added sources of anxiety including transplant evaluation, outcome, the shortage of organs, uncertainty of donation, and increased understanding that having a transplant may not offer a complete cure. The anxiety symptoms may increase the stress during intensive care unit stay, metabolic abnormalities, sleep deprivation, post operative complications, episodes of graft rejection and medications side effects.

The patients worry about the future, loss of independence, autonomy, privacy, and increase strain in relationship with family, friends, and work associates. It is essential that patients recognize these issues prior to transplant. Because anxiety and depression are associated with poor physical and psychological outcome. Hospitalization is a highly stressful situation to both for patients and their families which has negative effects on the patients' quality of life.

Another aspect to be considered that patients feel that they are a burden to the entire family. Patients engage with daily activities and well prepared mentally have decreased fatigue and enhanced physical and psychological wellbeing.

Conclusions: The transplant team's role is to support patients' immediate and long-term recovery with specific interventions to promote quality of life. Transplant coordinator has most interactions with patients, able to keep an effective bond with patients and their families. Thus, prove trust, respect, and freedom to share their concerns. A multi-disciplinary approach helps to improve outcomes.

EP_465 CELLULAR KIDNEY TRANSPLANT REJECTION TREATED WITH EQUINE ANTI-HUMAN T LYMPHOCYTE IMMUNOGLOBULIN

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Background: 35 year old female with end stage kidney disease secondary to IgA nephropathy. First deceased donor transplant Aug 2015. Type 2a vascular rejection with features suspicious for chronic rejection and antibody mediated rejection requiring plasma exchange and rabbit ATG May 2016. Kidney transplant failure Sep 2016 with return to kidney replacement therapy.Second deceased donor kidney transplant Apr 2022. Immediate graft function achieving stable serum creatinine (sCr) around 80 micromol/L at 3 months. Presentation: Transplant review Nov 2022, significant increase in sCr to 260 micromol/L with shortness of breath on exertion, orthopnoea, and hypertension.

Methods: Immunology: donor specific antibodies negative. Histology: adequate transplant biopsy showed severe tubulitis and with oedema and haemorrhage but no clear glomerulitis. Haemorrhage suggests vascular rejection although not directly seen. Possibility of antibody mediated rejection but indefinite, and donor specific antibodies negative. Possibility of recurrent primary disease. Impression: severe acute cellular rejection.

Results: Decision made to use equine ATG given patient had received rabbit ATG for first kidney transplant. Received 10 doses (9 at 10 mg/kg and 1 at 15 mg/kg). Lymphocytes suppressed to <0.2 by day 15 of equine ATG course. Transplant function improved to new baseline of sCr 120 micromol/L (Figure 1).

Conclusions: Concern that further rabbit ATG may be ineffective due to anti-rabbit antibodies. There is paucity of published evidence and experience to help guide decision making regarding the efficacy of a second course of rabbit ATG for transplant rejection. An alternative approach could be to initiate rabbit ATG and presume presence of anti-rabbit antibodies if a reduction in lymphocyte count is not achieved. Consideration of cumulative dose of rabbit ATG for first graft transplant rejection.

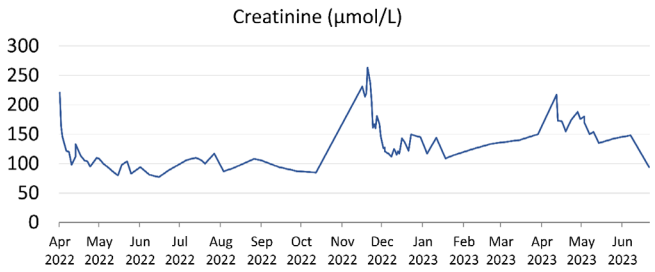

Fig. 1: A graph of serum creatinine against time, starting at time of transplantation.

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EP_466 A MULTIDICIPLINARY APPROACH TO MANAGING COVID-19 IN TRANSPLANT PATIENTS AT A LONDON TEACHING HOSPITAL

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Background: Transplant patients who test positive for Sars-Cov2 virus are at higher risk of severe disease and are eligible for antiviral medication as per NICE guidelines. However it is necessary to establish whether the patient has COVID-19 disease (pneumonitis) or requires pre-emptive treatment as well as considering the type of antiviral and need for steroids. At our Trust high risk inpatients are discussed in a daily COVID multidisciplinary team (MDT) meeting involving clinical virologists, specialist pharmacists and parent clinical teams. We present the transplant patients discussed in our MDT, describing our experiences in treatment of COVID-19 in this population.

Methods: Between October 2023 and July 2024 a total of 159 patients were discussed in our MDT, 12 (8%) of which had received organ transplants. These inpatients had tested positive for Sars-Cov2 on PCR from nasal/throat swabs or broncho-alveolar lavage.

Results: Of the 12 patients there were 4 renal, 2 heart, 3 lung and 3 heart-lung transplant recipients. The MDT reviewed their clinical status, Sars-Cov2 PCR cycle threshold (Ct) values, imaging and medication. Three patients were asymptomatic and did not require antivirals. Eight patients were for pre-emptive treatment; 5 patients received remdesivir, 2 sotrovimab and 1 molnupiravir. One patient received dexamethasone and sotrovimab for suspected COVID pneumonitis. No patients were treated with Paxlovid due to drug interactions with tacrolimus or poor renal function. One patient treated with remdesivir developed persistent infection and had further treatment with sotrovimab and molnupravir. This patient died with COVID-19 listed as a contributing factor. The remaining 11 patients recovered from Sars-Cov2 infection.

Conclusions: Transplant patients who test positive for Sars-Cov2 are a unique population who require careful management. Clinical symptoms, imaging and serial Sars-Cov2 PCR Ct values can help to determine whether a patient has COVID-19 disease or if a pre-emptive treatment approach is required. Drug interactions have a significant impact on choice of antiviral, co-administration of Paxlovid and tacrolimus is not recommended due to potential toxicity and alternative antivirals should be prescribed. An MDT can address these issues in an efficient and timely manner.

EP_467 M. ARGININI INFECTION IN A KIDNEY TRANSPLANT RECIPIENT: DIAGNOSTIC AND THERAPEUTIC CHALLENGES

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Background: *Mycoplasma arginini* is a Gram-negative bacterium that typically resides as a non-pathogenic colonizer in the respiratory and urogenital tracts of animals. In rare cases in immunocompromised individuals, especially those with hypogammaglobulinemia, it can cause significant infections. This case describes a kidney transplant recipient with M. arginini infection, highlighting the diagnostic and therapeutic challenges.

Results: A 56-year-old patient with a history of plasmocytoma, C3 glomerulonephritis, leading to end-stage renal failure and two kidney transplants, was hospitalized with a 3-week history of swelling, redness, and pain in her left arm (Fig.1). In addition to maintenance immunosuppressive, she had undergone multiple additional long-term immunosuppressive therapy to treat recurrent C3 glomerulonephritis on her graft. She also had reported one of her cats had bitten her on the forearm before the onset of symptoms. Laboratory tests showed a slightly elevated C-reactive protein. Despite treatment with β-lactam antibiotics, her symptoms worsened. An ultrasound examination revealed mild cellulitis and tenosynovitis in the affected arm. Surgical irrigation of the radiocarpal joint with collection of material for microbiologic analysis were performed, and *M. arginini* was isolated from the synovial fluid using polymerase chain reaction (PCR) and culture techniques. Antibiotic therapy was switched to doxycycline and she additionally received intravenous human immunoglobulin due to severe hypogammaglobulinemia, which resulted in resolution of inflammation. She received 10 weeks of doxycycline therapy. Oropharyngeal swabs from the patient's pets resulted in the isolation of Mycoplasma species, and they were treated with doxycycline.

Conclusions: *M. arginini* infections in humans are exceptionally rare and are primarily reported in immunocompromised individuals, particularly those with concomitant hypogammaglobulinemia. Although there are no optimal treatment guidelines for *M. arginini* infections, potent intracellularly acting antibiotics with a prolonged course of treatment, such as tetracyclines and macrolides, should be used to effectively treat infections caused by this pathogen.

Figure 1. Affected left wrist; picture taken after surgical procedure.

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EP_468 INCIDENCE OF VIRUS INFECTIONS AND GRAFTLOSS IN ABO INCOMPATIBLE KIDNEY TRANSPLANTATION IN JAPAN

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Background: The current study aimed to examine the incidence of perioperative infections and graft viability in ABO-compatible and ABO-incompatible renal transplant recipients.

Methods: We included 643 living donor renal transplant recipients registered in the Michinoku Renal Transplant Network from 1998 to 2021. Patients were divided into the ABO-compatible and ABO-incompatible kidney transplantation groups. We compared the characteristics of the two groups and evaluated the incidence of postoperative viral infections (cytomegalovirus and BK virus), graft loss-free survival, and overall survival between the two groups.

Results: Of 643 patients, 485 (75%) and 158 (25%) were ABO-compatible and ABO-incompatible renal transplant recipi- ents, respectively. Postoperative viral infections, rituximab use, and plasma exchange were significantly more common in ABO-incompatible than in ABO-compatible transplant recipients. However, there were no significant differences in terms of other background characteristics. The ABO-incompatible group was more likely to develop viral infections than the ABO-compatible group. Graft loss-free survival and overall survival did not significantly differ between the two groups. According to the multivariate Cox regression analysis, ABO compatibility was not significantly associated with graft loss- free survival and overall survival.

Conclusions: Although the incidence of postoperative viral infections in ABO-incompatible renal transplant recipients increased, there was no significant difference in terms of rejection events, graft loss-free survival, and overall survival.

EP_469 ASSOCIATION BETWEEN FRAILTY AND HEMOGLOBIN-TO-RED CELL DISTRIBUTION WIDTH RATIO IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The hemoglobin-to-red cell distribution width ratio (HRR) has been identified in several meta-analyses as a prognostic marker for assessing the outcomes of patients. This study aimed to evaluate the association between HRR and the frailty of kidney transplant recipients.

Methods: This prospective cross-sectional study included 583 adult kidney transplant recipients who underwent transplantation at Severance Hospital between 2000 and 2022. Recipients were divided into tertiles according to their HRR values measured one year after transplantation. Frailty was defined as a Fried phenotype score of 2 or higher. Logistic regression models were used to examine the relationships between HRR and frailty.

Results: Patients exhibiting frailty accounted for 11.7% of the total population, showing an increase in frailty as HRR decreased. The prevalence of frailty was higher in women (13.7%) compared to men (10.0%). Among women, there were no significant differences in physical function according to HRR, whereas men showed significant differences especially in the grip test based on HRR. In Logistic regression analysis, lower HRR was identified as an independent risk factor for frailty, which was also found to increase with longer post-transplant duration, larger waist circumference, older age, lower total protein levels, and lack of physical activity (Hazard ratio: 4.103; 95% confidence interval: 1.980–8.504; $P < 0.001$).

Conclusions: This study suggests that lower HRR values following kidney transplantation are associated with a higher risk of frailty of recipients.

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EP_470 MONITORING OF MEDICATION ADHERENCE BY ELECTRONIC HEALTH CARE DATA IN KIDNEY TRANSPLANT RECIPIENTS

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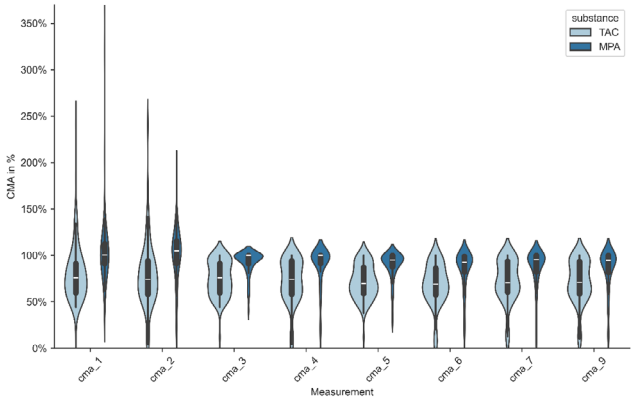
Background: Medication non-adherence to immunosuppressive drugs is a major challenge in the management of kidney transplant recipients and a major risk factor for rejection and early graft loss. Utilizing electronic healthcare data in the form of pharmacy refill records (PRR), offers a practical method for estimating adherence in this setting. Analysis of the value of PRR in the context of a multimodal assessment of non-adherence in a real world setting is crucial for its application in routine post-transplant care.

Methods: The AdTorque study was initiated to conduct a multimodal and longitudinal evaluation of adherence to immunosuppressive medications among kidney transplant recipients including PRR. All 287 adult kidney graft recipients transplanted at the Medical University Vienna between 2018 and 2019 were monitored for 2 years with a clinical follow-up of 4 years. PRR were analyzed using the standardized continuous measures of medication availability (CMA) calculations (CMA1-CMA9; primary analysis CMA7). These scores estimate adherence as a value from 0 to 100%, denoting complete non-adherence and perfect adherence, respectively.

Results: For this interim analysis only the 101 subjects with a complete record of dispensations and prescriptions for the first post-transplant year were included. Interestingly, PRR showed different adherence estimates between tacrolimus (TAC) and mycophenolic acid (MPA; mean CMA7: TAC: 72.4%; MPA: 87.3%, *p<0.001, **Fig. 1***). Such differences were also found in the more basic CMAs scores. No differences in CMA scores were found regarding biopsy proven graft rejection and de novo donor specific antibodies. Notably, no association was found between CMA scores and adherence assessed using the self-report questionnaire BAASIS®, which in contrast to PRR picks up on irregularities concerning the time of drug intake during the day.

Conclusions: This study suggests that when using PRR to estimate adherence in a post-transplant setting TAC and MPA need to be considered separately and that the customary 80% cutoff to identify adherence might not be applicable. In case granular data is not available the more simple CMA scores seem to provide similar insight to more sophisticated CMAs. Furthermore, PRR alone might not be conclusive in this setting due to their blindness to timing issues.

Figure 1



EP_471 OUTCOMES IN TRANSPLANT RECIPIENTS WITH REFRACTORY CYTOMEGALOVIRUS OR INTOLERANCE TO ANTIVIRAL AGENTS

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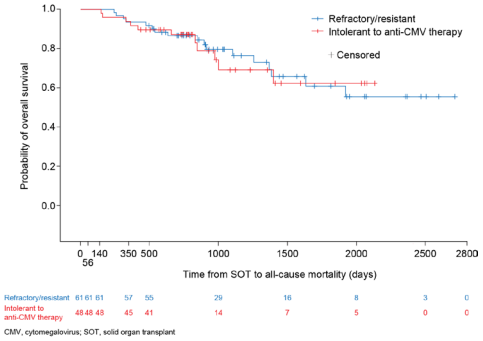
Background: Cytomegalovirus (CMV) infection remains a significant challenge in solid-organ transplant (SOT) recipients, particularly in cases of refractory or resistant infection (RR) and intolerance to antiviral therapy (I). Real-world data on these patient subsets are scarce. This study aims to provide insight into the burden of CMV infection and outcomes in SOT recipients with RR or I.

Methods: In a retrospective, medical chart review, data from adult SOT recipients with RRI CMV were collected from 15 transplant centers in Austria, Belgium, Canada, Greece, Italy, Israel, Netherlands, Poland and Sweden. Inclusion criteria required documentation of the first CMV episode post-transplant that was classified as RR or I (index CMV episode). Patients were followed for at least 12 months or until death. Descriptive statisti

Results: In total, 109 patients were analyzed (median age: 58 years; 58% male; donor +/recipient - CMV serostatus: 61%). Mean±SD follow-up after SOT was 2.9±1.6 years. Initial CMV management (n=99) was prophylaxis (n=74; 75%) or virological monitoring and pre-emptive therapy (n=25; 25%). Median (Q1–Q3) time from SOT until index CMV episode was 119 (46–231) days. At the index episode, 61 patients (56%) were classified as RR and 48 (44%) were classified as I only. Overall, 58 patients (53%) had a pre-emptively treated index CMV episode. Median duration of index CMV episode was 78 (44–174) days, and viremia clearance of index CMV episode was achieved in 83 patients (76%). After CMV index date, 46 patients (42%) required hospitalization related to CMV infection, and 63 patients (58%) had CMV-related outpatient visits. During all post-SOT CMV episodes, myelosuppression and nephrotoxicity occurred in 70 patients (64%) and 16 patients (15%), respectively. Graft loss was reported in 7 patients (6%) at a median (Q1–Q3) of 479 (357–870) days after index CMV date. All-cause mortality was 26% in the overall population, with a median survival time from index CMV of 0.8 years. Mortality was similar in the RR and I cohorts (**Figure**). Outcomes in the RR and I subgroups are shown in the **Table**.

Conclusions: This study highlights the poor prognosis and high burden of CMV RRI infection in SOT recipients, characterized by high rates of adverse events, substantial healthcare resource use and poor clinical events.

Figure. Cumulative probability of survival following solid organ transplant in patients with resistant/refractory CMV infection or intolerance to anti-CMV therapy



CMV, cytomegalovirus; SOT, solid organ transplant

Table. Outcomes in SOT recipients categorized as having resistant/refractory CMV or intolerance to anti-CMV therapies at index[a]

	Resistant/refractory (n=61)	Intolerant (n=48)
Time from SOT until index CMV episode (days), median (Q1–Q3)	97 (45–237)	137 (49–225)
Duration of index CMV episode (days), median (Q1–Q3)	160 (52–240)	56 (42–84)
Viremia clearance, n (%)[b]	41 (67)	42 (88)
Myelosuppression, n (%)	24 (39)	46 (96)
Nephrotoxicity, n (%)	13 (21)	3 (6)
Graft loss, n (%)	5 (8)	2 (4)
Time from index CMV episode to graft loss (days), median (Q1–Q3)	547 (457–870)	249 (18–479)
Mortality, n (%)	17 (28)	11 (23)
Time from index CMV episode to death (years), median (Q1–Q3)	1.0 (0.4–2.7)	0.6 (0.3–2.2)
CMV-related hospitalization, n (%)	28 (46)	18 (38)
CMV-related outpatient visit, n (%)	39 (64)	24 (50)

[a]Type of organ at index SOT: resistant/refractory cohort: kidney (n=29), lung (n=27), liver (n=3), heart (n=2); intolerant cohort: liver (n=26), kidney (n=12), lung (n=10)
[b]As reported by the physician based on medical records
CMV, cytomegalovirus; SOT, solid organ transplant

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EP_472 DO TRADITIONAL CARDIOVASCULAR RISK FACTORS PREDICT MACE IN HEART TRANSPLANTED PATIENTS? DOES ONE SIZE FIT ALL?

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Background: The stratification of the cardiovascular (CV) risk in heart transplanted (HT) patients is made considering the same factors of general population; however, this approach is not evidence-based. Moreover, despite the recommended use of statins to all patients, a target of LDL cholesterol is not defined. The aim of our study is to verify if the traditional risk factors can be used to stratify CV risk in HT patients.

Methods: In our single center study of prospectively collected data (EC code: PNC0000002), we included all adult patients HT in our Center (2013-23) surviving at least one year after HT. We collected data about CV and immunological risk factors at one month and one year after HT. Patients were stratified into low, intermediate and high/very high risk according to current ESC guidelines. The endpoint was freedom from MACE (excluding cellular rejection) at 10 years.

Results: Among 189 patients (73% males, 52?12 yrs), 30% had ischemic etiology (CAD), 22% diabetes, 70 % hypertension; donor age was: 46?14 yrs. Despite a wider use of statins over the first year (46.4% vs 77.9%, p<0.01) and a related decrease in LDL, still 55% of pts had LDL>100 mg/dl at 1yr. Stratifying CV risk according to ESC guidelines did not predict 10-yrs prognosis (80.4?14.9% vs 77.3?6.5% vs 85.2?7.2% vs 7.2?9.2% low vs intermediate vs high vs very high, p=0.6). At univariate analysis, we identified the following 1-yr variables: 1-yr LDL, (>110 mg/dl, HR:8.7), triglycerides > 140 mg/dl, HR:7.8 (both by ROC analysis), >2 episodes of cellular rejection (>2R) in the first year (HR:3.3), CMV infection (HR: 3.6), p<0.01 all, CAD with a borderline statistical significance (HR:2.8, p=0.08); mTOR inhibitors, DSAs, steroids, antiplatelets did not predict MACE. By scoring each of the above risk factors according to its HR (2 points for TG and LDL, 1 for the others), we created two risk groups (0- 3 vs ?4 points), that were able to stratify MACE (94.9?2.8% vs 64.7?9.3%, p<0.01), even after adjusting for donor age >45 yrs.

Conclusions: In HT patients, traditional tools seem not able to stratify CV risk. A score including metabolic risk factors (LDL cholesterol, triglycerides), rejection history, CMV infection and ischemic etiology seems to better stratify CV events regardless of donor age. These results reflect the multifactorial etiology of CAV.

EP_473 PSYCHOSOCIAL SUPPORT FOR FAMILIES AS AN INTERVENTION FOR IMPROVED TRANSPLANTATIONS OUTCOMES

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Background: This study examines the role of psychosocial support for family members of transplant patients as an intervention to improve outcomes. It posits that the quality of life of family members influences patient outcomes in both the short and long term (Young & Smith, 2016; Gregorio, Rodríguez, & Bernal, 2008). The goal is to evaluate the impact of various psychosocial interventions, such as counseling, support groups, and educational programs, on the emotional well-being of family members and their ability to support the patient (Brown & Williams, 2015).

Methods: A systematic review by Young et al. (2016) synthesizes multiple studies to provide a comprehensive overview of existing evidence. Additionally, findings from other relevant research, such as the impact of social support on health-related quality of life in chronic liver diseases (Johnson & Brown, 2021) and the psychosocial challenges faced by caregivers of liver transplant patients (Williams & Smith, 2018; Smith & Jones, 2017), are included.

Results: The studies indicate that family members of transplant patients often experience low quality of life, with persistent anxiety, stress, and depression post-transplant. This negatively impacts patients, as a poor psychosocial state of the family can affect transplantation outcomes (Williams & Smith, 2018; Brown & Johnson, 2018; Gregorio, Rodríguez, & Bernal, 2008).

Conclusions: Although specific research on the effectiveness of psychosocial support as an intervention is limited, the findings suggest that such interventions could potentially contribute to improved transplantation outcomes for both the patient and the family. A holistic approach to care, where the family plays an active role in the transplantation process, is essential. Regular psychosocial assessments, tailored support programs, and ongoing counseling are necessary to address the unique needs of family members throughout the transplantation journey (Smith & Williams, 2015; Johnson & Brown, 2020).

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EP_474 SCREENING FOR MEASLES MMUNITY IN ADULT RENAL TRANSPLANT CANDIDATES: A SINGLE UK CENTRE EXPERIENCE

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Background: Measles is one of the most contagious of all infectious diseases with a significant risk of mortality in immunocompromised individuals. In response to the increasing incidence of measles infection in 2024, updated guidance from the British Transplantation Society in June 2024 recommended all SOT (solid organ transplant) recipients and waiting list patients should have readily accessible information on documented completion of full measles vaccination or measles IgG status. We therefore introduced screening for measles IgG in all adult patients being assessed for renal transplantation at our centre who were born after 1970. Identifying non-immune patients before transplant immunosuppression is started allows a window of opportunity for these patients to receive the live MMR vaccine.

Methods: We collected data for all patients attending our renal transplant assessment clinics between September-October 2024. Where available, vaccination history was sought via the primary care electronic records.

Results: 58 patients were tested for measles IgG using NovaLisa® (Gold Standard Diagnostics) assay. 51 (88%) were positive, 7 (12%) were negative. There were no equivocal results. The majority of non-immune patients (5 of 7) were aged 25-35 years. Their vaccination history was: fully vaccinated (n=1), unvaccinated (n=1), incomplete/interrupted vaccine course (n=2), history unavailable(n=1). Vaccination was encouraged in the non-immunosuppressed patients before transplant listing. The older 2 non-immune patients were aged 46-54 years and had both previously received a renal transplant (and remained on transplant immunosuppression at the time of testing). Vaccination history was unavailable.

Conclusions: We identified that a significant proportion (12%) of prospective renal transplant candidates in our centre were not immune to measles at the time of transplant assessment. These patients were more likely to be younger (consistent with reduced vaccine uptake nationally for this age group) or previously transplanted. Pre-transplant screening has allowed for safe vaccination in non-immunosuppressed recipients.

EP_475 KETO ANALOGUES IN PATIENTS WITH CHRONIC KIDNEY DISEASE WITH OR WITHOUT KIDNEY TRANSPLANTATION

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Background: Keto analogues in combination with a (very) low-protein diet significantly reduces the progression to end-stage kidney disease. The question of their benefit and safety for kidney transplant recipients remains. This study aimed to show the renoprotective effect and safety of the use of this method in patients with chronic kidney disease and a kidney transplantation.

Methods: This was a retrospective monocentric study conducted by the transplant nephrology department in Martin, in which patients with chronic kidney disease, with or without kidney transplant therapy, who received a low-protein diet and supplementation with keto analogues were included (n = 59). The changes in their glomerular filtration rate, proteinemia, calcaemia, weight, and glycaemia and the side effects associated with a low-protein diet and keto analogue use were studied in the patients with chronic kidney disease with or without kidney transplantation.

Results: The kidney transplant recipients had a significantly more advanced stage of chronic kidney disease (p = 0,0001) than the non-transplanted patients at the time of the prescription of the keto analogues (p = 0,0001). Furthermore, the kidney transplant recipients had a significantly longer follow-up period (p = 0,0001), with a difference of 27 months within subgroups. During the observed period, we recorded a decrease in glomerular filtration, but without statistical significance. In our group, we did not confirm a significant occurrence of adverse effects associates with a low-protein diet and keto analogues.

Conclusions: Keto analogues reduce the progression of chronic kidney disease and stabilise glomerular filtration in patients with chronic kidney disease. Based on our analysis, treatment with keto analogues is effective and safe for kidney transplant recipients after kidney transplantation.

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EP_476 A RARE CASE OF CRYPTOCOCCUS SKIN AND BLOODSTREAM INFECTION IN A KIDNEY TRANSPLANT RECIPIENT - A CASE REPORT

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Background: *Cryptococcal* sepsis has primarily been described in patients suffering from advanced HIV associated acquired immunodeficiency syndrome (AIDS) and liver cirrhosis. The most reported clinical manifestation of disseminated *cryptococcus* sepsis is meningitis, which is frequently associated with fatal outcomes. *Cryptococcus neoformans* is a member of the candida family which is ubiquitously found in the soil. However, it is an opportunistic pathogen and does not lead to clinical manifestations in healthy individuals. Though treatment regimens for *cryptococcal* sepsis have been described, little work has been published on successful treatment and preservation of graft function in kidney transplant (KTX) recipients. Therefore, we report this case of a KTX recipient surviving *Cryptococcus* sepsis with severe cutaneous manifestations and metastatic dissemination.

Case: A 54-year-old male KTX recipient on long-term immunosuppressive therapy developed severe pain and a pink discoloration in his right lower leg after recent venous thrombosis and cytomegalovirus colitis. Despite initial antibiotic treatment with piperacillin/tazobactam, his condition worsened, with the emergence of painful blisters, elevated creatinine phosphokinase levels, and cutaneous lesions. Eventually, bacterial cultures of blisters and blood revealed *Cryptococcus neoformans*. Antimycotic therapy with fluconazole/flucytosine was initiated but escalated to amphotericin B due to worsening graft function. Despite treatment, abscesses, skin necrosis and small psoas lesions developed. After two months, *Cryptococcus* was no longer cultured, and the patient received an autologous skin graft. The patient improved with continued therapy and was ambulatory after three months.

Conclusion: *Cryptococcal* infection can occur in immunocompromised KTX recipients, presenting with atypical manifestations like cutaneous lesions. In our case, diagnosis was challenging due to inadequate initial response to antibiotics, but blood and blister cultures confirmed the infection. Treatment required adjustment due to graft dysfunction, highlighting the complexity of managing opportunistic infections in KTX patients.

EP_477 IMPACT OF BARIATRIC SURGERY ON STEATOTIC LIVER DISEASE AND LIVER TRANSPLANT PATIENTS: META-META-ANALYSIS

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Background: Bariatric surgery (BS) is a common, effective treatment for obesity, improving metabolic profiles and reducing mortality risk. However, its impact on patients with liver disease is unclear, with inconsistent results. In this umbrella review and meta-meta-analysis (MMA), we assessed existing literature on BS in such patients.

Methods: A systematic search from January 2013 to April 2024 was conducted. Two independent reviewers selected articles, assessed quality, and evaluated bias in the included systematic reviews. We examined BS effects on patients with liver disease, including those with metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic dysfunction-associated steatohepatitis (MASH), compensated and decompensated cirrhosis, and liver transplant (LT) recipients. MMA were performed with a random-effects model. The protocol was registered with PROSPERO (CRD42023410190).

Results: Nineteen systematic reviews were analysed, with six included for MMA. MMA revealed benefits of BS on MASLD/MASH patients with ALT and AST decreasing by 13 U/L and 6 U/L, respectively. Steatosis, steatohepatitis, and fibrosis resolved completely in 53%, 45%, and 25% of patients, respectively. Fibrosis stage reduced by 0.76, and MASLD activity score (MAS) decreased by 2 points (range 1-3). Complications following BS in compensated cirrhotics were 18%, with 5% experiencing liver decompensation, and 1% early mortality. However, decompensated cirrhotics had a higher mortality of 16-22% post-BS mortality. BS before-LT resulted in higher excess weight loss percentage but increased 1-year graft loss (12.5% vs. 3.1%). Immediate complications were fewer compared to BS during- or after-LT.

Conclusions: Our umbrella review and MMA highlights BS benefits in MASLD, MASH, and compensated cirrhotics but caution against it in decompensated cirrhosis. Furthermore, future meta-analyses should focus on primary studies investigating treatments such as endoscopic and pharmacological therapies and comparing them with surgical interventions.

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EP_478 LIVE DONOR KIDNEY TRANSPLANTATION HAS A SIGNFICANT SURVIVAL BENEFIT FOR OLDER TRANSPLANT RECIPIENTS

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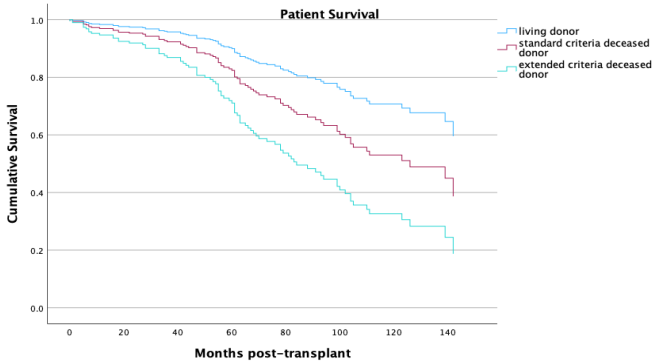
Background: The survival benefit of live donor (LD) compared to deceased donor (DD) kidney transplantation in older patients with end-stage renal disease (ESRD) in Europe is unclear. This study considered transplant outcomes in older recipients who received a kidney from a LD with that of a DD.

Methods: All consecutive kidney transplant recipients aged at least 65 yr. in Northern Ireland between 2010 and 2024 were analysed. Survival was analysed as time from transplant to death. Hazard ratios (HR) and confidence intervals (CI) were calculated using Cox regression models.

Results: The median age was 70 years. Median follow-up was 55 months. 114 (39%) patients received a LD kidney, 53 (18%) patients received a standard criteria DD kidney and 127 (43%) patients received an extended criteria DD kidney. 5-year survival was 87% for LD, 81% for standard criteria DD, and 63% for extended criteria DD recipients. Extended criteria transplantation was associated with a significantly increased risk of death (unadjusted HR 3.10; 95% CI 1.84-5.22, p<0.001) compared to live donor transplantation. Results were similar in models adjusted for age, sex, diabetes, cardiovascular disease and time on dialysis prior to transplant.

Conclusions: LD kidney transplantation offers a substantial survival benefit for older transplant recipients in Northern Ireland. This remains significant in patients with diabetes, cardiovascular disease and those on dialysis prior to transplant. Such striking survival benefit for LD kidney transplantation should be borne in mind when counselling potential transplant candidates (and their families) on kidney transplant options.



EP_479 REVEALING THE VIROME OF KIDNEY TRANSPLANT RECIPIENTS THROUGH PLASMA CELL-FREE DNA WHOLE-GENOME SEQUENCING

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Background: Plasma cell-free DNA (cfDNA) is a promising minimally invasive biomarker for post-transplant monitoring. Popular tests measure the donor-derived cfDNA (dd-cfDNA) in the recipient's plasma, a non-specific marker of loss of graft quiescence. Although this approach may have clinical value for monitoring graft health in certain contexts, it does not offer a comprehensive post-transplant monitoring. Investigating the plasma virome of transplant recipients could fill these gaps by providing relevant information regarding other post-transplant comorbidities related to over-immunosuppression.

Methods: Plasma samples from 182 kidney transplants, collected at the time of a kidney biopsy, were retrospectively selected (N=75 with normal kidney biopsy, N=75 with graft rejection, N=32 with polyomavirus nephropathy). Plasma samples from 111 non-transplanted individuals were collected as control group without immunosuppression. Plasma cfDNA was subjected to whole-genome sequencing. Sequencing reads were analyzed using an in-house developed pipeline, to estimate the viral load for the viral species detected in each sample.

Results: When compared to the gold standard blood qPCR technique, our results showed a remarkably high correlation with polyomavirus and cytomegalovirus PCR test results (Fig.1A and 1B), providing also taxonomic details (Fig.1A). By comparing transplanted versus non-transplanted individuals, we could observe differences in the structure of the plasma virome: in transplant recipients the most represented viral family is that of the Anelloviridae, a family of endemic viruses linked to individual immunocompetence; viral load of Anelloviruses was markedly increased in the transplant population compared to non-transplanted individuals, without significant differences across the 3 different transplant cohorts (Fig.1C).

Conclusions: Plasma cfDNA whole-genome sequencing showed comparable accuracy of gold standard qPCR in detecting viruses of interest, with the advantage of preserving taxonomic information and ability to detect multiple viruses in one single assay. The global plasma virome shows a different composition in immunosuppressed versus immunocompetent individuals, with no clear differences across different transplant cohorts.

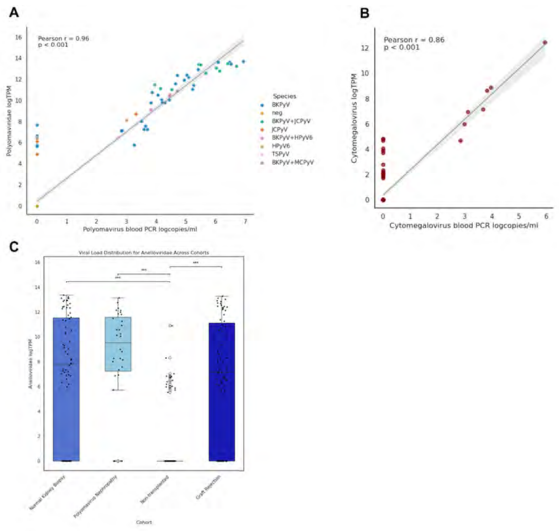

Figure 1: Correlation between blood qPCR test results for Polyomavirus **(A)** and Cytomegalovirus **(B)** and cfDNA sequencing based viral load for human Polyomaviruses and Cytomegalovirus, respectively. Viral load calculated with qPCR is expressed in log transformed viral copies/ml; viral load calculated via cfDNA sequencing is expressed as log transformed normalized read counts (TPM=transcripts per million). BKPyV = BK polyomavirus, JCPyV = JC polyomavirus, HPyV6 = Human polyomavirus 6, HPyV7 = Human polyomavirus 7, TSPyV = Trichodysplasia spinulosa polyomavirus, MCPyV = Merkel cell polyomavirus. **(C)** Box and whisker plot showing the viral load, expressed as log transformed normalized read counts (TPM), of Anelloviruses across the different cohorts.

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EP_480 LIVING KIDNEY DONATION IN PRESENCE OF MONOCLONAL GAMMOPATHY OF UNCERTAIN SIGNIFICANCE (MGUS): CASE SERIES

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Background: Monoclonal gammopathy of undetermined significance (**MGUS**) is a premalignant plasma cell dyscrasia that precedes multiple myeloma with a 1% risk of progression per year; 3.2% of individuals over 50 are affected by MGUS1,2. While in the setting of deceased donor kidney transplant MGUS represents an almost negligible risk for the recipient, Living Kidney donation (LKD) with MGUS is controversial because of donor long term safety issues, but it is an increasingly relevant topic due to the raising age of kidney donors and recipients.

Methods: We report 7 LKD (TABLE1) with history of MGUS prior to donation, who underwent screening at our center since 2019. Our haematological workup (FIGURE1) includes: serum electrophoresis, Monoclonal Component (MC) qualitative and quantitative study, plasma K/L free light chains, Bence Jones, lymphocyte cell typing. Abdominal ultrasounds and CT are routinely performed to rule out splenomegaly or lymphadenopathy. In case of MC detection,a haematological consult is performed to assess the indication to Bone Marrow Biopsy (BMB). BMB allows exclusion of multiple myeloma (MM) and a more precise definition of the future risk of progression from MGUS to MM, which will be thoroughly discussed with the potential LKD and the recipient.

Results: Only two donors (D) underwent donation. D1 had a 39 months MM free follow-up, her recipient did not develop hematological diseases at 5 years. D2 was lost at follow up because her recipient died of post operative cardiovascular complications. D3 and 5 had no MGUS progression at 16 years (MGUS known before LKD screening) and 17 months respectively, D4 follow-up is not assessable(<6months). D6 was diagnosed with MM, so he did not donate. D7 withdrew his consent after being informed of the risks.

Conclusions: In our experience LKD with MGUS is possible, after a thorough study, a multidisciplinary evaluation and an adequate information of both D and R. D safety should be granted through long term follow up. Further data are needed to draw more definite conclusions.

Figure 1

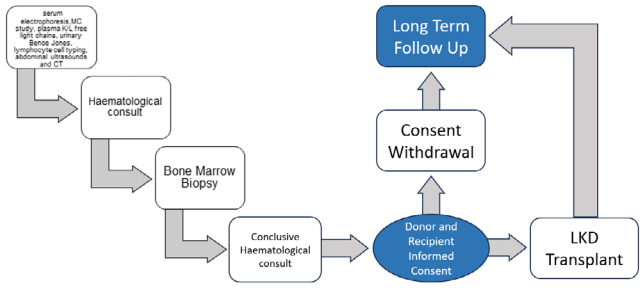

Table 1

DONORS AGE	SEX	CREATININE ELECTROPHORESIS	k/λ	BJ	URINE IMMUNOFIXATION	LYMPHOCYTE PROFILING BMB	HAEMATOLOGICAL OPINION	DONATION	FOLLOW-UP
Donor 1	64 F	1,02 mg/dL	IgG kappa >0,5 g/dl	2,36	+	/	no circulating clones	/	NO ABSOLUTE CONTROINDICATION	performed	No malignancies at 39 months
Donor 2	56 F	0,87 mg/dL	IgG-kappa >0,5 g/dl	1,37	-	negative	no circulating clones	plasma cells <10%	NO ABSOLUTE CONTROINDICATION	performed	Lost at follow-up
Donor 3	60 F	0,86 mg/dL	Klg-lambda 0,69 g/dl	0,86	-	negative	no circulating clones	plasma cells <5%	NO ABSOLUTE CONTROINDICATION	not yet performed	No malignancies at 16 years
Donor 4	59 M	0,83 mg/dL	IgA-lambda >0,5 g/dl	0,9	+	free lambda light chains	no circulating clones	plasma cells <5%	NO ABSOLUTE CONTROINDICATION	not yet performed	+6 months
Donor 5	84 F	0,79 mg/dL	negative	0,63	-	negative	no circulating clones	not performed	NO ABSOLUTE CONTROINDICATION	not yet performed	No malignancies at 17 months
Donor 6	59 M	1,04 mg/dL	IgG-lambda 0,52 g/dl	2,06	-	negative	no circulating clones	plasma cells <10%	DONATION CONTROINDICATED	not performed	/
Donor 7	70 M	0,96 mg/dL	IgM kappa >0,5 g/dl	1,35	/	not performed	no circulating clones	not performed	NO ABSOLUTE CONTROINDICATION	consent withdrawal	No malignancies at 8 months, then lost at follow up

1. Mouhieddine TH et al. Monoclonal gammopathy of undetermined significance. Blood. 2019 Jun 6;133(23):2484-2494.

2. Kaur J et al. Monoclonal Gammopathy of Undetermined Significance: A Comprehensive Review. Clin Lymphoma Myeloma Leuk. 2023 May;23(5):e195-e212.

EP_481 REMOTE QUANTIFICATION OF BLOOD TACROLIMUS LEVELS: A PROOF-OF-CONCEPT SELF-TESTING PLATFORM

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Background: Tacrolimus monitoring is crucial for post-transplantation follow-up. Remote sampling methods based on Dried Blood Spots (DBS) or Volumetric Absorptive Microsampling (VAMS) combined with testing in central laboratories proved comparable to conventional venous sampling while minimizing patient burden. However, the turnaround time for lab-testing and subsequent patient feedback hampers a prompt and efficient adjustment of the tacrolimus dose.

Methods: A bioluminescent sensor enabling tacrolimus quantification in the physiological concentration range (5.5 – 16.5 nM) had been developed. We developed a proof-of-concept portable platform enabling remote quantification of blood tacrolimus levels. It comprises a simple microfluidic cartridge, a hand-held reader and a smartphone application. We validated this platform against the gold standard, liquid chromatography tandem mass spectrometer (LC-MS/MS), using whole blood samples spiked with tacrolimus. Method agreement was evaluated using Passing-Bablok regression and Bland-Altman analysis.

Results: Method agreement was adequate for tacrolimus. The platform quantifies tacrolimus in 15 minutes using only 10 µL of capillary whole blood.

Conclusions: This proof-of-concept platform was validated for tacrolimus, enabling remote immunosuppressant therapeutic drug self-monitoring for organ transplanted patients. Potentially leading to significant savings of 3,5 h for patients and 157 € of societal cost per test as well as improved patient care. We are now working on bringing this platform to market, potentially revolutionizing tacrolimus monitoring in transplant patients.

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EP_482 A DECADE OF ABO INCOMPATIBLE KIDNEY TRANSPLANTATION: RESULTS AND LESSONS LEARNED

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Background: Living donor kidney transplantation (LDKT) is the best option for renal replacement therapy, as it offers better outcomes and quality of life for patients. Traditionally, transplants have been performed between donors and recipients with compatible blood type. However, in recent years, ABO-incompatible transplants have emerged as an effective alternative for patients on the waiting list without a compatible donor.

Methods: A single-center retrospective study was conducted, including ABO-incompatible LDKT patients in our hospital between 2013 and 2023, with a minimum follow-up of 1 year. Desensitization protocol with anti-CD20 monoclonal antibodies, specific immunoadsorption (IA), and polyclonal immunoglobulins was implemented. Induction immunosuppression consisted of thymoglobulin, prednisone, tacrolimus, and mycophenolic acid.

Results: Twenty-four patients were included. The average age of donors and recipients was 55 ± 8 and 54 ± 9 years, respectively, with a majority of female donors (80%) and male recipients (60%). Marriages represented the most common relationship (68%). The mean follow-up time was 42 months. 80% of patients required pre-transplant IA (average of 4 sessions), while 41% required post-transplant IA (average 3.5 sessions). All patients had pre-transplant isoagglutinin (ISO) titers <1/8, and post-transplant ISO titers remained low in most cases. 16% of patients experienced acute rejection (cellular and/or humoral). One patient developed graft thrombosis 15 days post-transplant due to humoral rejection mediated by ISO. Graft survival was 96% in the first year and remained stable throughout the follow-up, with mean serum creatinine levels of 129 ± 46 µmol/L and no proteinuria. Patient survival was 94%. No higher rates of infections or neoplasms were observed.

Conclusions: Despite the immunological challenges inherent in ABO-incompatible LDKT, current desensitization protocols allow for acceptable rates of acute rejection and provide satisfactory long-term graft and patient survival.

EP_483 OCCUPATIONAL AND ENVIRONNEMENTAL INFECTIOUS RISKS PREVENTION IN KIDNEY TRANSPLANT RECIPIENT ON JOB RETENTION

Camille Dauptain[1], Cécile Vigneau[2], Christophe Paris[1], Pierre Tattevin[3], Anastasia Saade[4]

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Background: Few kidney transplant recipients return to work, despite most being of working age. The impact of infectious risks on quality of life and professional reintegration remains underexplored. This study evaluates the benefit of consultations to prevent environmental and occupational infectious risks in facilitating return to work, compared to data in the literature. The primary objective is to compare the prevalence of recipients returning to work one year post-transplant with the 30% reported in the literature. Secondary objectives include assessing employment prevalence before transplantation and the impact of infectious risk consultations on return-to-work rates and quality of life.

Methods: This single-centre prospective cohort study, conducted at Rennes University Hospital, enrolled kidney transplant patients aged 18–64 years from August 2022 to February 2024. Infectious risk prevention consultations were standardised, with one-year follow-up. Data included demographics, comorbidities, infectious exposures, transplant status, and socio-professional characteristics. Statistical analyses were performed using R Studio®. Ethics Committee approval was obtained.

Results (preliminary): Of 52 participants, 24 were male, with a median age of 50 [41–54] years. Pre-transplant employment prevalence was 44% [30–59%]. Inactive patients were more likely to have undergone haemodialysis (P = 0.009), while active patients had more occupational health follow-up (P < 0.001). Permanent employment contracts significantly predicted continued employment (OR: 10.7 [2.6–58.3]). Environmental infectious risks were low, while occupational risks were slightly higher among inactive patients (14% vs. 9%) without statistical significance. After 559 [328–649] days, 14/30 returned to work at one year, 11 requiring workstation adjustments, independent of occupational risk assessments.

Conclusions: Early infectious risk consultations supported lifestyle guidance post-transplant. Final results will present return-to-work prevalence, associated factors, and patient quality of life outcomes.

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EP_484 RECURRENCE OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION: OVER 40 YEARS OF EXPERIENCE IN OUR CENTRE

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Background: Focal Segmental Glomerulosclerosis (FSGS) is a common cause of kidney disease. Its primary form is rare, but recurrence in kidney transplantation (KT) occurs in 30-60%, compromising short-term graft survival. Despite advances in understanding and treatment, KT in this population remains a challenge. Our study aims to describe the characteristics of patients with FSGS recurrence in kidney transplantation.

Methods: Retrospective study of KT patients with recurrent FSGS at our centre since 1982. Clinical, analytical, and histological data, as well as transplant characteristics, were collected.

Results: A total of 117 FSGS patients with KT were identified: 20,5% with secondary forms, 6,8% genetic, and 38,5% primary. 40 patients were unclassifiable. Among the primary cases, 11 recurrences (24,4%) were observed, with a mean age at disease onset of 26±18 years, proteinuria of 11±2,7g/day, and albuminemia of 16,6±3,9g/L. At KT, 73% had nephrotic syndrome. Two patients received living donor KT, and 9 deceased donor KT. The median time to recurrence was 6,2±8 months. 90% presented nephrotic-range proteinuria, 36% with nephrotic syndrome. 3 patients received plasmapheresis, 3 rituximab, and 3 methylprednisolone. All were on ACE inhibitors/ARBs, and calcineurin inhibitor levels were increased. 3 patients achieved complete remission, 2 partial remission and 5 had no response, with graft loss and reinitiation of hemodialysis. 2 patients received a second KT, with one recurrence. Patients with graft loss had higher pre-transplant proteinuria (9.8 vs 6.2g/day) and received older grafts (58.2 vs 35.8 years), all from deceased donors. They presented delayed graft function more frequently (60% vs 0%, p=0.061), earlier recurrence (71 vs 283 days), along with higher proteinuria at diagnosis (9.2 vs 6.6g/day) and more acute rejection (60% vs 17%). Recurrence within 3 months was associated with earlier disease onset (20 vs 34 years) and more severe hypoalbuminemia (15 vs 20g/L, p=0.065).

Conclusions: According to our results, patients with FSGS diagnosed at an earlier age, with more severe hypoalbuminemia, who receive a KT from older donors, with higher proteinuria at the time of transplantation, would benefit from more rigorous post-transplant monitoring to detect and address early recurrence.

EP_485 LIPOPROTEIN(A) IN SOLID-ORGAN TRANSPLANT RECIPIENTS OF THE SWISS TRANSPLANT COHORT STUDY

***Julien Vionnet*[1], Linard Hoessly[2], Oriol Manuel[3], Adriana Koller[4], Baris Gencer[5], Dela Golshayan[6], Angela Koutsokera[5], Roger Hullin[5], Fadi Haidar[7], Nicolas Goossens[8], Giulia Magini[8], Daniel Sidler[9], Annalisa Berzigotti[10], Michele Martinelli[11], Kerstin Huebel[12], Andreas Kremer[13], Andreas Flammer[14], Macé Schuurmans[15], Christian Kuhn[16], Juerg Steiger[17], Pierre-Yves Bochud[5], Jean Villard[18], Michael Koller[2], Nicolas Mueller[19], Manuel Pascual[20], Florian Kronenberg[4], Tinh-Hai Collet[21]**

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Background: Cardiovascular diseases (CVD) affect solid-organ transplant (Tx) recipients with a higher incidence compared to the general population. High lipoprotein(a) [Lp(a)] levels is a genetically determined causal risk factor for CVD in the general population, but this has not been studied in Tx recipients.

Methods: STCS is a comprehensive nationwide cohort study enrolling all Tx recipients since May 2008. Clinical and biochemical data was prospectively collected until December 2019 from consecutive, first-time, single-organ Tx recipients. In a subset of Tx patients at 2 sites (Lausanne and Geneva), pre-Tx Lp(a) levels and apo(a) isoforms were determined by ELISA and Western blot, respectively. In liver Tx recipients, Lp(a) levels and apo(a) isoforms were repeated one year after Tx.

Results: Pre-Tx Lp(a) levels and apo(a) isoforms were determined in 982 Tx recipients (81 heart, 136 lung, 241 liver and 524 kidney). The mean age at Tx was 53.1 (SD 13.3) and 334 (34%) were women. The overall median pre-Tx Lp(a) level was 9.94 mg/dL (range 0.02-290.05)**.** The pre-Tx Lp(a) level was lowest in liver Tx [1.93 mg/dL (0.02-135.62)], compared to heart [12.33 mg/dl (0.75-191.39)], lung [11.61 mg/dl (0.31-216.50)], and kidney [17.88 mg/dl (0.09-290.05)] recipients (p<0.001) **(Figure 1).** The number of patients with low molecular weight (LMW) apo(a) isoforms (i.e. at least one isoform with <23 kringle IV repeats) was higher in liver (32.0%) compared to heart (22.5%), lung (20.4%) and kidney (19.8%) recipients (p<0.01). One year after liver Tx, median Lp(a) levels increased to 8.29 mg/dL (0.08-142.50), with a median change of Lp(a) of 4.85 mg/dL (-77.79; 141.27) (p<0.001) **(Figure 1).** The molecular weight of Lp(a) isoforms changed in 74 (40.7%) liver Tx recipients, decreasing to LMW in 29 and increasing to high molecular weight in 45 patients **(Table 1).**

Conclusions: Pre-Tx Lp(a) levels were lowest in liver Tx recipients. One year after liver Tx, Lp(a) levels significantly increased, not only due to the acquisition of the donor Lp(a) isoform, but also to the improvement in liver function. Further studies are needed to understand the potential of Lp(a) as a cardiovascular risk biomarker in the Tx population.

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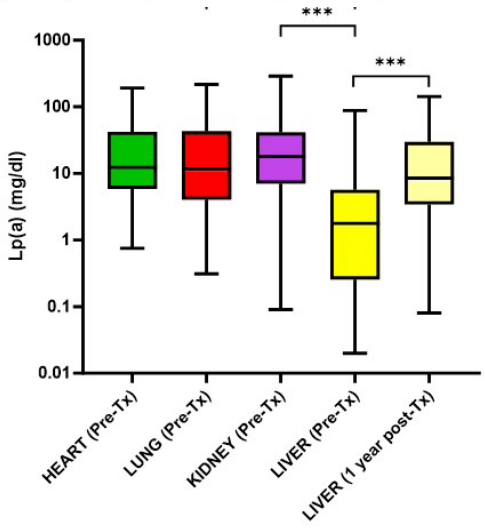
Figure 1. Lipoprotein (a) levels in heart, lung, kidney, and liver transplant recipients.



***p<0.001

Table 1. Change in Lp(a) levels and apo(a) isoforms one year after liver transplantation.

		Change in Lp(a) levels			
		Decrease: < −5 mg/dL	No change: −5 ≤ x ≤ +5 mg/dL	Increase: > 5 mg/dL	Total
Change in apo(a) isoforms	HMW → LMW	0	6	23	29
	No change	5	46	57	108
	LMW → HMW	13	21	11	45
	Total	18	73	91	182

LMW, low molecular weight Lp(a) isoform (≤ 22 kringle IV repeats)
HMW, high molecular weight Lp(a) isoform (> 22 kringle IV repeats)

EP_486 RENAL TRANSPLANTATION MEDICATION COUNSELLING - EDUCATIONAL TACROLIMUS VIDEO

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Background: Long-term transplant graft survival relies on adherence to immunosuppressive medication. Non-adherence can lead to acute rejection and renal graft failure. Patients need proper education on immunosuppression to ensure therapeutic drug levels and reduce rejection risk. Imperial College NHS Trust (ICHT) Renal and Transplant Centre uses tacrolimus for maintenance immunosuppression post-transplant. Medication education is time-consuming, with the renal pharmacy team spending an average of 120 minutes per patient. ICHT serves a diverse population with over 100 languages spoken, leading to variations in health and digital literacy.

Methods: **QI Methodology:** The project aimed to reduce the average time for counselling new renal transplant patients by 20%. Two Plan Do Study Act (PDSA) cycles were conducted over two months. • **PDSA Cycle 1:** Implemented a tacrolimus counselling video in two languages, English and Hindi. • **PDSA Cycle 2:** Updated the medication aid template to an Excel format. The template was tested and finalized for all new renal transplant patients.

Results: • **PDSA Cycle 1:** Improved face-to-face counselling time to 83.5minutes per patient but had little impact on mediboard completion time. • **PDSA Cycle 2:** Reduced mediboard completion time to 36.5minutes per patient, leading to an overall reduction in counselling time by 26% to 89 minutes.

Conclusions: The SMART objective was met, with identified limitations and areas for improvement. A patient and staff satisfaction questionnaire showed positive effects. The tacrolimus video is available in English and Hindi. Both interventions are sustained and embedded into practice, with perceived efficiency and ease. Further PDSA cycles are planned to develop the project further

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EP_487 PROJECT REVASTART: ENHANCING POST-TRANSPLANT AND LVAD PATIENT REHABILITATION AND REDUCING HOSPITAL STAY

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Background: After heart, liver, and lung transplantation (HTX, LTX, and LoTX, respectively), as well as after Left Ventricular Assist Device (LVAD) implantation, patients may be medically ready for discharge but not sufficiently recovered due to deconditioning. For these patients, the Revastart project was established in a rehabilitation center near the transplant institute. This project combines geriatric rehabilitation care and medical specialist rehabilitation to bridge the gap between being medically ready and discharge home. This approach facilitates further recovery in a rehabilitation setting rather than prolonged hospital stays until discharge home.

Methods: In preparation for the project's launch, monthly meetings were held between healthcare providers from the transplant institute and providers from both the geriatric rehabilitation care and medical specialist rehabilitation organizations. Clear guidelines from both the hospital and RevaStart were established for patient transfer. A specific training program, focusing on wound care, lifestyle guidelines, and medication management, was developed by hospital providers and followed by all Revastart healthcare professionals. Subsequently, the first patient was transferred to RevaStart. Weekly multidisciplinary meetings are held to maintain communication between the hospital and RevaStart regarding transferred patients. On indication, healthcare providers also visit patients at RevaStart. Data was retrospectively collected from discharged patients to Revastart.

Results: In November 2023, the first patient was transferred to Revastart. Since start, the program has received 2 LVAD, 3 HTx, 5 LTx, and 2 LoTx ,with a mean age of 57.4 years, 17% of whom were female. The median rehabilitation duration was 5 weeks (IQR 3-6), after which all patients were discharged to their homes. Of the 12 patients, only one was readmitted to the hospital from Revastart after a week. This patient was eventually discharged home from the hospital.

Conclusions: Since the project's inception, 12 patients have been transferred for rehabilitation. This has facilitated faster and more frequent rehabilitation outside the hospital, significantly reducing hospital stay durations. This contributes to delivering the right care in the right place.

EP_488 PROGNOSTIC ROLE OF THYROID HORMONES IN ACUTE-ON-CHRONIC LIVER FAILURE PATIENTS UNDERGOING LIVER TRANSPLANTAION

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Background: Acute-on-chronic liver failure (ACLF) is associated with a high mortality rate, with liver transplantation (LT) often being the only curative option. Thyroid hormone abnormalities are common in critically ill patients, including those with ACLF, and may influence post-transplant outcomes. This study explores the prognostic significance of thyroid hormones (TSH, fT3, fT4) in predicting survival in ACLF patients undergoing LT.

Methods: This retrospective study analyzed 95 ACLF patients, with 43 undergoing LT. Thyroid hormone levels (TSH, fT3, fT4) were assessed in relation to post-transplant survival. Differences between survivors and non-survivors were evaluated using the Mann-Whitney U test, and correlations with clinical scores (MELD, CLIF-C ACLF) were analyzed using Spearman's correlation. Statistical significance was set at $p < 0.05$.

Results: Post-transplant non-survivors exhibited significantly lower fT3 levels compared to survivors (mean: 2.04 vs. 2.57 pg/mL, $p = 0.045$). fT4 levels were marginally lower in non-survivors, though the difference was not statistically significant. TSH levels showed no significant difference between groups ($p = 0.689$). Correlation analysis revealed an inverse relationship between fT3 and CLIF-C ACLF scores ($r = -0.338$, $p = 0.003$) and between fT4 and MELD scores ($r = -0.398$, $p < 0.001$). Thyroid dysfunction, particularly low fT3 levels, was associated with worse post-transplant outcomes.

Conclusions: Low fT3 levels are a significant predictor of mortality in ACLF patients undergoing LT and correlate with disease severity scores. These findings suggest that thyroid hormone assessment may provide additional prognostic information to guide patient selection and perioperative management in LT candidates. Future prospective studies are warranted to confirm these results and further elucidate the role of thyroid hormones in ACLF.

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EP_489 IMPACT OF STANDARD IMMUNOSUPPRESSION ON COMPLICATIONS IN OLD KIDNEY TRANSPLANT PATIENTS: A SEX-SPECIFIC ANALYSIS

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Background: Infection and cancer are leading causes of mortality in older kidney transplant recipients, often resulting from the combined effects of maintenance immunosuppression (IS) and age-related immunosenescence. This study aimed to explore sex differences in response to immunosuppressive treatment, as these differences may impact outcomes such as infectious complications and malignancies.

Methods: We evaluated the outcomes of kidney transplants in recipients aged over 60 years (n=148) compared to younger recipients (n=272) from the age groups 18-34, 35-49, and 50-60 years. The groups were matched for calculated reaction frequency, donor-recipient HLA mismatches, and CMV serostatus. The study included transplants performed between April 2009 and March 2019. Comparisons were made between males and females within the four age groups concerning the occurrence of CMV viraemia within the first 6 months and the incidence of new non-skin malignancies, using multivariate analysis and hazard ratios.

Results: CMV viraemia occurred in 44% of older recipients (50-60 and >60 years) compared to 19% in the 18-34 year group. Age >60 was associated with a more than two-fold increased risk of CMV (HR=2.67; 95% CI=1.50-4.75). A significant interaction between age and sex (p=0.029) revealed that older women were at higher risk for CMV infection, though this effect was attenuated after adjusting for confounding factors (Figure1(a)). Malignancy, particularly skin cancer, was more common in older recipients, with those >60 years having a significantly higher risk (HR 7.26; 95% CI=1.69-31.10). A significant interaction between age and sex showed that older male recipients had the highest risk of malignancy, although this was somewhat attenuated after adjustment (p<0.001) (Figure1(b).

Conclusions: Older kidney transplant recipients face increased risks from immunosuppression, with sex-specific differences in outcomes. Older women are more prone to CMV infection, while older men are at higher risk for malignancy. These findings highlight the need for sex- and age-adjusted immunosuppression to improve outcomes and reduce complications.

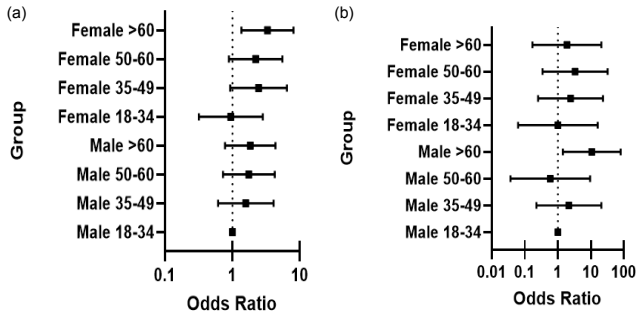

Figure 1: Forest plot of odds for developing a) CMV and b) risk of malignancy, according to age and sex. Male recipients aged 18-39 were used as the reference group.

EP_490 MANAGEMENT AND OUTCOME OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS RECURRENCE IN KIDNEY ALLOGRAFT IN A GREEK COHORT

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Background: Idiopathic focal segmental glomerulosclerosis (FSGS) frequently recurs in kidney allografts and significantly impairs their longevity. No robust data exists regarding the optimal management of FSGS patients undergoing kidney transplantation (KT). This study aims to record treatment approaches and outcomes and to define prognostic factors of FSGS recurrence.

Methods: Data of patients with idiopathic FSGS, transplanted in our center between 1993 and 2024, was retrospectively studied. Patients' and disease-specific characteristics, treatment approaches and graft outcomes were recorded.

Results: 59 KT of patients with idiopathic FSGS were performed from 1993 to 2024. 64.4% (38/59) were male. Median time from diagnosis to renal failure was 8 years (IQR 3-12), median dialysis time 33.5 months (IQR 12-96) and mean age at KT 37.4±13.1 years. In 33 cases (56%), there was a living donor. Prophylactic treatment (plasmapheresis before and/or after KT) was applied in 37 cases (62.7%). Recurrence was observed in 28 cases (47.5%) in a median time of 22 days (IQR 9.5-38). Median creatinine at time of recurrence was 2.66mg/dl (IQR 1.5-3.29) and median proteinuria 5.06g/day (IQR 3.22-7.70). In logistic regression analysis, prophylactic treatment emerged as the only factor significantly protecting from recurrence (OR 0.032, p=0.018). Plasmapheresis was performed in all cases of recurrence. Rituximab was added in 14/28 cases (50%), ACTH in 7/28 (25%) and abatacept in one. Complete remission was achieved in 7/28 cases (25%) and partial remission in 14/28 (50%) in a median time of 3 months (IQR 2-4 and 2-10 respectively). In a median follow-up time of 49 months (IQR 22-101), death-censored graft loss was observed in 50% (14/28) of patients with recurrence and only in 16.1% (5/31) of those without (p=0.034).

Conclusions: Plasmapheresis can reduce the risk of FSGS recurrence after KT. Nevertheless, effective treatment of disease recurrence still remains an unmet need.

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EP_491 IMPACT OF IMMUNOSUPPRESSION MODIFICATIONS ON BK POLYOMAVIRUS NEPHROPATHY IN KIDNEY TRANSPLANTS

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Background: BK virus-associated nephropathy (BKVAN) reduces kidney graft survival. As there is no effective treatment, we often need to minimize immunosuppression to control viral replication, even in patients at high immunological risk. This study aims to describe the characteristics of patients with BK virus-DNAemia and BKVAN and assess the impact of immunosuppression changes on graft outcomes.

Methods: We retrospectively analyzed all kidney transplant recipients from 01/05/2019 - 31/12/2023 with BK virus-DNAemia >10,000 copies/mL or biopsy-proven BKVAN. Graft biopsies were performed by clinical indication or by protocol at 1-year post-transplant. Acute rejection (AR) episodes were categorized according to Banff 2019 classification. BKPyV-DNAemia was monitored every two months during the first year and at each visit in the second year.

Results: 23 patients (8.2% of 282 kidney transplants in the study period) met inclusion criteria, all of them with viremia. 13 patients developed BKVAN and 10 had only BKPyV-DNAemia. There were no statistically significant differences between both groups in the percentage of hyperimmunized (median virtual PRA 86%) patients (38.5% vs 30%, p= 0.51) and or previous AR (53.8% vs 50%, p=0.59). Median follow up was 29 months after transplantation. 14.3% of the total graft losses in the study period were attributed to BKVAN, after a median time of 13.5 months from viremia onset. Conversion from mycofenolate (MPA) to mTOR inhibitor (mTORi) was made after the onset of viremia prior to performing a biopsy. Immunosuppression adjustments and graft outcomes are shown in the table.

Conclusions: Changes in immunosuppression regimen performed after viremia onset appear to be safe even in highly sensitized patients. An immunosuppressive regimen based on mTORi might potentially reverse BKVAN.

	BK virus-DNAemia (N=10)	BKVAN (N=13)	p
Switch from MPA to mTORi	9	12	0.59
Tacrolimus discontinuation	2	8	0.08
Graft biopsy	8	13	0,18
Post-conversion acute rejection	2	3	0.63
Re-biopsy after BKVAN diagnosis	-	6	-
Resolution of BKVAN following immunosuppression adjustment	-	3	-
Graft loss due to BKVAN	0	4	0.08

EP_492 BK POLYOMAVIRUS AND RENAL TRANSPLANT: TEN YEARS OF RETROSPECTIVE DATA FROM A SINGLE CENTER

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Background: BK virus (BKV) infection can lead to allograft nephropathy (BKVN) and graft loss in kidney transplant recipients (KTRs). This study explores the relationship between different viraemia degrees and BKVN, examining classical and other factors, clearance and graft survival.

Methods: We conducted a retrospective cohort study involving 156 KTRs diagnosed with BKV viraemia between January 2013 and December 2023, with follow-up data available through December 2023.

Results: Forty-seven (30,5 %) patients with viraemia developed BKN. Immunosuppressive induction therapy consisted of anti-CD25 in 36,2% and antilymphocyte antibodies in 61,7% of BKN patients. Baseline immunosuppressive regimen was calcineurin inhibitors (TAC) with mycophenolic acid (MPA) and prednisone (PDN) in 61,6% with BKN, or TAC with an mTOR inhibitor (iMTOR) and PDN in 38% with BKN. IMTOR withdrawal occurred in 59.5% of BKN patients without statistical association. Switched to an iMTOR+FK regimen were used in 32.1% patients, 21.8% had a reduction in FK, and 5.1% iMTOR-only therapy. Almost 36 % were monitored with no change in therapy. Additional treatments included Leflunomide (5 patients), intravenous immunoglobulin in 26 patients or photopheresis in 14 cases. Clearance was achieved in 42,2% with BKN. Interstitial fibrosis (CI >2) was found in 48.3% of BKN cases. Graft rejection after BKVN occurred in 34%. Graft loss was recorded in 63% of the BKVN patients—a statistically significant finding. The average time to graft loss was 22.3 months. Mortality was observed in only 10% of the BKVN patients. In multivariate high BK load (>10,000 copies/mL) at first replication and deceased donor status were significant predictors of BKVN, p = 0.031. No significant differences were found between immunosuppressive strategies and graft loss. Twenty-nine had probably BKN (>10.000 cp/ml) without proven BKN .

Conclusions: BK viral loads at initial replication, exceeding 10,000 copies/mL, and deceased donor status are key factors linked to BKVN. No significant differences in graft loss were observed across treatments. We didn´t found proven BKN by biopsy in an important number of patients with high replication, due to unknown individuals' protective factors or insufficient specificity by biopsy that encourage us to look for new biomarkers.

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EP_493 A MULTICENTER OBSERVATIONAL STUDY OF PTLD RISK AND PROGNOSTIC FACTORS AMONG SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Post-transplantation lymphoproliferative disease (PTLD) remains a potentially fatal complication of solid organ transplantation. The risk of PTLD development varies in relation to the type of transplanted organ and is considered one of the lowest among kidney transplant recipients (KTRs), intermediate among liver transplant recipients (LTRs) and high for lung transplant recipients (LngTRs).

Methods: To investigate the factors contributing to PTLD development and treatment outcomes, we created a multicenter registry which included KTRs, LTRs and LngTRs, diagnosed with PTLD. The chi-squared test was used to analyze the differences in group composition, and univariate Cox regression was applied to determine the impact of factors upon PTLD onset and patient survival.

Results: Our registry consisted of 58 KTRs, 40 LTRs, and 5 LngTRs from 6 transplantation centers in Poland. The median time from transplantation to PTLD onset was significantly longer among KTRs (117 months) than among LTRs (49 months, P < 0.001) and LngTRs (5 months, P < 0.001). Among KTRs, older age at first transplantation correlated with earlier disease development (P = 0.01). LTRs treated with tacrolimus developed PTLD later, compared to LTRs treated with cyclosporin (P = 0.042). CNIs did not significantly affect the development of the disease among KTRs. Reduced immunosuppression was associated with better survival among KTRs (HR = 0.34, P = 0.017). The LngTR group was too small for meaningful analysis.

Conclusions: We identified clear differences in the factors affecting PTLD onset and survival between KTRs and LTRs. Organ-specific analyses are needed to improve our understanding of PTLD risk factors, treatment choices, and clinical outcomes.

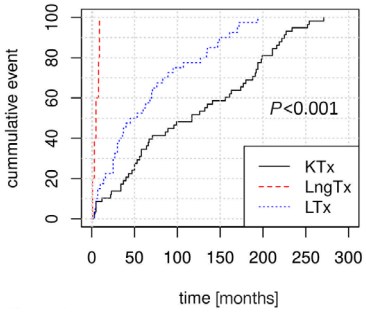

FIGURE 1. Kaplan-Meier estimator curves depicting differences in the time of PTLD onset between kidney transplant recipients (KTRs), liver transplant recipients (LTRs), and lung transplant recipients (LngTRs).

TABLE 2. Factors affecting the time of PTLD onset

Parameter	HR	95% CI	*P* value
KTRs			
Age at 1st Tx	1.03	1.00–1.05	0.01
LTRs			
TAC	0.21	0.05–0.95	0.042
CsA	4.8	1.06–21.78	0.042

CsA, cyclosporin; TAC, tacrolimus; Tx, transplantation. P values for univariate Cox regression.

EP_496 DO WARM AND COLD ISQUEMIA TIMES INFLUENCE DELAYED GRAFT FUNCTION IN A TRANSPLANT WITH DONATION AFTER CARDIAC DEATH?

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Background: The kidney transplant (KT) programme with a donor after cardiac death (DCD) has already been consolidated in our country. However, excessive warm and/or cold ischemia time can influence the clinical evolution of the transplant.

Methods: We studied 75 KT from DCD, from 15th August 2017 to 29th November 2023. The variables collected were; donor and recipient age, sex, transplant number, cause of ESRD, time on dialysis, type of immunosuppression, days of admission, cold and warm ischemia times, delayed graft function (DGF) defined as the need for haemodialysis in the first week, rejection (type and treatment), complications, number of HLA mismatches, and graft and patient survival. In addition, creatinine, glomerular filtration rate (GFR), and tacrolimus levels were collected at discharge, at 6 months, and annually thereafter.

Results: see attached table. 36 patients (46%) had DGF while 39 did not (54%). The mean cold ischemia time was 12 hours and 33 minutes (4.05-27.46) and the mean warm ischemia time was 12 minutes (5-29). We studied the association of warm ischemia time and cold ischemia time with DGF. Logistic regression was used (SPSS version 28).

The Odds Ratio (OR) indicated that for each minute that warm ischemia time increased, the risk of DGF would increase by 1.375, but it was not statistically significant (p 0.384). The same causal relationship was found with cold ischemia time and although the OR indicated that for each hour that cold ischemia time increased, the risk of DGF would increase 1.112 times, it was not statistically significant (p 0.063).

Conclusions: Although in the study carried out there is 46% of DGF, cold and warm ischemia time do not seem to influence the development of DGF, possibly due to the sample size.

ASSOCIATION OF THE WARM ISQUEMIA TIME WITH DGF		
Odds ratio (OR)	P value	IC 95% for OR
1.375	0.384	0.89-1.042
ASSOCIATION OF THE COLD ISQUEMIA TIME WITH DGF		
Odds ratio (OR)	P value	IC 95% for OR
1.112	0.063	0.994-1.243

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EP_497 PREDICTIVE VALUE OF CARDIAC BIOMARKERS ON LONG-TERM CARDIOVACULAR OUTCOMES IN KIDNEY TRANSPLANT PATIENTS

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Background: Cardiovascular disease is the leading cause of death among kidney transplant recipients. However, the identification of a specific prognostic risk biomarker remains challenging.

Methods: We conducted a prospective cohort study involving 73 patients that underwent a kidney transplantation (KTx) between September 2015 and February 2017. Median follow-up time was 9 years. High-sensitivity cardiac troponin (hs-cTn) and PCSK9 levels were measured at admission, 1 month and 6 months after KTx. Possible predictive value of those biomarkers with major adverse cardiovascular events (MACE) were examined during the follow-up period. MACE was defined as any hospital admissions with myocardial infarction, stroke, unstable angina, atrial fibrillation, heart failure, pulmonary embolism, any coronary revascularization procedure and any cardiovascular-related death.

Results: The mean age of recipients was 45.4 years and 60% were male. Only two patients had diabetic nephropathy, while 44% were hypertensive. Mean levels of PCSK9 were 199.8ng/ml before transplantation and were increased after transplantation (month 1: 276.2ng/ml, month 6: 245.9ng/ml). On the contrary, levels of hs-cTn progressively reduced after transplantation (mean hs-cTn before, at 1 and 6 months were 40pg/ml, 17 pg/ml, 13pg/ml respectively). During the 9 years of follow-up 21.9% of patients had a MACE. There was a significant association between MACE and elevated hs-cTn at 1 month (p=0.014). There was no association between MACE and PCSK9 at any timepoint. The Kaplan-Meier survival estimated rate for the study cohort at 8 years was 93% and there was a trend for worst survival in those with elevated hs-cTn at 1 month (p=0.08). During follow-up eight recipients died, half of them from a cardiovascular event. The mean creatinine levels at the end of follow-up were 1.49 ±0.67 mg/dl.

Conclusions: At one-month post-transplantation, elevated troponin levels could serve as a predictive biomarker for long-term cardiovascular outcomes.

EP_498 ABERNETHY MALFORMATION (CPSS) AND LIVER TRANSPLANTATION: CASE SERIES AND LITERATURE REVIEW

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Background: CPSS is a multisystem disease involving hepatic, neurological, pulmonary, metabolic and endocrine dysfunction. Classified into 2 types based on the degree of portal diversion. Tumor development particularly associated with Type 1 CPSS and include FNH, adenoma, HCC and hepatoblastoma. Associated with mutations in CTNNB1 gene.

Methods: 4 cases CPSS and liver tumors underwent LT. Clinical records, outcomes and literature were reviewed. 4y male, with neonatal hepatitis and 11cms tumor in left liver with atrophied right lobe. Type Ia CPSS. At 6y developed jaundice, CT showed enlarging FNH with central hemorrhage. Underwent DBD LLS LT at 8y. Well differentiated hepatocellular neoplasm. 11y female with FNH resected aged 4y. Developed dysplastic nodule and deranged liver function on follow up. Type Ib CPSS and associated ASD, VSD, PDA. Underwent DBD LLS LT at 13y. Explant well differentiated HCC. 8y male presented with deranged liver function tests. Imaging: multiple, bilobar focal lesions. Type Ia CPSS. Dominant lesion biopsy proven adenoma which rapidly enlarged. DBD whole LT aged 19. Explant showed multiple FNH, adenomas with recent hemorrhage. 37y old male with early stage HCC on follow up for multiple liver nodules with Type II CPSS. Dominant lesion treated with transarterial chemo-embolization and stereotactic radiotherapy. DBD LT aged 38y. Residual lesions were FNH with dysplastic changes. All 4 have good graft function long term.

Results: Over 30 cases of LT for CPSS are reported. Indications include hepatic encephalopathy, HPS, pulmonary hypertension and liver tumors. Age at LT range 3 months to 38 years. Optimal management is CPSS ligation as early as possible. HCC may occur early (1y), but multiple FNH are precursors to later malignancy. Imaging characterization is difficult due to portal diversion.

Conclusions: CPSS is a multisystemic disorder with complex biochemical and hormonal abnormalities. In our institution over 80 patients have been managed for CPSS with 4 undergoing LT. Literature reports a heterogenous group with good outcomes after LT.

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EP_499 CYTOMEGALOVIRUS SPECIFIC CYTOTOXIC T-CELL THERAPY IN AN ORTHOTOPIC HEART TRANSPLANT RECIPIENT

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Background: A 54-year-old man underwent orthotopic heart transplant in October 2021 for hypertrophic cardiomyopathy. Induction immunosuppression (IMS) was omitted (donor hepatitis B virus (HBV) core antibody-positive). Maintenance IMS comprised tacrolimus, mycophenolate mofetil, and corticosteroids. Baseline serologies were cytomegalovirus (CMV) donor positive /recipient negative. CMV viraemia was undetectable post-transplant. CMV prophylaxis was stopped pre-discharge due to leukopenia requiring granulocyte-colony stimulating factor. He was discharged clinically well after 11 weeks with negative HLA antibodies, good graft function, and no rejection on 3 endomyocardial biopsies (EMBs).

Methods: CMV viraemia (6,595 IU/ml) was detected day 21 post-discharge. Treatment began with valganciclovir (VGC), followed by IV ganciclovir (GCV) (day 28-114). Readmitted on day 36 with fatigue, nausea, diarrhoea, and reduced graft function. EMB on day 28 showed 'exceptionally florid CMV myocarditis.' CMV levels peaked at 347,433 IU/ml (day 40), fell to 680 (day 81), but rebounded on treatment to 34,158 IU/ml (day 111). GCV resistance (UL97 A594V mutation) necessitated foscarnet (day 114-146). Viral load fell but rebounded on Letermovir (LTV) prophylaxis (day 147-161). Further therapy included LTV/foscarnet (day 161-172), LTV monotherapy (day 173-200), and LTV/foscarnet (day 201-224). Foscarnet nephrotoxicity prompted a change to high-dose LTV (day 251-260). Finally maribavir (day 261-317) yielded low-level viraemia (<1,000 IU/ml). To sustain viral suppression an experimental CMV-specific cytotoxic T-cell (CTL) therapy derived from his haploidentical son was given on day 278.

Results: Seroconversion to CMV IgG+ day 287. Discharged day 318 without antiviral therapy. He remains clinically well, CMV IgG+ with undetectable viral levels.

Conclusions: Virus-specific T-cell therapy is a promising treatment option for refractory CMV, enabling lasting serological response and humoral immunity in select cases.

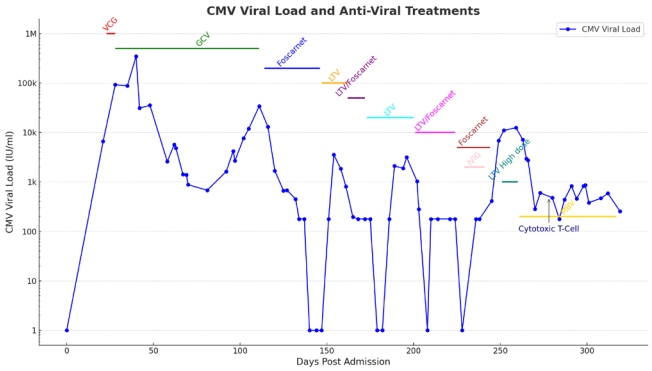

Figure 1. CMV Viral Load and anti-viral treatments used.

EP_500 POTENTIAL CARDIOVASCULAR BENEFITS OF DENOSUMAB IN KIDNEY TRANSPLANT RECIPIENTS: A FOCUS ON AORTIC ARCH CALCIFICATION

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Background: Several studies have identified aortic arch calcification (AoAC) as an indicator of cardiovascular disease risk. A research has shown that long-term use of denosumab, a treatment for osteoporosis, can improve AoAC in hemodialysis patients. However, similar studies have not yet been performed in kidney transplant recipients (KTRs).

Methods: We analyzed 98 KTRs who used denosumab every 6 months for the treatment of osteoporosis from 2018 to 2023. We assessed the severity of AoAC by AoAC score, calculated by calcification parts divided 16 * 100 (%) with simple chest X-ray. We investigated biochemical parameters, cardiovascular event, graft failure and patient death.

Results: Among them, 48 KTRs showed a change in AoAC score. The mean age at the time of denosumab administration was 63.5 ± 6.8 years. The mean AoAC score 1 year after denosumab administration had significantly decreased from 34.6% to 32.2% (P = 0.034) compared to the score before denosumab. There were no significant differences in the levels of calcium, phosphorus, parathyroid hormone, vitamin D, creatinine, and tacrolimus trough between pre- and post-denosumab. No cardiovascular events occurred in the study population. There were no significant differences in graft failure and death among the KTRs.

Conclusions: The potential use of denosumab to reduce AoAC in KTRs is promising. While initial findings in hemodialysis patients highlight denosumab's potential to ameliorate cardiovascular risks by improving calcification markers, extending this application to KTRs could offer a significant breakthrough. Further research could confirm these benefits and revolutionize post-transplant care, ultimately improving patient outcomes and longevity.

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EP_501 IMPACT OF CMV VIRAL LOAD KINETICS ON GRAFT SURVIVAL IN CMV SEROPOSITIVE KT RECIPIENTS UNDER PREEMPTIVE STRATEGIES

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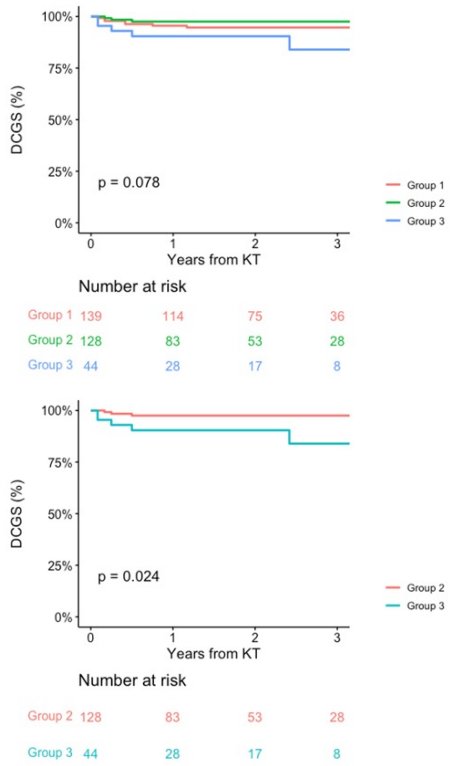
Background: Cytomegalovirus (CMV) infection remains a significant complication in kidney transplant recipients. Despite advancements in antiviral therapies, the impact of CMV viral load kinetics, especially doubling time, on graft survival is not well understood. This study investigates the relationship between CMV viral load kinetics and graft outcomes in the context of a preemptive management strategy.

Methods: We conducted a retrospective analysis of 554 adult CMV seropositive kidney transplant recipients treated at Severance Hospital from June 2020 to December 2023. Patients underwent preemptive antiviral therapy guided by a highly sensitive CMV qPCR assay with a lower quantification limit of 34.5 IU/ml. CMV infection was defined as any detectable viral load within 1-year post-transplant. CMV-infected patients (n=311) were stratified into three groups based on viral load doubling time: Group 1 (no increase in viral load, n=139), Group 2 (doubling time <14 days, n=128), and Group 3 (doubling time ≥14 days, n=44).

Results: Among the 559 recipients, 55.6% (n=311) experienced CMV infection. The median CMV peak titers for Groups 1, 2, and 3 were 169.0 [60.9–682.5], 1140.0 [354.0–3155.0], and 178.0 [100.5–716.0] IU/ml, respectively, showing statistically significant differences (P < 0.001). The median doubling times of CMV viral load for Groups 2 and 3 were 4.5 [3.1–7.3] days and 34.3 [18.7–62.4] days, respectively. Group 3 demonstrated the lowest 3-year DCGS at 84%, compared to 94.7% in Group 1 and 97.5% in Group 2. Multivariate Cox regression analysis identified a doubling time of viral load ≥14 days as a significant risk factor for graft failure (adjusted HR: 4.61; 95% CI: 1.06-20.1).

Conclusions: CMV viral load kinetics in CMV seropositive kidney transplant recipients show inter-patient variability under preemptive strategies, and notably, CMV infection with a viral load doubling time ≥14 days demonstrates negative correlation with death-censored graft survival.



EP_502 IGG3/KAPPA DEPOSITION DISEASE WITH FEATURES OF CRYOGLOBULINEMIC GLOMERULONEPHRITIS IN A KIDNEY TRANSPLANT RECIPIENT

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a life-threatening complication of transplantation, with most of the cases being associated with Epstein-Barr virus (EBV) and occurring within the first post-transplant year. Herein we present a case of late fatal monoclonal immunoglobulin deposition disease with IgG3/kappa specificity.

Methods: Case presentation with detailed pathological examination.

Results: A 40-year-old male received a kidney allograft from a deceased donor in 1999 after two years on dialysis for treatment of end-stage kidney disease caused by chronic glomerulonephritis without biopsy. The posttransplant course was complicated by deep venous thrombosis, and he was diagnosed with factor V Leiden mutation. In October 2016, he developed a nephrotic range of proteinuria and erithrocyturia. The biopsy revealed a diffuse proliferative pattern of glomerular injury with membranoproliferative features and several large intraluminal thrombi, suggesting a cryoglobulinemic component. There are large subendothelial and mesangial dense deposits restricted to IgG3-kappa by immunofluorescence. Therefore, an entire immunoglobulin was deposited in the glomeruli, with gamma 3 heavy chain and kappa light chain, and strong complement activation via classical pathway, resulting in extensive inflammatory reaction in the glomeruli. In contrast to a typical light chain deposition disease, this case included both heavy and light chain and results in glomerular inflammatory deposition disease, sometimes referred to as “light and heavy chain deposition disease”. EBV DNA revealed 996 copies/mL. Extensive examination failed to find hematologic disease. Unfortunately, the patient refused further treatment and died four years later.

Conclusions: Monoclonal paraprotein deposition diseases in the kidney have been associated with lymphoproliferative disorders (CLL and various types of lymphocytic lymphoma), plasma cell dyscrasias, and overt multiple myeloma. This complication in the kidney in a subgroup of patients can antedate the diagnosis of the lymphoproliferative disorder or an unequivocal bone marrow abnormality by several months or even years.

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EP_503 MALIGNANT NEOPLASMS FOLLOWING PANCREAS TRANSPLANTATION

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Background: Transplant recipients face a significantly higher risk of malignancies due to prolonged immunosuppression. This study evaluated the incidence and types of malignancies following pancreas transplantation (PT) at a single center.

Methods: We retrospectively analyzed 501 pancreas transplant recipients who underwent surgery between July 1992 and December 2024. The median follow-up was 107 months (range, 0~388 months).

Results: Among 501 recipients, 38 malignancies were diagnosed in 37 patients (7.4%). The median age at transplantation was 39.7 years (range, 17–66 years), and the median time to cancer diagnosis was 77.9 months (range, 3–207 months). Post-transplant lymphoproliferative disorder (PTLD) was the most common malignancy (n=12), followed by gynecologic cancer (n=7), thyroid cancer (n=4), hematologic malignancies (n=4), lung cancer (n=3), skin cancer (n=2), breast cancer (n=2), and single cases of tongue, rectal, stomach cancer and Kaposi's sarcoma. Treatment included surgical resection (n=25), chemotherapy or medical treatment (n=11), and observation (n=1). The mean survival of 55.3 months post-diagnosis (range: 2–240 months). The mean post-diagnosis survival was 55.3 months (range, 2–240 months). Seven patients died from malignancy. Graft rejection occurred in 11 patients, with seven cases resulting in kidney and pancreas graft failure.

Conclusions: The incidence of post-transplant malignancies in pancreas transplant recipients at our center was 7.4%, higher than in the general population. These findings underscore the importance of implementing tailored cancer screening programs and rigorous post-transplant monitoring to enable early detection and timely management of malignancies in this high-risk population.

EP_504 EARLY DETECTION AND COMPLETE PREVENTION OF BKV NEPHROPATHY BY URINE BKV-PCR MONITORING

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Background: BK virus-associated nephropathy (BKVN) occurs in approximately 2–3% of kidney transplant recipients, and its prognosis is poor due to the lack of effective antiviral treatments. The primary therapeutic goal is to reduce immunosuppression to eliminate the virus from the graft and bloodstream. Monitoring BK virus (BKV) in urine and plasma is critical for early detection and management. It is well known that plasma BKV levels above 10^4 copies/ml are associated with BKVN. This study investigated the relationship between urinary BKV levels, plasma BKV positivity, and BKVN development using urinary BKV-PCR monitoring.

Methods: We analyzed 104 kidney transplant outpatients (age 24–83 years; 63 males, 41 females) at Shonan Kamakura General Hospital. All patients received tacrolimus, mycophenolate mofetil, methylprednisolone, and basiliximab for induction. BKV-PCR was performed on urine and plasma samples to assess positivity rates, copy numbers, and their correlations.

Results: Of the 104 patients, 31 (29.8%) had urinary BKV ≥10^2 copies/ml, 13 (12.5%) had plasma BKV ≥10^2 copies/ml, and 2 (1.9%) developed BKVN. Among 16 patients with urinary BKV ≤10^6 copies/ml, 3 (18.8%) showed plasma BKV positivity. In contrast, among 15 patients with urinary BKV ≥10^7 copies/ml, 10 (66.7%) were positive in plasma. Plasma BKV positivity was rare (7.7%) when urinary BKV levels were ≤10^5 copies/ml, and no cases of plasma BKV positivity occurred without concurrent urinary positivity. These findings suggest urinary BKV precedes plasma BKV positivity, with plasma positivity observed when urinary levels exceed 10^6 copies/ml. The 2 BKVN cases had delayed PCR monitoring, with plasma BKV positivity already present at initiation. Early intervention following urinary BKV monitoring prevented BKVN in other cases.

Conclusions: Plasma BKV positivity indicates advanced viral replication, limiting early intervention. Urinary BKV monitoring via PCR enables earlier detection of viral activation. Prompt reduction or modification of immunosuppression upon detection of urinary BKV ≥10^5 copies/ml can effectively prevent BKVN in nearly all cases.

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EP_505 DIFFERENT NEUROENDOCRINE TUMOURS ARISING AFTER KIDNEY TRANSPLANTATION

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Background: Neuroendocrine tumors (NETs) are rare cancers that can develop in various cells of the neuroendocrine system. There is limited information on NETs in kidney transplant recipients (KTR). This report outlines our experience treating KTR diagnosed with NETs.

Methods: We included patients diagnosed with NETs after kidney transplantation in our study. We retrospectively collected and analyzed medical charts and records.

Results: Among 2,282 patients who underwent kidney transplantation at our institution from October 1973 to December 2023, eight patients were diagnosed with NETs. Four of these patients had Merkel cell carcinoma, two had pancreatic neuroendocrine tumors, and two were diagnosed with a carcinoid tumor of the appendix. Treatment approaches included surgery, radiation, and modifications to immunosuppression protocols. Unfortunately, all four patients diagnosed with Merkel cell carcinoma passed away within a year of their NET diagnosis. One patient with carcinoid died and one developed terminal kidney allograft failure and required hemodialysis. Two patients with pancreatic NETs are currently alive and have stable kidney allograft function.

Conclusions: In summary, neuroendocrine tumors are rare but aggressive cancers. Merkel cell carcinoma is highly aggressive in immunocompromised patients. Therefore, regular skin examinations and high level of awarness are essential for early detection and intervention.

EP_506 ALTERED THYMIC FUNCTION IS ASSOCIATED WITH INCREASED RISK OF SEVERE COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Kidney transplant recipients are at heightened risk for severe infections, including COVID-19, due to lifelong immunosuppression. T-cell receptor excision circles (TRECs), markers of thymic output, have emerged as potential biomarkers for assessing immune competence and predicting infection risks. However their utility in transplant populations remains underexplored.

Methods: This single-center retrospective study included 733 kidney transplant recipients, with TRECs levels measured at the time of transplantation using qPCR. Patients were stratified into four risk groups based on their TREC levels (log-transformed). Severe COVID-19 outcomes, defined as ICU admission or death, were assessed using Kaplan-Meier survival analysis and Cox proportional hazards models, adjusting for demographic, clinical, and immunological factors.

Results: Of the 733 recipients, 62 (8.5%) experienced severe COVID-19 outcomes. Kaplan-Meier analysis revealed distinct survival rates without severe COVID-19 across TREC risk groups, with 5-year rates of 96.1%, 90.9%, 83.5%, and 68.0% for the lowest to highest quartiles, respectively ($p<0.0001$) (**Figure 1A**). Multivariable Cox analysis identified TREC levels as an independent predictor of severe COVID-19 outcomes (HR 0.40, 95% CI 0.26–0.61, $p<0.001$), independently of age, BMI, diabetes, and prior kidney transplant. Analyses among COVID-19-positive patients confirmed that lower TREC levels were significantly associated with higher ICU admission and mortality rates (**Figure 1B**).

Conclusions: TRECs levels at transplantation are independent factors of severe COVID-19 outcomes in kidney transplant recipients. These findings underscore the potential of TRECs as a biomarker for immune vulnerability and risk stratification in transplant populations, with possible implications for personalized patient management.

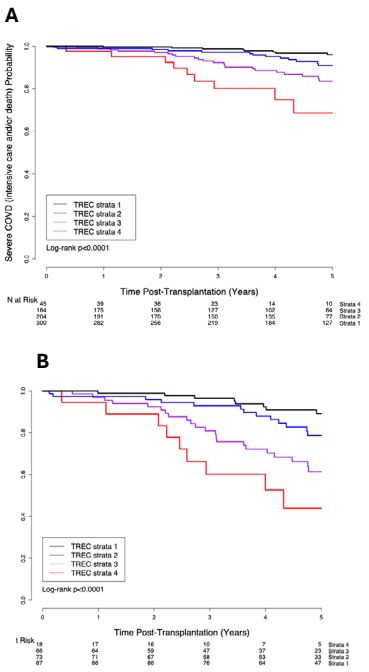

Figure 1: Kaplan-Meier curves of survival rates without severe COVID-19 in the cohort according to the levels of TRECs.

Panel A correspond to the survival rates without severe COVID-19 in the cohort and Panel B among the patients with COVID-19 infection.

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Infectious diseases, malignancies & long term challenges

EP_507 CORTICAL NECROSIS OF RENAL GRAFTS: A RETROSPECTIVE MULTICENTER FRENCH STUDY

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Background: Cortical necrosis is a severe renal complication with a poor prognosis. Its epidemiology has been described in native kidneys, but data on kidney transplant recipients remain scarce.

Methods: Our retrospective multicenter French cohort study included kidney transplant recipients between 1987 and 2023, with a diagnosis of cortical necrosis of the graft confirmed by imaging or graft biopsy.

Results: The study included 148 patients, with a median follow-up of 39.5 months (range: 1–1482). Males accounted for 57.4% of recipients, and the recipient median age at transplantation was 53.4 years. Median Body Mass Index of recipients was 24.9 kg/m². Anti-HLA antibodies were present in 64.2% of recipients. This was the first transplant for 83.8% of recipients, a second transplant for 14.9%, and a third or subsequent transplant for 4%. The median cold ischemia time was 15 hours. Grafts were obtained from deceased donors in 75.7% of cases whom 25% of donors had experienced cardiac arrest. The median donor age was 55 years. Grafts had one artery in 73.6% of cases, two arteries in 18.2%, and three or more arteries in 8.3%. The median time to event onset was 0 days (range: 0–11,662). At diagnosis, 50% of patients were anuric. Diuresis resumed in 39.1% of patients, with a median time of 8 days. Dialysis dependence was observed in 80.7% of patients at diagnosis, and 76.4% remained on dialysis at the last follow-up. On imaging, cortical necrosis appeared patchy in 54.1% of cases and diffuse in 45.9%. The primary etiology was vessel thrombosis and postoperative complications (49%), followed by undetermined causes (11%) and shock (9%). Rejection caused 18% of cases, including 7% with acute antibody-mediated rejection. Rare causes included antiphospholipid syndrome (3%) and other thrombotic conditions (1% each). For cortical necrosis occurring >30 days post-transplant, rejection accounted for 50%, including 11% acute antibody-mediated rejection.

Conclusions: Donor and recipient characteristics do not appear to differ significantly from those of the general transplant population. Beyond surgical or post-operative causes, rejection emerges as the leading cause of cortical necrosis in renal grafts. We suspect that inflammation and endothelial injury triggered by rejection play a critical role.

EP_508 POST KIDNEY TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN PEDIATRIC RECIPIENTS

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Background: Post-Transplant Lymphoproliferative Disease (PTLD) is the most common malignancy complicating after solid organ transplantation (SOT) in children as well as adults , and it's represented by lymphoid cell proliferation that happens post-organ transplant. There is limited knowledge about the prevalence of PTLD in children post kidney transplant in Saudi Arabia. The aim of this study is to identify the prevalence and risk factors of PTLD in children post kidney transplant .

Methods: Retrospective cohort study conducted at King Faisal Specialist Hospital and Research Center, Saudi Arabia. A total of 477 pediatric recipient aged ≤18 years were included , who underwent kidney transplant between 2011 to 2021. Primary outcome: The prevelance of Post-Transplant Lymphoproliferative Disease , determined using the WHO criteria for diagnosis. Secondary Outcomes: Survival rate , graft survival and risk factors of PTLD

Results: 10 out of 477 patients had a confirmed diagnosed of PTLD with The prevalence rate of 2.1%. Survival rate was 100% . With good graft survival, mean eGFR of 87 ml/min/1.73m2 after 1 year. Ongoing analysis is being conducted to evaluate the risk factors, including the immunosuppressant regimens and EBV serostatus.

Conclusions: The survival rate of pediatric patients with PTLD post kidney transplant is excellent, with good graft survival outcomes.

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EP_509 PROTEOMIC SIGNATURE OF LATE GRAFT FAILURE IN KIDNEY TRANSPLANTATION

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Background: Although short-term outcomes have improved significantly over the decades, long-term graft survival after kidney transplantation remains suboptimal. We investigated whether serum proteomics could reveal biomarkers of chronic graft injury and enhance risk prediction beyond standard clinical parameters.

Methods: We conducted a matched case-control analysis of 79 kidney transplant recipients (KTR), comprising 30 cases with and 49 controls without graft failure, enrolled in the TransplantLines Biobank and Cohort. Graft failure was defined as a return to hemodialysis or re-transplantation. Matching was performed on age, sex, eGFR, BMI, and post-transplant time. Proteomic data were measured at baseline alongside clinical parameters. A machine learning-based feature selection approach identified proteins associated with time-to-death-censored graft failure. We then performed forward selection of proteomic markers added iteratively to a clinical-only base model, including the mentioned variables, and proteinuria. Protein–protein interaction networks and DBSCAN were used to explore biological pathways and subcluster structures.

Results: Over a median 4.6-year follow-up, 30 KTRs (38%) experienced graft failure. Baseline age, eGFR, and post-transplant time were 49.5 ±14.3 years, 37.5 ±15.9 mL/min/1.73 m², and 2.6 [0.6–7.6] years, respectively. Feature selection identified 122 proteins, significantly enriched in complement activation, coagulation, and lipoprotein metabolism. In the proteomic-only model, beta-2 microglobulin and cystatin C showed strongest signals, both surrogates of kidney function. In forward selection (accounting for clinical variables at baseline), apolipoprotein C1 and apolipoprotein L1— key members of a 14-protein subnetwork enriched in lipoprotein metabolism—were identified as top candidates. Despite biological plausibility, these markers did not meaningfully improve predictive performance compared to the clinical-only model.

Conclusions: These proteomic analyses highlight important biological mechanisms potentially driving chronic graft injury. Larger studies with extended follow-up may clarify the role of these proteomic signatures in risk stratification and inform future mechanistic and therapeutic investigations.

EP_510 ALLOGRAFT STORAGE FLUID CONTAMINATION AND ITS EFFECTS ON LIVER TRANSPLANT: A SINGLE CENTER PROSPECTIVE STUDY

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Background: Microbial contamination of allograft storage fluid (ASF) may contribute to donor-derived infections in liver transplant (LT) recipients. In the absence of specific guidelines, the management and potential antimicrobial treatment of patients with contaminated ASF remain center-specific. Furthermore, implications of ASF contamination are not well understood.

Methods: This prospective, single-center longitudinal study included patients undergoing LT between 2021 and 2022. Routine ASF cultures were performed, alongside microbial analysis of surplus vascular allograft samples (e.g., portal vein and vena cava) when available. All samples were centralized in a reference microbiology laboratory and subjected to MALDI-TOF identification following plating on agar and enrichment broths, with an incubation period of five days.

Results: The study analyzed 210 LTs. The median recipient age was 59 years, and the median MELD-Na score at transplant was 15. Among these, 38 (18.1%) were urgent LTs, and 57 (27.1%) involved recipients with high infectious risks. The median donor age was 67 years, and 32 grafts (15.2%) were obtained from donations after cardiovascular determination of death (DCD). ASF contamination was identified in 198 cases (94.3%), with cultures positive for high-risk pathogens in 67 cases (31.9%). Of these, 9 patients (4.3%) developed infections attributable to ASF pathogens. No significant differences in ASF culture outcomes were observed between grafts retrieved from DCD and those from brain death donors (DBD). Recipients with ASF positive for high-risk pathogens experienced longer median ICU stays (4 vs. 3 days, p=0.012) and increased 90-day mortality (13% vs. 5%, p=0.031). However, rates of overall and infectious complications, as well as graft functional recovery, were comparable.

Conclusions: ASF contamination represents a potential risk factor for donor-derived infections in LT recipients, and the presence of high-risk pathogens is associated with increased peri-transplant mortality. These findings support the implementation of routine ASF microbial testing during transplantation. Notably, despite the greater technical complexity of the donation process, DCD allografts demonstrated ASF contamination rates comparable to those of DBD allografts.

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EP_511 REPEAT KIDNEY TRANSPLANTATION IN PEOPLE LIVING WITH HIV: A UK SINGLE CENTRE EXPERIENCE

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Background: Antiretroviral therapy (ART) has transformed the care of people living with Human Immunodeficiency Virus infection (PLWH). Kidney transplantation (KT) in the context of HIV is well established but few studies have reported outcomes of re-transplantation in HIV+ recipients and there are no published UK data that describe re-transplantation in PLWH. Thus, we sought to analyse outcomes at our centre for re-transplantation events in HIV+ kidney transplant recipients.

Methods: We identified all HIV+ and HIV- KT recipients of a second kidney allograft on a prospectively maintained KT database at our centre and analysed patient and graft survival using Kaplan-Meier methods. HIV+ and HIV- KT recipients were matched in a 1:2 ratio for age, ethnicity and transplant type (deceased or living donor, kidney only or simultaneous pancreas-kidney). In cases of death with a functioning graft, the follow-up period was censored at the date of death as functioning allograft.

Results: Of the 83 HIV+ KT recipients, 9 (median age 50 years, 67% male, 89% black ethnicity, median CD4 341 cells/mm^3) were re-transplanted. Seven patients received a deceased donor kidney, 1 patient received a living kidney and 1 underwent a simultaneous pancreas-kidney transplant. One-year patient survival was 100% in both groups. Three-year patient survival was 75% and 87.5% in the HIV + and HIV- groups respectively. HIV+ graft survival was 100% at 1 year and 71.4% at 3 years, whilst HIV- graft survival at 1 year and 3 years was 94% (Figure 1).

Conclusions: Preliminary experience suggests that patient and graft survival for re-transplantation are not majorly impacted by recipient HIV status. US studies suggest inferior outcomes in re-transplanted patients, and while this finding may not necessarily be translatable to UK practice given the population heterogeneity between the US and UK, further large-scale UK studies are necessary.

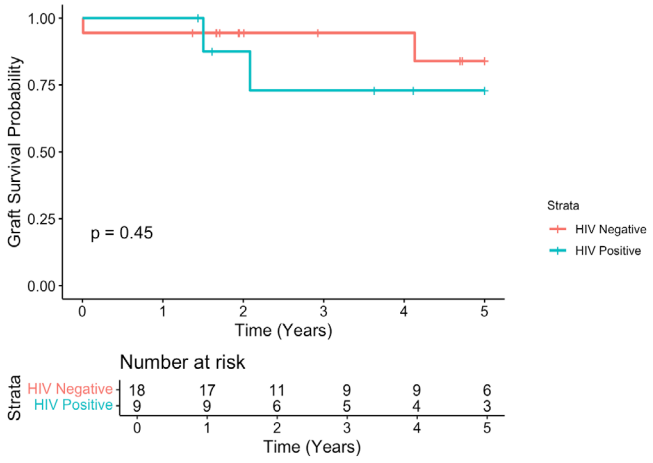

Figure 1: Kaplan-Meier of graft survival probability by recipient HIV status

EP_512 IMMUNOTHERAPY IN KIDNEY TRANSPLANT PATIENTS WITH CANCER: THE LATEST CHALLENGE

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Background: Cancer is one of the main causes of morbidity and mortality in kidney transplant (KT) patients. The use of immune checkpoint inhibitors (ICPIs) in these patients has been controversial because of the lack of robust evidence regarding their efficacy and safety. However, recent studies indicate that with and adequate management of the basal immunosuppression and a multidisciplinary approach in the follow-up of these patients, its use is feasible. Our study aims to describe our experience and results of using ICPIs in KT patients.

Methods: Prospective study of KT patients with cancer who have received treatment with ICPIs. Before starting ICPIs treatment, according to our protocol, mycophenolate acid was discontinued, tacrolimus levels were reduced (to 4-6ng/ml) and treatment with 5mg of prednisone was maintained. Epidemiological, clinical and analytical data were collected, as well as immunological complications related to ICPIs treatment.

Results: Were included 6 patients, 66% male, mean age 63 +/- 7 years. Cancer's origin: 16% cutaneous, 50% bowel, 34% lung. All patients were in an advanced stage of cancer and had not responded to other treatments. Median creatinine level at the start of treatment: 125 umol/L. Mean of baseline tacrolimus levels: 7.5 ng/ml. ICPIs used: 84% Pembrolizumab and 16% Atezolizumab. Mean follow-up time was 9 months. No episodes of rejection were observed. Any patient developed de novo DSA. 33% developed acute tubulointerstitial nephritis, which were treated with high doses of prednisone, resulting in a good response. Mean tacrolimus levels during treatment: 5.2 ng/ml. Median serum creatinine levels (at 1m, 3m, 6m after KT): 138 umol/L, 130 umol/L and 146umol/L, respectively. 100% of patients had a very good oncological response. Mortality rate: 0%. One patient started dyalisis 6 months after completing treatment, but he had poor renal function prior to the treatment.

Conclusions: Our results indicate that ICPIs can be appropriate treatments for KT patients with cancer, with acceptable complications on the renal allograft and very good oncological outcomes. Large studies are needed to confirm these results and optimize the management of immunosuppression in this context.

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EP_513 30-YEAR SURVIVAL AFTER PEDIATRIC AND ADULT LIVER TRANSPLANTATION

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Background: With the inaugural liver transplantation performed at our center in 1972, we report the first 30-year outcome data for pediatric and adult liver transplantation.

Methods: A retrospective single-center analysis was conducted on patients who underwent liver transplantation between 1972 and 1994 at Hannover Medical School.

Results: A total of 916 liver transplantations were performed on 770 patients (152 pediatric, 618 adult). The overall 10-, 20-, and 30-year survival rates were 41% (n=318), 28% (n=218), and 16% (n=127). Thirteen Percent of adult (n=80) and 31% (n=47) of pediatric transplantations survived more than 30 years post-transplantation. For adult transplantations, the mean donor age was 25 years, with a mean recipient age of 35 years, and a mean donor BMI of 22. The mean hospital stay was 53 days. Severe complications (Clavien-Dindo >3a) occurred in 39% of patients, with 34% requiring reoperation. Fourteen percent of patients underwent retransplantation during the initial hospital stay, while 9% received another transplant in the subsequent course. Sixty-seven percent of patients experienced rejection, with 71% of these rejection episodes occurring within the first 5 years post-transplantation. Twenty-three percent of patients developed malignancies during follow-up, predominantly those transplanted in adulthood. Among pediatric transplant recipients with complete follow-up, 59% had children, while one patient was unable to conceive due to infertility. Furthermore, 95% of these patients completed vocational training.Two-thirds of long-term survivors developed chronic renal insufficiency, with 11% receiving kidney transplants. Twenty-three patients died after a post-transplantation period exceeding 30 years, three (2%) due to graft-related pathologies.

Conclusions: In contrast to existing data on 10- and 20-year survival outcomes, graft-related mortality diminishes after 30 years of survival post-transplantation.

EP_514 THE EFFECT OF EXERCISE AND NUTRITIONAL CARE DURING THE IN-HOSPITAL PHASE IN SINGLE ORGAN TRANSPLANT RECIPIENTS

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Background: In 2023, a total of 1,429 transplants were performed in the Netherlands. Organ transplantation is an invasive, high-risk procedure with significant costs. There is increasing focus on improving physical capacity and lifestyle to enhance transplant outcomes. Several studies have demonstrated the positive effects of (pre)habilitation on transplant outcomes. However, research focusing on paramedical care during the in-hospital phase and its impact remains limited. To improve our understanding of paramedical care during the in-hospital phase, we are working to optimize our paramedical care pathways across the continuum of care. As part of this initiative, we aim to conduct a systematic review of all published studies examining the impact of paramedical care during the hospital phase of solid organ recipients.

Methods: We will search databases for studies up to 08 May 2024. Four reviewers independently assess full text for inclusion based on predetermined in- and exclusion criteria. We will include studies of any study design that investigate physical therapy and/or dietary care during the in-hospital phase after single organ transplantation. Independent reviewers will extract clinical outcomes. as well as outcomes related to the exercise intervention and nutritional status. We plan to do a quantitative meta-analysis when there are three or more studies of sufficient homogeneity. When meta-analysis is not possible, best-evidence (i.e., narrative) synthesis will be undertaken.

Results: A total of 4672 papers were identified by the bibliographic search. We will assess the risk of bias of the randomized controlled trials (RCTs) with the Risk of Bias tool 2 (RoB 2) and non-randomized studies of interventions using the Risk Of Bias In Non-Randomized Studies –of Interventions (ROBINS-I). We will rate the certainty of evidence with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Conclusions: The review will focus on factors that may influence the provision of care and the clinical reasoning process, ensuring that care teams are well-informed. By addressing these critical elements, we aim to support healthcare providers in delivering optimal, patient-centered care throughout the transplant journey and improve their quality of life.

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EP_515 LIVER TRANSPLANTATION FOR HDV/HBV CONFECTION IN ITALY: AN INTENTION-TO-TREAT ANALYSIS OF LONG-TERM OUTCOMES

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Background: Patients with HDV/HBV-related end-stage liver disease candidates for liver transplantation (LT) have traditionally been regarded as a special population, as HDV infection is considered the most severe form of chronic viral hepatitis. However, outcomes of HDV/HBV coinfected LT recipients are controversial.

Methods: A nation-wide study analyzed, with an intention-to-treat(ITT) approach, the long-term outcomes of HDV/HBV-coinfected patients waitlisted for LT in Italy, between 2011-2020, compared to HBV-monoinfected LT candidates, and investigated the strategies adopted to prevent disease recurrence.

Results: Out of 1,731 HBV-infected LT candidates, 1,237 (71.5%) had HBV-monoinfection and 494 (28.5%) HDV/HBV-coinfection. At listing, HDV/HBV-coinfected patients were significantly younger, listed mainly for decompensated cirrhosis, and with less hepatocellular carcinoma (HCC:26% vs 65.8%, *P*<0.0001) compared to HBV-monoinfected patients. HDV/HBV-coinfected patients were transplanted earlier and showed better 5-year ITT-survival (83.2%, 95%CI:79.4–83.4%) than HBV-monoinfected patients (71.6%, 95%CI:68.8-74.2%; *P*<0.0001). ITT-multivariable analysis identified the presence of HCC, advanced recipient age, and high-MELD-Na scores as mortality risk factors. Five-years after LT, 99.1% of patients received oral nucleos(t)ide analogues [entecavir (n=250, 60.4%), tenofovir dipivoxyl (n=108, 26.1%) and lamivudine (n=52, 12.6%)]. At last follow-up, immunoglobulins against HBsAg (HBIg) were administrated in 91.8% of cases, while 8.2% had suspended HBIg treatment. In the HDV/HBV-coinfected group, HBV and HDV viral recurrences were 1.1% and 0.2%, respectively (none of patients who ceased HBIg after LT), whereas recurrent or *de novo* HCC were 8.9% and 0.3%, respectively.

Conclusions: In Italy, HDV/HBV-coinfected patients waitlisted for LT showed more favorable outcomes compared to HBV-monoinfected patients, both before and after LT. Viral recurrence was rare in the HDV/HBV cohort, and there were few cases of recurrent or *de novo* HCC. These excellent results, derived from the largest cohort reported so far, suggest that HDV/HBV-coinfected LT recipients don't represent a risky population and may be considered for simpler long-term antiviral prophylactic strategies.

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EP_516 EARLY MULTIDISCIPLINARY FOLLOW-UP IN HEART TRANSPLANT PATIENTS: A 12-MONTH ANALYSIS OF THE CURE-AT-HOME PROJECT

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Background: International guidelines recommend multidisciplinary follow-up for heart transplant (HT) patients. However, the benefits of early implementation remain unclear. Center-based approaches often prove challenging during outpatient follow-up, suggesting home-based alternatives as a potential solution. Our center has implemented a multidisciplinary outpatient follow-up program in conjunction with a personalized mobile application (CURE-AT-HOME project). This study aims to analyze the outcomes of patients enrolled in the CURE-AT-HOME project who completed the 12-month follow-up period.

Methods: We included patients who had fully completed the 12-month CURE-AT-HOME project. Patient outcomes, including clinical parameters, metabolic profile, bioelectrical impedance analysis, cardiopulmonary exercise testing, and hand-grip strength tests (dominant and non-dominant upper limb, DL and NDL respectively) were performed at baseline (T0), 6 months (T6), and 12 months (T12) of the program. Student's t-test analysis was conducted to correlate variables between different timepoints: T0 vs T6, T6 vs T12, and T0 vs T12.

Results: From January 2023 to December 2024, 40 patients were enrolled. Of these, 14 (35%) completed all the assessments scheduled in the 12-month program and represent the study population. The mean age was 51 years, and 9 were men (64.3%). There was an optimization of hemoglobin values (T0vsT6 p=0.04, T6vsT12 p=0.85, T0vsT12 p=0.08). A reduction in resting heart rate was observed (T0vsT6 p=0.005; T6vsT12 p=0.08, T0vsT12 p=0.001), along with an increase in maximum exercise heart rate (T0vsT6 p=0.0006, T6vsT12 p=0.015, T0vsT12 p=0.0001). There was an increase in peakVO2 consumption (T0vsT6 p=0.002, T6vsT12 p=0.074, T0vsT12 p=0.003) and strength in both limbs (DL T0vsT6 p=0.0022, T6vsT12 p=0.02, T0vsT12 p=0.0001, NDL T0vsT6 p=0.0066, T6vsT12 p=0.03, T0vsT12 p=0.0006). A normalization of the phase angle was noted (T0 5.9 0.6, T6=6.18 0.81), with a reduction in extracellular water (T0vsT6 p=0.0004).

Conclusions: The 12-month results of the CURE-AT-HOME project demonstrated improvements in metabolic profile, strength, and functional capacity for HT recipients.

EP_517 NOCARDIA AND RENAL TRANSPLANTS IN CATALONIA: A MULTICENTRIC REVIEW OF ANTIBIOTIC TOLERANCE

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Background: Nocardiosis is one of the opportunistic infections characteristics of transplant patients. The first-line treatment is trimethoprim-sulfamethoxazole (TMP/SMX) at high-dose and long-duration. However, this drug carries a risk of nephrological side effects.

Methods: A retrospective multicenter study was performed in the six kidney transplant units in our region. All KT diagnosed with nocardiosis in the last 15 years were included.

Results: Among KT patients in the six RTUs (1000 transplants per year in total), 26 cases of nocardia infection were diagnosed. Characteristics are detailed in Table 1. Duration of treatment: 8 months [5.25–11.5]. 68% of patients received combined treatment with carbapenems/cephalosporins plus a specific antibiotic: TMP/SMX was administered to 20 patients (76.92%). Treatment was discontinued or dose reduced in 80% (16 patients) due to adverse effects, predominantly nephrotoxicity (renal failure, metabolic acidosis or hyperkalemia). Only 3 completed the therapy without dose adjustments. Linezolid was used in 11 patients (42.3%), discontinued in 90% (10 patients) due to myelotoxicity. Tedizolid was administered to 10 patients (38.46%), in 4 of them (15.38%) as a first-line therapy. Two patients (20%) discontinued treatment due to myelotoxicity.

Conclusions: Common treatments are poorly tolerated: 80% of patients receiving TMP/SMX experienced renal adverse effects, and 90% of those treated with linezolid developed myelotoxicity. Tedizolid is the best-tolerated drug so far, 20% rate of myelotoxicity.

BASELINE CHARACTERISTICS	n = 26
Patient characteristics	
Age, years (median [Q1-Q3])	75 [66.4-19.12]
Gender, male (%)	69%
Transplant characteristics	
Cadaveric Donor (%)	100%
Induction immunosuppression – Antithymocyte globulin (%)	 73%
Maintenance immunosuppression – Prednisone, CNI, MPA	 84.62%
Infection characteristics	
Time after transplant, mo (median [Q1-Q3]) – Infection during the first year after KT (%)	19.83 [8.43-46.3.] 36%
Kidney function – Creatinine, µmol/L (median [Q1-Q3])	 167 [131.5-259]
Clinical presentation: – Respiratory (%) – Musculo- skeletal (%) Fever, yes (%)	 65.38% 15.38% 26.92%
Mortality – Due to nocardiosis (%) – During the hospital admission (%) – During the treatment (%) – After ending the treatment (%)	 3.85% 7.69% 15.38% 34.61%

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EP_518 A DECADE ON: EXPERIENCE AND OUTCOMES IN HIV POSITIVE TO POSITIVE DECEASED DONOR TRANSPLANTATION

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Background: Transplantation remains the standard of care for people with HIV and end stage kidney disease (ESKD), conferring significant survival benefit in comparison to remaining on dialysis. There is a paucity of data regarding long term outcomes for HIV+ recipients receiving organs from a HIV+ donor. Almost a decade following the UK's first HIV positive to positive (HIV +/+) kidney transplant, we sought to analyse patient and graft outcomes in our HIV +/+ cohort.

Methods: We identified all HIV+ kidney transplant (KT) recipients on a prospectively maintained KT database at our centre and analysed patient and graft survival using Kaplan-Meier methods. HIV +/+ and HIV -/+ recipients were matched in a 1:2 ratio for age and ethnicity. In cases of death with a functioning graft, the follow-up period was censored at the date of death as functioning allograft.

Results: Of the 83 HIV+ KT recipients, a total of seven recipients (mean age 55 years, 57% male) received a KT from a HIV+ donor. Recipient characteristics are shown in Table 1. Patient survival at 1-year, 3-years, and 5-years in HIV +/+ recipients was 100%, 85.7% and 71.4% respectively and 100%, 92.9% and 84.6% respectively in HIV -/+ recipients. Graft survival for HIV +/+ recipients at 1-year, 3-years, and 5-years was 100%, 85.7% and 71.4% respectively (Figure 1). No recipients in the HIV +/+ group developed HIV superinfection.

Conclusions: There remains a disparity between organ supply and demand. Survival for people with HIV has improved dramatically since the advent of antiretroviral treatment and thus a need to maximise access to transplantation is paramount. Preliminary results suggest that outcomes are not majorly impacted by donor HIV status. This study, while limited in scope, provides an impetus to extend our analyses to include national data in order to inform selection of recipients for HIV+ organs and to determine whether such organs can be offered universally to all HIV+ recipients.

Characteristic	HIV +/+ (n=7)	HIV -/+ (n=14)
Age	54.8 ± 5.8	49.6 ± 10.2
Male (%)	57.10%	64.20%
Mean recipient CD4 count (cells/mm^3)	360	471
Donor age	49.5 ± 11.5	43.0 ± 12.6
Graft Number	1 (n=5), 2 (n=2)	1 (n=14)
Graft cold ischaemia time (mean, hours)	17	15

Table 1: Demographics and Characteristics

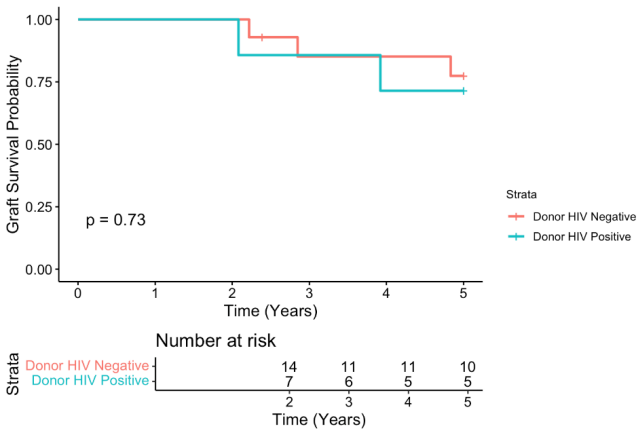

Figure 1: Graft survival probability in HIV+/+ vs HIV -/+ recipients

EP_519 THE LONG-TERM JOURNEY OF LIVER TRANSPLANT RECIPIENTS WHO TRANSITIONED TO ADULTHOOD

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Background: Pediatric liver transplantation (pLT) offers excellent survival rates, enabling many patients to reach adulthood and transition to the adult healthcare service (AHS). AIM.To describe the short- and long-term outcomes of patients who underwent pLT at Padua University Hospital, focusing on the achievement of ideal outcome after transitioning to AHS.

Methods: All patients who underwent pLT between 1993 and 2022 were included. Short-term (i.e., 6 months) and long-term (i.e., ≥20 years) outcomes were assessed. For those who transitioned to AHS, the rate of achieving an ideal outcome—defined as a combination of perfect graft function, no immunosuppression side effects, and no late reLT—was evaluated.

Results: 197 pLTs were performed in 167 children (90 males [53.8%], median age at transplant 4 years). Among 30 re-LTs (15.2%), 21 (10.6%) were performed urgently. Biliary atresia was the most common underlying condition (31%), while oncological indications accounted for 16%cases. Patient and graft survival rates at 1, 5, 10, and 20 years were 87%, 84%, 80%, and 76%, and 76%, 75%, 70%, and 63%, respectively (Fig.1). Nineteen (11%) patients did not survive beyond 6 months after their first pLT, with the need for urgent re-LT identified as an independent predictor of survival in multivariate analysis (p = 0.05). Among 27 patients who, at the time of analysis, had survived ≥20 years after pLT, all but one were still receiving immunosuppression; 7(26%) developed at least one major medical complication, 1(3.7%) underwent re-LT due to chronic rejection, and 1(3.7%) died of sepsis. Of the 48 patients who transitioned to AHS, an ideal outcome was achieved in 47%, 44%, and 45% of patients at 12, 36, and 60 months after transition, respectively.

Conclusions: Medical complications, whether related or unrelated to the graft, during the long-term follow-up of patients undergoing pLT significantly impact global health and the achievement of an ideal outcome.

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EP_520 MYCOPHENOLATE MOFETIL IS NOT ASSOCIATED WITH RISK OF BK NEPHROPATHY IN PATIENTS RECEIVING ALEMTUZUMAB INDUCTION

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Background: The 3C study reported higher rates of BK Nephropathy (BKN) in patients receiving Alemtuzumab compared with Basiliximab induction when maintained on tacrolimus (FK) and mycophenolate mofetil (MMF) immunosuppression. Whether the use of FK monotherapy post-Alemtuzumab reduces the risk of BKN is not known. This study aims to investigate the incidence and outcomes of BKN following Alemtuzumab induction in patients receiving maintenance with FK+MMF compared with FK monotherapy.

Methods: In a retrospective single centre study, we investigated 693 consecutive kidney transplant recipients. All patients received Alemtuzumab and tacrolimus, with patients with a CRF≥85% being maintained on MMF in addition. MMF was also added to treatment in FK patients who develop DSA or rejection. All BKN was histologically confirmed.

Results: Overall, 45 (6.5%) patients had BKN which was confirmed after a median follow up of 2.7 (1.5-3.7) years. Patient characteristics by BKN diagnosis is shown in Table 1. The 1-yr BKN free survival was 95.0%. BKN free survival was no different in the FK+MMF versus the FK group, p=0.53, with 8 (6.9%) FK+MMF and 37 (5.4%) FK patients having BKN confirmed. There was no difference in death censored allograft survival following BKN between the cohorts, p=0.41. Overall BKN was more common in patients with either rejection and/or DSA. 18 (40.0%) and 16 (35.6%) BKN patients had either rejection and/or DSA respectively, compared with 106 (16.4%) and 77 (11.9%) without BKN, p<0.01. In the FK group, 11/37 (29.7%) developed BKN after rejection, whilst 7 (28.9%) experienced rejection following BKN. In the FK+MMF group, 2 developed BKN before and 2 after rejection.

Conclusions: Incidence of BKN is not higher in patients receiving FK+MMF compared with FK monotherapy following Alemtuzumab. Stratification of MMF use to prevent adverse alloimmune outcomes in these patients should remain the priority over concerns of BKN at the time of transplant.

Table 1. Clinical characteristics

		No BK N=648 (%)	BK N=45 (%)	P value
Age (years)		56 (46-65)	56 (48-64)	0.37
Male		392 (60.5)	31 (68.9)	0.26
Caucasian		191 (29.5)	9 (20.0)	0.18
Pre-emptive		98 (15.1)	9 (20.0)	0.38
Diabetes		246 (38.0)	16 (25.6)	0.75
Donor Type	DD LD SPK	517 (79.8) 118 (18.2) 13 (2.0)	34 (75.6) 9 (20.0) 2 (4.4)	0.52
Primary Allograft		577 (89.0)	39 (86.7)	0.62
ABDR Mismatch		4 (3-5)	4 (3-5)	0.025
cRF%		0 (0-54)	13 (0-59)	0.47
MMF-FK group		108 (16.7)	8 (17.8)	0.85

EP_521 ZOONOSES, EMERGING VIRAL INFECTIONS: SURVEILLANCE AND IMPACT ON THE TRANSPLANTATION SYSTEM

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Background: WHO estimates that more than 60% of human pathogens are zoonotic, accounting for 75% of all emerging pathogens in the last decade. Given the close relationship between human, animal and environmental health ('One Health'), human activities and climate change influence the transmission and spread of diseases. Arboviral diseases are zoonoses caused by viruses transmitted through the bite of arthropod vectors such as mosquitoes, ticks and phlebotomus; Italy is currently considered an endemic area for West-Nile-Virus (WNV) Toscana Virus and Tick-Borne-Encephalitis, but in recent years there have been increasing reports of human cases of Arbovirosis. Several cases of donor to recipient transmission in the transfusion, solid organs, tissues and cells sectors have been described

Methods: The national authority responsible for transplantation has a surveillance role based on an integrated model involving a close collaboration between the surveillance systems of the National Health Authorities for human and animal health; this model enables rapid and effective communication of informations and actions to be taken. The activity involves the support of infectious disease experts and is based on the introduction of prevention measures modulated on the basis of epidemiological trends, the type of biological substance used, their specificity and their use

Results: In 2024 there were 460 human cases of WNV, 693 cases of Dengue of which 213 were autochthonous, 7 and 15 imported cases of Zika and Chikungunya. No donor to recipient transmission reported

Conclusions: Prevention of transmission through blood, organs, tissues and cells contributes to patient safety. Future scenarios will see an exponential increase in new viruses and the transplantation network will necessarily have to implement training programmes dedicated to increasing the expertise of operators, in order to maintain high quality and safety standards

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EP_522 RISK OF END STAGE RENAL DISEASE AFTER LIVER TRANSPLANT IN A CONTEMPORARY COHORT

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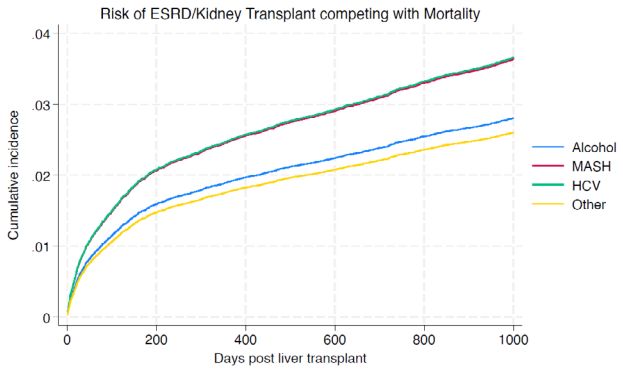
Background: Since the introduction of MELD-based liver allocation in the US in 2002, the proportion of liver transplant candidates with pre-existing CKD has increased, as has the overall comorbidity burden of liver transplant candidates. Data regarding end-stage renal disease (ESRD) rates among liver transplant recipients in the post-MELD era is lacking.

Methods: We utilized data from the Scientific Registry of Transplant Recipients, which includes all solid organ transplants performed in the US, linked to the United States Renal Data Systems, which collects data on patients administered chronic dialysis within the US, using 5 identifiers (social security number, first and last name, date of birth and sex). Descriptive statistics were generated, comparing those who developed ESRD (defined as chronic dialysis or kidney transplantation) with those who did not. We constructed multivariable cox models for mortality as well as ESRD. We also performed analyses for time to ESRD where death was considered a competing risk.

Results: We identified 126,440 adult liver transplant alone recipients transplanted 2/28/2002-12/31/23 with a median follow up time of 1491 days (IQR 398-3263 days); multi-organ transplant recipients were excluded. Overall, 5.7% of liver transplant recipients developed ESRD. In univariable analyses, male sex, Black race, pretransplant diabetes, hypertension, hepatitis B or C, and liver disease due to metabolic associated steatohepatitis (MASH) were all associated with ESRD. In our competing risk analyses we found that the risk of ESRD after liver transplantation was elevated in patients with MASH (SHR 1.30, 95% CI 1.17-1.49) and hepatitis C (HCV) (SHR 1.31, 95% CI 1.21-1.42) as shown in Figure 1. Index immunosuppression with tacrolimus-based regimens was protective (SHR 0.87, 95% CI 0.78-0.97) whereas rapamycin increased ESRD risk (SHR 1.35, 95% CI 1.15-1.58).

Conclusions: The risk of kidney failure after liver transplantation in the contemporary post-MELD era remains elevated, even when accounting for the increased of risk death that liver transplant recipients with multiple comorbidities face. Tacrolimus-based immunosuppressive regimens are associated with decreased ESRD risk after liver transplantation.



EP_523 RENAL ALLOGRAFT OUTCOMES IN RECURRENT MEMBRANOUS NEPHROPATHY: A SINGLE CENTRE EXPERIENCE

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Background: Membranous nephropathy (MN) may recur after kidney transplantation, but its impact on graft survival is unclear. This study aimed to determine frequency of MN recurrence and explore its impact on patient and graft outcomes.

Methods: We undertook a retrospective observational study of patients with MN who underwent kidney transplantation, or who developed MN post-transplant, at a single centre between 1978 and 2022. We determined MN recurrence rate and analysed graft and patient survival stratified by the development of MN post-transplant.

Results: 43 patients were included, median age at transplant 48 (IQR 34-57.5) years and 33 (76%) males. 38 patients had known MN (33 idiopathic and 5 secondary MN), and 5 patients developed de novo MN. 54 kidney transplants (53 kidney alone, and 1 combined liver- kidney) were identified, with 10 patients having more than one transplant. 34 (63%) transplants were from deceased donors and 6 (14%) were pre-emptive. Antibody to phospholipase A2 receptor (anti-PLA2R) was positive (?2RU/ml) in 10 (26.3%) patients and negative (<2RU/ml) in 10 (26.3%) patients at the time of transplant, while results were unavailable in 18 (47.4%) cases. MN recurred in 11 (29%) patients over a median follow-up of 10.3 (IQR 5.4-17.25) years. The median time to recurrence was 36 months. MN recurrence presented with median serum creatinine 185?mol/l, urine protein:creatinine ratio 444.5 mg/mmol, and median anti-PLA2R level of 20 RU/ml. Recurrence occurred in 7 (70%) patients who were anti-PLA2R positive at the time of transplant and no patients who were negative (p=0.0031). 5 (45.5%) patients with recurrence were treated with rituximab and 6 (54.5%) patients were managed conservatively. 13 patients died, and 21 graft failures occurred. There were no differences in patient or allograft outcomes between patients with and without MN recurrence (**Figure**).

Conclusions: MN recurred in 29% of cases, and there was more recurrence if anti-PLA2R was positive at the time of transplantation. The development of MN post-transplant had no impact on patient or allograft survival in this small single centre cohort.

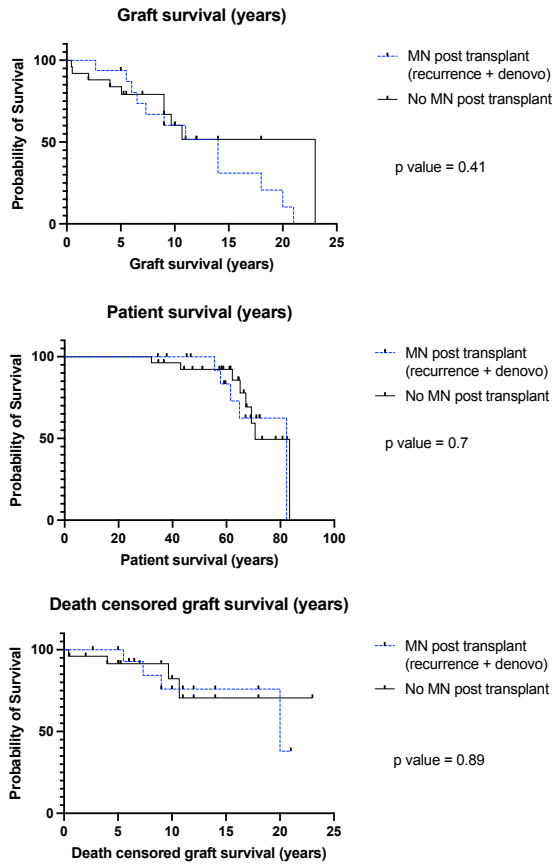

Figure: Patients and allograft outcomes after kidney transplant stratified by MN recurrence.

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EP_524 TEN YEARS AND BEYOND: SINGLE CENTER STUDY ASSESSING LONG-TERM SURVIVAL AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is the gold standard for end-stage liver disease. Advances in surgical techniques, postoperative care, and pharmaceuticals have improved outcomes in recent decades. However, long-term post-LT outcomes, particularly beyond 10 years, are poorly documented. This study aims to describe long-term post-LT survival and identify associated factors.

Methods: We conducted a retrospective study of patients who underwent liver transplantation at our center between January 2002 and June 2015. We analyzed recipient (age, hepatitis C virus positivity, hepatocellular carcinoma) and donor (age) characteristics. Long-term patient and graft survival were compared using the Kaplan-Meier method.

Results: We included 558 patients with a mean follow-up of 12±6 years. At follow-up, patient and graft survival rates were 78% and 70%, respectively. Infections were the leading cause of death (28.5%, 35 cases), followed by tumors (22%, 27 cases, including 14 with de novo neoplasms and 13 with primary tumor recurrence), and cerebrovascular or cardiovascular events (14%, 17 cases). Nine recipients (7%) died from hepatitis C virus (HCV) relapse, but patients with HCV-related cirrhosis (177 cases, 31.7%) had similar long-term survival (p=0.233). In contrast, hepatocellular carcinoma (HCC) patients (113 cases, 20%) had lower survival (70% vs. 80%, p=0.029). Donor age alone did not significantly affect survival (p=0.089 for patient survival, p=0.272 for graft survival), but the combined age of donor and recipient (>100 years) negatively impacted both graft (p=0.023) and patient survival (p=0.040). Recipient age >50 years (360 cases, 64%) was linked to lower patient survival (p=0.011), though this effect was not significant for those >60 years (p=0.876).

Conclusions: Our results show excellent long-term survival after LT. Despite the pre-direct-acting antivirals era, HCV positivity did not adversely affect long-term survival, unlike HCC. Donor age alone did not impact outcomes, even without graft reconditioning. However, the combined advanced age of donor and recipient is a detrimental factor. A strict selection of recipients >60 years, especially considering comorbidities, could improve long-term outcomes compared to recipients aged 50-59 years.

EP_525 INCIDENTAL MLIGNANCY IN LIVER RESECTION SPECIMENS AFTER TRANSPLANTATION: A GREEK CENTER'S EXPERIENCE

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Background: Orthotopic liver transplantation (OLT) is the only curative treatment for patients with end-stage cirrhosis, a major risk factor for the development of liver cancer. The objective of this study was to assess the frequency of incidental neoplastic findings in the histopathological examination of hepatectomy specimens from patients undergoing OLT.

Methods: Data from a prospectively maintained database, spanning from 2018 to the present, were analyzed. Histological examinations of hepatectomy specimens were reviewed, and unexpected findings were documented. The initial surgical indication was also evaluated. All patients with malignant findings in their histology reports were cross-checked with their clinical files to confirm that these findings were not previously known.

Results: Pathology reports from 80 patients (58 males, 22 females) were reviewed. The patients' ages ranged from 20 to 69 years (median 56.5 years). In 6 cases, the underlying cause of cirrhosis was revised. In 9 cases (11.25%), previously undetected malignancies were found, including hepatocellular carcinoma (HCC) (66,67%), intrahepatic cholangiocarcinoma (11.11%), combined cholangiocarcinoma and HCC (11.11%), and mixed hepatocellular-cholangiocarcinoma (11.11%). The most common underlying liver disease was alcohol-related cirrhosis (27,5%). The median interval between the last preoperative imaging and the transplantation was 72 days (range: 53-315 days).

Conclusions: The incidence of unexpected malignancies in explanted liver specimens was 11.25%, aligning with published data. Despite regular imaging surveillance of patients on the OLT waiting list, a significant proportion of liver cancers are only identified postoperatively.

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EP_527 POLYOMAVIRUS BK NEPHROPATHY, 10-YEAR OUTCOME OF BOLOGNA TRANSPLANTATION CENTER

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Background: BK polyomavirus (BKPyV) is a small DNA virus, a member of the Polyomaviridae family. It infects renal tubular and uro epithelial cells, resulting in a mostly asymptomatic and quiescent infection in most of the population. However, in kidney transplant recipients, BKPyV can reactivate and result (5 to 10% of cases) in a nephropathy pattern associated with risk of dysfunction and transplant loss5. The focus of this study was to examine long-term clinical outcomes (10 years) of kidney transplant patients who had developed BKPyV infection (> 10,000 copies/ml) after transplantation.

Methods: The study represents a retrospective analysis conducted on a cohort (No. 57) of kidney transplantation patients from the Bologna Transplantation Center who had developed BKPyV infection in the decade from 2014 to 2024, with an overall follow-up of 10 years.

Results: We observed: 1) high overall patients survival (100% of patients); 2) good transplant survival (one case of graft failure). During the follow-up period, 11 patients (19.3%) developed DSA (only one within two months of infection); of these, 9 patients (15.8%) also achieved clearance of plasma BKPyV-DNAemia, while 2 patients (3.5%) had persistent plasma BKPyV-DNAemia despite of the reduction of immunosuppression. The most interesting result from our analysis is the worst renal function trend (estimated from creatinine values) in patients with persisting BKPyV-DNAemia or patients with BKPyV-DNAemia loads persisting >1000 copies/mL (Figure 1). However, our result is not statistically significant due to the small sample size (only 57 patients).

Conclusions: In conclusion, BKPyV nephropathy represents a complex clinical challenge; further studies are needed to elucidate pathogenetic mechanisms and develop new diagnostic and therapeutic strategies that can improve prognosis.

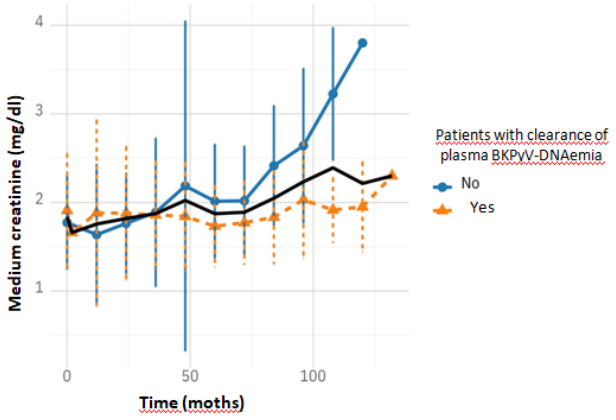

Figure 1

EP_528 CLINICAL PRESENTATION AND PROLONGED VIRAL PERSISTANCE OF DENGUE IN RENAL TRANSPLANTS RECIPIENTS

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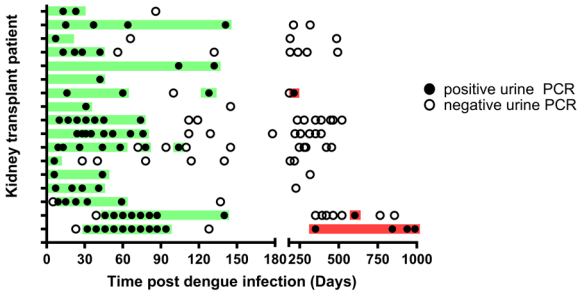
Background: Dengue is a mosquito-borne viral infection threatening approximately half of the global population. Its clinical presentation in immunocompromised patients, especially renal transplant recipients (RTRs), is poorly documented. Although the virus is typically cleared within 15 days, cases of persistent infection have been reported in RTRs. This study aims to characterize the clinical presentation and persistence of dengue in RTRs.

Methods: A retrospective cohort study was conducted on RTRs diagnosed with dengue using WHO 2009 diagnostic criteria, at the University Hospital of La Réunion between January 2019 and December 2022. A subset of patients underwent serological and virological follow-up.

Results: Thirty-seven patients were enrolled in the cohort. Diagnosis was confirmed by blood RT-PCR in 83.8% of cases or serology. 78% required hospitalization, and 11% developed severe dengue. Acute kidney injury (AKI) occurred in 54% of cases, most being transient. Two patients (10%) required dialysis. No death or persistent kidney failure was observed by the end of hospitalization. The mean duration of viremia was 12 days, with a maximum of 53 days. The mean duration of viruria was 90 days, with a maximum of 351 days. Three patients exhibited asymptomatic reactivation of urinary RT-PCR after several months, including one case after 600 days.

Conclusions: This study suggests that dengue in renal transplant recipients typically results in favorable outcomes, despite a high incidence of transient acute kidney injury. Although the virus is rapidly cleared from the bloodstream, shedding was prolonged in the urine, indicating that the kidney may serve as a potential viral sanctuary. Further research is needed to explore the clinical significance of viral persistence in this immunocompromised population

Urinary dengue PCR surveillance after infection in kidney transplant



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EP_529 EFFICACY AND SAFETY OF RAVULIZUMAB FOR THE MAINTENANCE OF AHUS REMISSION AFTER KIDNEY TRANSPLANT

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare thrombotic microangiopathy (TMA) triggered by complement dysregulation. Ravulizumab, a next generation complement inhibitor provides immediate and sustained complement C5 inhibition. The aim of this study was to assess clinical efficacy, safety and tolerability of ravulizumab in aHUS patients.

Methods: Patients with a clinical diagnosis of aHUS treated with eculizumab for at least three months were switched to ravulizumab. The first ravulizumab infusion was administered at least two weeks after the last eculizumab dose, followed by a second infusion two weeks later and subsequent doses every eight weeks.

Results: Four patients with end-stage renal disease due to aHUS had previously undergone kidney transplant. At the time of switching to ravulizumab, none required dialysis, and no new dialysis events occurred during treatment. Estimated glomerular filtration rate (eGFR), platelet count, lactate dehydrogenase (LDH), creatinine, haptoglobin and hemoglobin levels remained stable throughout the study. No clinical signs of TMA or adverse event (AE) relapses were reported. Genetic testing confirmed at least one aHUS associated variant in the complement system in all patients. No meningococcal infections were reported during the study.

Conclusions: Long-term treatment with ravulizumab proved to be well tolerated and associated with sustained hematologic and renal parameters, and improved quality of life. Furthermore, the close attention to vaccinations status and preventive antibiotic therapy ensured no meningococcal infections during the treatment. Decision which patients required lifelong treatment involved consideration of a wide range of factors. Our study provides compelling evidence on the complexity of safety aspects of ravulizumab treatment.

Patient	Date of transplantation	Complement-related genetic mutations	Anti-complement factor H (CFH) antibody status	Duration of eculizumab treatment	Start of ravulizumab treatment	Final decision regarding treatment continuation
I 41, M	01/05/2023	*CFH C3 CD46*	Negative	1 year	10/06/2024	Continue treatment
II 42, W	28/04/2022	*CFH C3*	Negative	3 years	14/02/2024	Continue treatment; verification in future
III 49, W	24/09/2019	*CFH*	Negative	4 years	14/02/2024	Continue treatment; verification in future
IV 21, W	29/01/2019	*CFH*	Negative	6 years	02/05/2024	Continue treatment; verification in future

EP_530 MANAGING DRUG RESISTANT CYTOMEGALOVIRUS POST SIMULTANEOUS KIDNEY PANCREAS TRANSPLANT: A COMPLEX CASE

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Background: A 51-year-old male underwent DBD simultaneous kidney-pancreas (SPK) transplant with alemtuzumab induction, HLA mismatch 112, and cytomegalovirus (CMV) IgG status Donor positive/Recipient positive (D+/R+). He received 3 months oral valganciclovir (VGCV) chemoprophylaxis as per standard protocol. Discharged day 8 with primary graft function of both organs on standard immunosuppression (IS) – tacrolimus and mycophenolate (early switch to azathioprine at 3months due to diarrhoea). Six months post-transplant, he developed loss of appetite, diarrhoea despite azathioprine switch, and abdominal pain with CMV viral load (VL) 5.47 log10 IU/mL.

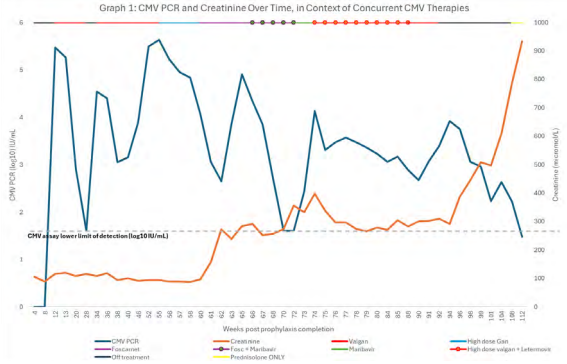
Methods: A stepwise review was conducted. The patient required multiple treatments over 20 months for complex CMV infection, alongside IS reduction (Table 1). Graph 1 illustrates the effect of various CMV treatments on renal function and CMV VL. Viral mutations conferring resistance to VGCV and ganciclovir (GCV) were detected. The case was further complicated by a significant decline in renal function during foscarnet treatment. Biopsy revealed T-cell-mediated rejection, treated with methylprednisolone and increased IS. The patient experienced severe foscarnet-related neuropathy. Further treatment changes to maribavir and then letermovir plus high-dose VGCV were used with no significant change to VL. No further treatment options available, and CMV treatment was weaned. He was maintained on dual IS of azathioprine and prednisolone for 3 months before azathioprine was stopped due to pancytopenia and persistent CMV VL.

Results: CMV treatments and IS minimisation negatively impacted renal function. The patient returned to haemodialysis 31 months after SPK transplant, with the pancreas transplant maintained on tacrolimus and prednisolone. The most recent CMV VL was undetectable at 38 months post-transplant.

Conclusions: This case highlights the challenges of managing drug-resistant CMV in transplant recipients. Despite various treatment options (VGCV, GCV, foscarnet, maribavir, and letermovir), the patient had persistent CMV viraemia and treatment-related complications, resulting in kidney graft loss. The patient is now being reassessed for a kidney after pancreas (SPK) transplant.

Table 1: Summary of Antiviral Treatments and Immunosuppression reduction:

Weeks post-transplant	CMV Treatment	Immunosuppression
0-12	Valganciclovir prophylaxis	
20		Tacrolimus + Azathioprine
24	Valganciclovir	Tacrolimus + reduced dose Azathioprine
25	Valganciclovir	Tacrolimus. Azathioprine stopped
44	OFF treatment	Tacrolimus. Azathioprine restarted
56	Valganciclovir	
68	High dose ganciclovir	Tacrolimus. Azathioprine stopped, prednisolone 5mg daily added
72	High dose foscarnet	
78	Foscarnet/Maribavir	Rejection: Methylprednisolone 3days 500mg IV +Tacrolimus+ Azathioprine + prednisolone
84	Maribavir	
86	High dose valganciclovir/letermovir	
92		Tacrolimus stopped. Azathioprine + prednisolone
100	High dose valganciclovir	
104	CMV treatment stopped	
120		Azathioprine stopped. Prednisolone monotherapy (10mg daily)
124	Renal Graft Failure (return to haemodialysis)	Pancreas graft functioning. Tacrolimus restarted at week 140 post transplant



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EP_531 INFLUENCE OF PRIOR CANCER ON OUTCOMES IN KIDNEY TRANSPLAN RECIPIENTS

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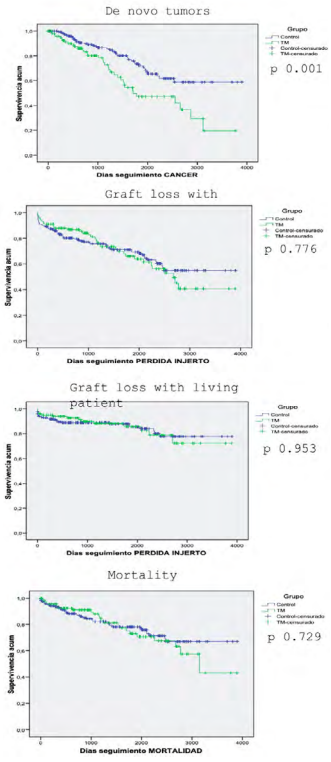
Background: The increased life expectancy of kidney disease patients has led to a growing number of individuals with cancer prior kidney transplantation (KT). Cancer has been identified as the leading cause of mortality among kidney transplant recipients (KTR). It is reasonable to anticipate that patients with cancer prior KT may experience poorer outcomes in terms of mortality, graft loss, and post-transplant tumors. Available data on this population remains limited. The objective is to determine whether KTR with a history of cancer prior to KT have higher rates of mortality, graft loss or the development of tumors comparing with those of recipients without a cancer history.

Methods: A retrospective observational study was conducted on a total population of 298 KTR between January 2014, and April 2024. The study group comprised 100 patients with a cancer prior to transplantation (C-KTR), while the control group included 198 patients without a history of cancer (nonC-KTR). Controls were matched based on similar baseline characteristics. Analyses were performed using SPSS software, with a 95% CI and a significance threshold of p<0.05.

Results: There were no differences in baseline characteristics except on mean age (66±9.9 in C-KTR Vs 64±9.8 in nonC-KTR). The median follow-up period was 43.8 [16.7-71.3] months. Of a total of 82 tumors, 42 occurred in nonC-KTR and 36 in C-KTR, indicating that C-KTR had more predisposition to have a new cancer compared with nonC-KTR (HR 2 (95% CI: 1.3–3.2; p=0.002). There were 97 cases of graft loss, 63 patients in nonC-KTR and 34 patients in C-KTR, without significant differences. The most common cause of graft loss was death with a functioning graft in both groups. During the follow-up period, 65 patients died, 42 in nonC-KTR and 23 in C-KTR, with no differences between groups. The leading cause of death in both groups was infection, but followed by cardiovascular causes in nonC-KTR and cancer-related causes in C-KTR

Conclusions: This study suggests that a history of cancer prior to KT is not associated with increased mortality or graft loss. However, it does indicate a higher incidence of de novo tumors and cancer-related mortality in this population. This study suggest the importance of a strengthen cancer surveillance and a modified immunosuppressive treatment in this group of patients



EP_532 SINGLE-CENTER STUDY OF CANCER MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS WITH LONG-TERM FOLLOW-UP

Miriam Baztan-Ilundain[1], Gabriel Buades-Lucas[2], Javier Lavilla-Royo[2], Jose Maria Mora-Gutiérrez[3], Laura Juliana Castañeda Infante[1], Loreto Fernandez-Lorente[2], Nuria Garcia-Fernandez[4], Ana Hurtado-Pamies[2], Catalina Ulloa[2], Paloma Leticia Martin Moreno[4]

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Background: Kidney graft survival has improved due to advances in immunosuppressive therapy. However, improving long-term survival of patients with functioning grafts remains a challenge due to high cancer mortality rate, among other causes.

Methods: A retrospective study was conducted including patients who underwent kidney transplantation during the period from 2005 to 2014. A total of 300 kidney transplants (292 patients) were analyzed. We studied causes of graft failure and all-cause mortality, and compared cancer mortality with other causes. The quantitative variables were assessed by student's t test, while categorical variables by Chi-square test. Data was analyzed with SPSS.

Results: The graft loss rate was 36.4%, of which 56.4% was due to death of the patient with a functioning graft. During the study period, there were 62 deaths (21.2%), with a quarter of these due to cancer (25.8%). Cancer mortality rate was greater than cardiovascular mortality (19.4%) (Figure 1). In the group of patients who died of cancer compared to other causes, the only statistically significant difference was the lower rate of treatment with calcineurin inhibitors (Table 1). The most common malignance found in our population was lung cancer (43.7%).

Conclusions: The main cause of graft loss in our population was patient death. This occurred in 25% of the cases due to oncological pathology. In our cohort, cancer mortality exceeds cardiovascular mortality, the main etiology being lung cancer. The reason for the lower rate of treatment with calcineurin inhibitors in the group of patients with malignancy at the time of death, is probably due to the switch to other immunosuppressants at diagnosis. This demonstrates the impact of cancer in kidney transplant units. Early detection protocols different from those used in the general population are necessary in order to prolong the survival of kidney transplant recipients.

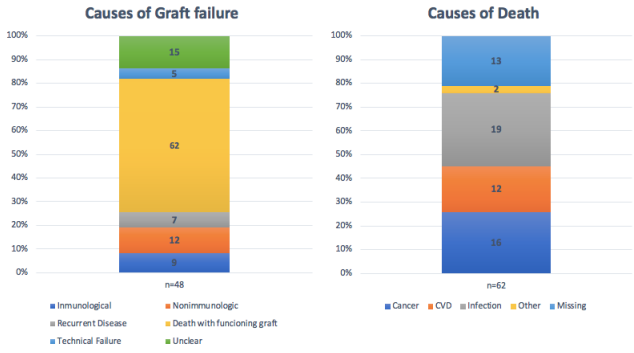

Figure 1. Causes of Graft Failure and causes of Death
Abbreviations: CVD, cardiovascular disease

Cause of death	Cancer n=16	Others n=46	p value
Recipient age			0.197
Mean ± SD	72 ± 9.6	69.9 ± 11.6	
Patient survival (months)			0.186
Mean ± SD	90.8 ± 47.1	111.4 ± 54.7	
Recipient sex			0.347
Male	13 (81.25%)	33 (71.4%)	
Female	3 (18.75%)	13 (28.6%)	
Smoker			0.515
Yes	10 (62.5%)	27 (58.7%)	
No	6 (37.5%)	19 (41.3%)	
Calcineurin inhibitors			0.001
Yes	8 (50%)	42 (91.3%)	
No	8 (50%)	4 (8.7%)	

Table 1. Demographic data of deceased patients due to cancer compared to other causes
Abbreviations: SD, standard deviation

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Infectious diseases, malignancies & long term challenges

EP_533 NUTRITIONAL STATUS INFLUENCE OVER EARLY POSTOPERATIVE INFECTION RISK IN KIDNEY TRANSPLANT

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Background: Kidney transplantation is considered the best renal replacement therapy (RRT). Malnutrition is one of the stronger predictors of morbidity and mortality in End-Stage Kidney disease patients. Moreover, nutritional status in hospitalized patients severely affects the clinical outcomes, increasing the risk of complications. The Nutritional Risk Index and Geriatric Nutritional Risk Index are indexes used to evaluate the risk of malnutrition in hospitalized adults, which have been validated for dialysis patients as prognostic indexes of nutrition-related morbidity and mortality. Infections remain a common complication of renal transplantation. Early post-transplant infections occur in the first month post-surgery and are typically health care-associated infections. The objective of this study was to evaluate the prevalence of early postoperative infections and its possible relationship with the nutritional status in renal transplantation.

Methods: A longitudinal retrospective study was conducted, including all patients who received a kidney transplant, a total of 140, between January 2020 to December 2023, at a tertiary-level hospital.

Results: 140 patients were included in this study, 53 females (37.9%) and 87 males (62.1%), with a mean age of 53± 15 years. The average GNRI was 110,1±11,6, equivalent to adequate nutrition, and only 16.4% patients were at risk of malnutrition. The mean NRI was 111,4±11,8 (no risk of malnutrition), and only 17.2% patients had moder-ate-to-severe risk of malnutrition. Thirty patients (21.4%) required oral nutritional supplementation at discharge, especially modular protein supplements (86.7%). 52 patients (37.1%) presented an infection during their stay. The most frequent infections were the urinary tract. Malnutrition calculated by GNRI or NRI correlated to a longer postoperative hospital stay and a higher rate of infectious complications ($p<0.05$), as well as, albumin, prealbumin, age, hyperimmunized status and hospital stay.

Conclusions: Malnourished patients have a higher risk of early postoperative complications, including infection and a longer hospitalization stay. The evaluation of nutritional status for the detection and treatment of malnutrition is strongly recommended in ESKD patients on the waiting list for a kidney transplant.

EP_534 POST-TRANSPLANT MALIGNANCIES IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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Background: Vascularized composite allotransplantation (VCA) restores complex defects when conventional reconstruction is not feasible. Lifelong immunosuppression is required to prevent allograft rejection increases the risk of post-transplant malignancies. This study evaluates the incidence of malignancies in VCA recipients, treatment strategies, and outcomes.

Methods: A systematic review following PRISMA 2020 guidelines included VCA patients who developed a subsequent malignancy. Data collected were VCA transplant details, malignancy characteristics, surveillance strategies, and treatment approaches.

Results: The review included 19 studies with 15 distinct VCA patients: six face, six upper extremity, one lower extremity, one scalp, and one abdominal wall. The cohort was predominantly male (73.3%), with a mean age of 48.7 years. A total of 18 malignancies were reported, the most common being post-transplant proliferative disorder (PTLD) with six (40%) patients, four (26.7%) with basal cell carcinoma, and four (26.7%) with squamous cell carcinoma. Less reported malignancies included cervical in situ carcinoma, gastric cancer, hepatocellular carcinoma, and Epstein-Barr Virus (EBV) associated smooth muscle tumors. Among recipients, one patient was cytomegalovirus (CMV) positive and two were EBV positive, while five donors were CMV positive and EBV positive. Aside from PTLD, most malignancies arose from non-allograft locations (91.7%) compared to their allograft. The mean time from transplant to malignancy diagnosis was 51.5 months. Malignancies were primarily detected by physical examination (55.6%) and radiologic imaging (33.3%). Treatment strategies ranged from surgical excision to chemotherapy and radiation. Of all patients, 40.0% achieved remission, while 33.3% succumbed to their malignancy.

Conclusion: Post-transplant malignancies in VCA recipients remain a significant challenge, with PTLD being the most common. Most malignancies arose at non-allograft sites and were diagnosed an average of four years post-transplant, emphasizing the need for comprehensive and long-term monitoring. Despite available treatment strategies, the substantial mortality rate highlights the need for surveillance protocols and balancing immunosuppression regimens to mitigate risks.

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EP_535 REDUCING UNNECESSARY URINE MCS TESTING IN CHRONIC RENAL TRANSPLANT RECEPIENTS WITH NEGATIVE URINE DIPSTICK

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Background: This study evaluated the cost-effectiveness and efficiency of reducing unnecessary urine microbial culture and sensitivity (MCS) testing in chronic kidney transplant recipients. It investigates the potential savings and workload reduction from avoiding MCS tests in patients with negative dipstick results, as current practice involves routine testing regardless of dipstick findings.

Methods: This retrospective study included 250 chronic renal transplant patients (more than three months post-transplant) at a single UK center. During a two-year period, 2,500 urine samples were collected from these patients across 10 routine clinic visits. Samples from patients on prophylactic antibiotics, those with indwelling urinary catheters, and those with incomplete data were excluded from the primary analysis. Samples were classified according to dipstick and culture results.

Results: Analysis of 2,137 urine samples revealed 1,079 instances of negative dipstick and culture results. This indicates that 1,079 MCS tests (54.46%) performed following negative dipstick results were likely unnecessary, incurring an estimated cost of £32,736 (at £30.34 per urine MCS test). Extrapolating this over two years suggests a potential cost saving of £65,247. Additionally, among the 94 patients (4.9%) with negative dipstick results who had positive culture results, only 9 (10%) required treatment, highlighting an additional opportunity for cost reduction through selective MCS testing. The 808 cases (40.7%) with negative dipsticks in which MCS was not performed align with appropriate clinical practice.

Conclusions: Urine dipstick shows a higher negative predictive value, indicating that routine MCS after negative dipstick results is inefficient, leading to significant avoidable NHS expenditure and increased workload. Implementing a protocol that limits MCS to clinically indicated cases (such as positive dipstick results or symptoms) could result in substantial cost savings and enhanced efficiency while maintaining quality patient care.

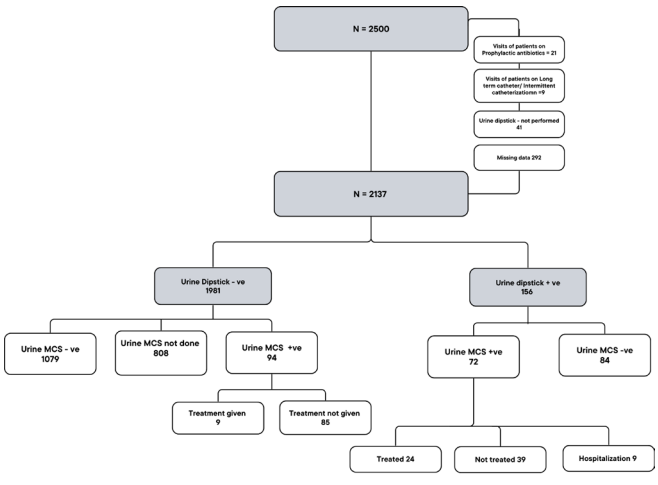

Fig 1: Analytical flow chart of clinic visit

EP_536 INFECTIONS IN KIDNEY AND RENAL-PANCREAS TRANSPLANT PATIENTS COLONIZED WITH ESBL ENTEROBACTERIA AND MRSA

Miriam Montero Estopiña[1], Valentina Blanco Fernández[2], Rosana Gelpi[3], Javier Paúl-Martinez[4], Omar Enrique Taco Sánchez[5], Mónica Bolufer-Cardona[6], Maria Molina[7], Laura Cañas[8], Jordi Bover[9], Jordi Ara[8], Anna Vila-Santandreu[4], Angela Casas[10]

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Background: Infections caused by multidrug resistant (MDR) bacteria represent a growing challenge for the public health, especially in immunocompromised patients, like solid organ transplant recipients. This study analyzes the incidence of colonization by methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales in kidney and kidney-pancreas transplant patients.

Methods: A cross-sectional and retrospective study was conducted at Germans Trias i Pujol University Hospital throughout 2023, evaluating 106 patients through nasal and rectal cultures performed on the day of transplantation and, assessing the development of infections in the following 6 months.

Results: According to the results, the colonization rate for ESBL was 3% and that of MRSA was 1%. During the follow-up period, no associated infections occurred in any of the colonized patients. The surgical antibiotic prophylaxis utilized at the center (cefazolin for kidney recipients or meropenem with vancomycin for kidney-pancreas recipients) may have contributed to reducing infection problems, even in immunocompromised individuals.

Conclusions: These results highlight the value of surveillance cultures in detecting MDR bacteria colonization, modifying strategies of prophylaxis, and preventing its spread within the hospital environment.

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EP_537 ROLE OF LAPAROSCOPIC MICROWAVE ABLATION BEFORE LIVER TRANSPLANTATION: INSIGHT FROM THE MOST EXTENSIVE WORLDWIDE SERIES

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Background: The role of laparoscopic microwave ablation (LMWA) as a specific treatment modality for patients with hepatocellular carcinoma (HCC) in the context of potential liver transplantation (LT) is still controversial. We sought to analyse the prognostic factors of patients with HCC undergoing LT after LMWA.

Methods: We retrospectively analysed the most extensive single-centre series of LMWA for HCC, focusing on patients receiving LT during the follow-up. Patients deemed ineligible for liver resection or percutaneous ablation were considered for LMWA. The clinical intent of the LMWA indication might be curative (one to three HCC nodules smaller than three cm in child A cirrhosis) or noncurative (beyond curative criteria, downstaging intent). Uni and multivariable survival analyses were performed.

Results: Between January 2014 and December 2023, 239 out of 1,371 HCC patients undergoing LMWA (17.1%) at our institution were transplanted, representing the study cohort. Among the enrolled patients, 55% were older than 60 years, 13% were female, 58% had viral cirrhosis, 32% had a MELD score greater than 10, 30% had nodules larger than 3 cm in diameter, 21% had more than three nodules, and 9% had an AFP value exceeding 100 ng/ml. LMWA was initially used with the aim of downstaging in 149 (62%), whilst 90 patients underwent salvage LT following curative-intent LMWA. Furthermore, 73 (31%) patients underwent more than one LMWA procedure, and 65% of them waited over 12 months before receiving LT. The one-, three-, and five-year survival rates were 96%, 88%, and 78% for patients receiving treatment with curative intent, while they were 99%, 90%, and 82% for those undergoing downstaging intent (p=0.40). Initial clinical intent, time before LT, and number of LMWA procedures were not associated with the post-LT outcome. Only initial high alpha-fetoprotein levels and impaired liver function were negative prognostic factors.

Conclusions: LMWA can be safely used before LT with a curative or a downstaging intent, assuring a high survival outcome.

EP_538 LIVER TRANSPLANTATION: A THERAPEUTIC OPTION FOR HEPATITIS B FLARE POST ONCO-HAEMATOLOGICAL TREATMENT

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Background: Liver transplantation (LT) is the curative treatment for acute and chronic hepatitis B virus (HBV) infections. However, LT indication becomes challenging when HBV flare arises following chemotherapy for onco-haematological diseases due to concerns about cancer recurrence. Limited outcome data make decision-making difficult. We evaluated LT outcomes for HBV flare in patients with recent history of onco-haematological diseases.

Methods: We reviewed cases between 2006 and 2024 to identify LT for HBV flare following chemotherapy for onco-haematological diseases. Data included cancer type, chemotherapy, HBV prophylaxis, donor and recipient characteristics, and post-LT outcomes. Range or incidences are given.

Results: Among 730 LT cases, 5 involved HBV flare following chemotherapy for non-Hodgkin (n=4/5) and Hodgkin lymphoma (n=1/5). Patients (aged 46–59y, 2/5 male) received rituximab-based regimens (n=4/5). One patient received tenofovir prophylaxis for known past HBV infection. HBV flare occurred 0-2 months after chemotherapy. All patients had positive HBV DNA and complete lymphoma response at the time of HBV flare. Antiviral treatment was unsuccessful in all cases. Three patients required ICU admission, and the model for end-stage liver disease score at LT ranged 29-40 points. All LT were performed from brain-dead donors aged 21–81y, with cold ischaemia times ranging 202-588min. Post-LT course was uneventful, with ICU stays of 0–10 days and hospitalization of 26–47 days. All patients received hepatitis B immunoglobulin and 3 received tenofovir post-transplant. Over a median 8yr of follow-up, no HBV recurrence occurred, and graft, patient and cancer recurrence-free survival rates were 100%.

Conclusions: LT is a viable life-saving option for patients experiencing HBV flare following recent onco-haematological disease with early complete remission. While our results demonstrate excellent mid-term patient and recurrence-free survival rates, validation of this therapeutic approach requires further evaluation through larger, multicentre studies with longer follow-up—especially given that these patients would otherwise face a poor prognosis.

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EP_539 HIGH-DOSE IVIG FOR MANAGING ADENOVIRUS INTERSTITIAL NEPHRITIS IN A PEDIATRIC KIDNEY TRANSPLANT: A CASE REPORT

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Background: Adenovirus is a prevalent viral infection associated with various complications in immunocompromised individuals, particularly kidney transplant recipients. Adenovirus nephritis can lead to significant morbidity, and its management remains controversial. This case report highlights the effective management of adenovirus interstitial nephritis in a pediatric kidney allograft recipient using high-dose intravenous immunoglobulin (IVIG).

Methods: We present a 15-year-old male kidney transplant recipient who developed adenovirus nephritis characterized by fever, hematuria, and rising creatinine levels. Initial evaluations revealed moderate hydronephrosis, and subsequent renal biopsy indicated acute T-cell mediated rejection with concurrent adenovirus infection confirmed through PCR and immunohistochemical staining.

Results: The patient was treated with high-dose IVIG (500 mg/kg/day for seven days) and reduction of immunosuppressive therapy. This approach resulted in a significant clinical improvement, with a decrease in creatinine levels and resolution of hematuria. Follow-up adenovirus PCR showed a reduction in viral load, indicating a favorable response to treatment.

Conclusions: This case underscores the potential efficacy of IVIG as a treatment for adenovirus nephritis in pediatric kidney transplant recipients. It highlights the importance of early recognition and tailored management strategies to improve outcomes in this vulnerable population. Further studies are warranted to establish standardized treatment protocols.

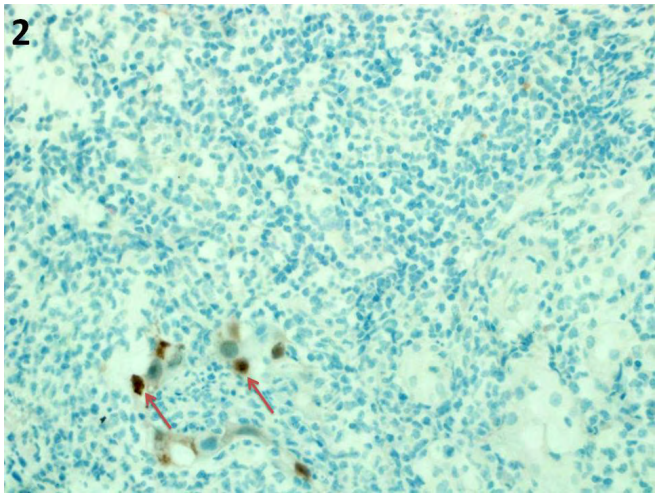

Figure 1: Immunohistochemical staining for adenovirus demonstrated nuclear positivity in the tubular epithelial cells (arrows) (x400).

EP_540 OUTCOMES OF HEART TRANSPLANTATION IN PATIENTS WITH CARDIAC SARCOMA

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Objective: The aim was to evaluate outcomes of heart transplantation (HTx) for cardiac sarcoma (CS).

Methods: From January 2010 to December 2024 HTx was performed in 276 patients and 3 (n=2 – male) of them due to CS without invasion into other organs and in the absence of data for metastasis. Their age was 42, 57 and 32-year-old, respectively. We analyzed retrospectively their outcomes, including complications and survival.

Results: Explanted heart histological results revealed myxofibrosarcoma of the heart was verified in 2 patients, hemangiopericytoma - in 1. Tacrolimus, mycophenolic acid, methylprednisolone and basiliximab were prescribed. Two months after all of them underwent conversion to everolimus and a rapid reduction of steroids. In patients №1 and №3, after 1 year and 1 month, respectively, brain metastases were detected; craniotomy with microsurgical tumor removal was performed. In 3 months patient №1 underwent 3 craniotomies due to recurrent development of metastases of the brain and later mediastinal metastasis was also detected and was surgically removed. She received 6 courses of polychemotherapy (PCT): Doxorubicin, Ifosfamide, Mesna with positive effect. Recipient №3 was diagnosed with adrenal glands metastases. In April 2024 after 3 courses of PCT (Doxorubicin with Ifosfamide) due to cancer progression PCT was discontinued, then he underwent 2 courses of radiation therapy (RT) for brain metastases with positive effect. In 7 months metastases in the skeletal bones were detected in patient №2; PCT (Doxorubicin, Ifosfamide, Zoledronic acid) was prescribed. After the 2nd course PCT was discontinued and then suspended due to severe chronic neutropenia and stabilization of the oncological process. Since July 2024 Sorafenib (№2 and №3) and Denosumab (№2) were initiated. 11 months of HTx due to progression of cancer 3rd recipient died. After completion of PCT and RT allograft function remained normal in all of them. On January 2025 2 patients were alive and survived 27 and 22 months, retrospectively.

Conclusion: HTx in CS patients improves their prognosis but multidisciplinary post-transplant follow-up is recommended. Due to high risk of cancer progression immunosuppression should be minimized from the early-term follow-up and frequent imstrumental methods to exclude methastases prescribed.

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EP_541 ASSOCIATION BETWEEN GRAFT DYSFUNCTION AND HCC RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: The inflammatory and cytokine milieu associated with initial graft dysfunction may predispose to hepatocellular carcinoma (HCC) recurrence following liver transplantation (LT). This study aims to investigate the correlation between early graft dysfunction and HCC recurrence.

Methods: A retrospective analysis was conducted on patients undergoing LT for HCC at the Padua Transplant Center between 2010 and 2022. Exclusion criteria included LT < 18 years of age, re-LT, and transplants for non-HCC indications. The incidence of early allograft dysfunction (EAD) and initial poor function (IPF) was assessed, along with their correlation with post-transplant HCC recurrence.

Results: Among 1097 LT procedures, 485 patients met the inclusion criteria. Of these, 26 developed IPF, and 116 developed EAD. EAD, and not IPF, was significantly associated with a reduced patient OS and RSF (5-year RFS 70.4% vs. 81.9%, p = 0.031), and graft survival (5-year graft survival 54.3% vs. 70.1%, p < 0.0001).Variables associated with an increased risk of HCC recurrence at Cox univariable analysis were: AFP at listing > 400 (p < 0.001), pre-LT radiological HCC nodules > 3 (p=0.056), previous abdominal surgery (p = 0.009), HCC surgical resection > 1 (p = 0.052), RFA procedure > 3 (p = 0.003), TACE procedure > 3 (p = 0.024), AFP at LT > 400 (p < 0.001), sodium level (p = 0.015), MELD-Na > 15 (p = 0.028), Child-Pugh score (p = 0.059), recipient portal vein thrombosis (p = 0.075), donor weight (p = 0.067), severe post-reperfusion syndrome (p = 0.011), AST peak within 7 pod > 2000 (p = 0.082), EAD (p = 0.034), post-LT portal vein stenosis (p = 0.002), hepatic veins thrombosis (p = 0.002), histological max diameter > 5 cm (p = 0.065), number of HCC nodules > 3 (p = 0.012), TTV > 115 cm^3 (p = 0.002), HCC grading > G2 (p = 0.020), micro vascular invasion (p < 0.001), and macro vascular invasion (p = 0.002). Multivariable analysis model confirmed EAD, AFP at LT > 400, histological max diameter > 5 cm, TTV > 115 cm^3, HCC grading > G2, and MELD-Na > 15 as significantly associated with HCC recurrence.Neither EAD nor IPF were associated with increased HCC-related death at competing risk analysis.

Conclusions: EAD, but not IPF, is associated with an increased risk of HCC recurrence and reduced graft survival. However, EAD does not appear to influence HCC-related mortality.

Table 1. Variables associated to HCC recurrence after LT at multivariable analysis

Variables	HR[1]	95% CI[1]	p-value
EAD (yes)	1.77	0.94, 3.35	0.078
AFP at LT > 400 ug/L	7.25	2.77, 19.0	<0.001
Histological max diameter > 5 cm	0.37	0.13, 1.08	0.068
Histological number of HCC nodules > 3	1.15	0.58, 2.24	0.7
Histological TTV > 115 cm^3	1.90	0.92, 3.92	0.083
HCC Grading > G2	3.70	0.89, 15.3	0.071
MELD-Na > 15	0.50	0.28, 0.89	0.019

[1] *HR = Hazard Ratio, CI = Confidence Interval*

LT, liver transplantation; EAD, early allograft disfunction; AFP, alpha-feto protein; HCC, hepatocellular carcinoma; TTV, total tumor volume; MELD, model for and stage liver disease.

EP_542 BANFF WORKING GROUP CLASSES DO NOT CORRELATE WITH THE BK POLYOMAVIRUS VIRAL LOAD

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Background: Although kidney graft biopsy using immunohistochemistry remains the gold standard to confirm BKPyV nephropathy, guidelines suggest treatment based on BK viremia findings. The Banff working group on BKPyV nephropathy classified the disease severity into three grades based on histology. Herein, we sought to determine the association of plasma load with kidney allograft biopsy findings.

Methods: All patients with BK viremia who underwent kidney allograft biopsy at our institution were included in investigation. We reviewed patients' records to obtain clinical data and demographic information. Patients with inadequate tissue samples were excluded from the investigation.

Results: An adequate tissue sample was obtained by indication biopsy in 29 patients (9 female) at the median of 7 months (range 1-101 months) after the transplantation. Two patients received cyclosporine and all other tacrolimus combined with mycophenolate mofetil and steroids. Median number of copies in plasma was 10250 (range 10-10^6 copies/mL). Ten patients had class 1, 14 class 2, and 5 class 3 BKPyV nephropathy. There was no statistically significant correlation between the BKPyV viral load and histopathology findings (f-ratio 0.34694, p= 0.71, one-way ANOVA test). All patients received intravenous immunoglobulins with reduction of immunosuppression.

Conclusions: In conclusion, Banff working group classes in our cohort do not correlate with the BKPyV viral load. While PCR test tests vary considerably and the prognostic predictive value of BK-DNAemia levels remains limited, we suggest kidney allograft biopsy for tailoring immunosuppressive therapy reduction in patients with BK nephropathy.

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EP_543 KIDNEY TRANSPLANTATION IN PATIENT WITH TUBULOCYSTIC RENAL CARCINOMA OF NATIVE KIDNEY

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Background: Tubulocystic renal cell carcinoma of the kidney is a rare entity with less than one hundred cases reported so far. It is now a well-established entity in renal neoplastic pathology and has been recognized as a distinct entity in the 2012 Vancouver classification of renal tumors. Current guidelines on listing patients for renal transplantation suggest that no delay is required for subjects with small or incidentally discovered RCC (renal cell carcinoma), while the recommendations for patients who have been treated for other types of renal cell carcinomas are conflicting.

Methods: case report.

Results: Male patient, 43 years old, diagnosed with IgA nephropathy at the age of 10, with progression to CKD. He was on a chronic hemodialysis program for 3 years. Among the comorbidities, he had arterial hypertension. Two years ago, he developed severe aortic stenosis, for which he was treated with replacement of the aortic valve with a mechanical valve, and was on chronic anticoagulant therapy. In the patient, a tumor mass of the native left kidney was verified 3 years ago. His father was evaluated and examined as a potential kidney donor with compatible blood group and no contraindications were found. Radical left nephrectomy was performed. Pathohistological finding revealed renal tubulocystic carcinoma, 3 cm in diameter, without necrosis, Fuhrman nuclear grade III, without lymphatic or venous invasion, without invasion in renal vein, hilus and perinephritic adipose tissue, Gerota's fascia or ureter. Lymph node and hilus adipose tissue had normal histology, without metastasis. After 3 years he was reconsidered for kidney transplantation treatment. Clinical examinations did not verify the presence of malignancy or pathological lymphadenopathy. Transplantation was performed with basiliximab in induction therapy, and with a standard immunosuppressive protocol (TAC + MMF + steroid), without complications. Graft function and patient are stable in follow up period.

Conclusions: Patients with tubulocystic renal carcinoma should be considered for treatment with a kidney transplantation with an individual assessment of the overall risk and benefit. Searching the literature, we did not come across a described case of kidney transplantation in a patient with a history of this type of native kidney cancer.

EP_545 PROGNOSTIC FACTORS IN ACUTE-ON-CHRONIC LIVER FAILURE: IMPACT OF LIVER TRANSPLANTATION

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Background: Acute-on-chronic liver failure (ACLF) is a critical condition associated with high mortality. Orthotopic liver transplantation (OLT) is a lifesaving intervention for selected patients, but identifying factors that predict survival both with and without transplantation is essential for patient selection and management. This study examines key clinical and biochemical predictors of outcomes in ACLF patients.

Methods: A retrospective analysis was conducted on 95 ACLF patients, including 43 who underwent OLT. Clinical and laboratory parameters such as age, MELD/MELD-Na scores, CLIF-C ACLF scores, platelet counts, fibrinogen levels, serum bilirubin, and oxygenation markers (PaO2/FiO2) were analyzed. Statistical comparisons were performed using the Mann-Whitney U test and Spearman correlation, with a significance threshold of $p < 0.05$.

Results: Non-survivors exhibited significantly higher CLIF-C ACLF scores (mean: 56.5 vs. 46.9, $p < 0.001$) and lower PaO2/FiO2 ratios (mean: 342.6 vs. 413.6, $p = 0.023$). Elevated FiO2 levels were also associated with increased mortality ($p = 0.005$). Survivors demonstrated higher fibrinogen levels (median: 166 vs. 125 mg/dL, $p = 0.024$). Age was a significant factor, with non-survivors being older on average (52.5 vs. 46.6 years, $p = 0.025$). MELD and MELD-Na scores showed no significant differences between survivors and non-survivors, indicating their limited prognostic value in this cohort.

Conclusions: CLIF-C ACLF scores, oxygenation markers (PaO2/FiO2 and FiO2 levels), fibrinogen levels, and age are significant predictors of mortality in ACLF patients, irrespective of OLT status. These findings highlight the importance of comprehensive preoperative assessment incorporating these parameters to improve prognostic accuracy and guide clinical decisions. Further studies are needed to validate these results and enhance prognostic tools in ACLF management.

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Infectious diseases, malignancies & long term challenges

EP_546 INTRAVENOUS IMMUNOGLOBULINS IN THE TREATMENT OF COMMUNITY RESPIRATORY VIRUSES IN LUNG TRANSPLANT RECIPIENTS

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Background: Community respiratory viruses (CRVs) in lung transplant recipients have been associated with the risk of developing Chronic Lung Allograft Dysfunction (CLAD). Currently, there are no proven effective therapies available. The use of intravenous immunoglobulins (IVIg) has shown to be effective in treating multiple conditions. However, there is a need of more clinical data to evaluate its use in the treatment of CRVs in lung transplant recipients. This study aims to evaluate the efficacy and tolerability of IVIg in treating CRVs in lung and heart-lung transplant patients.

Methods: Retrospective analysis of electronic records of adult lung and heart-lung transplant patients with IVIg for different CRVs between January 2016 and July 2023 at a single centre was conducted. Virus identified, mean baseline lung function before, and 3 months after IVIG treatment were collated to determine potential benefits, and any reported drug adverse effects.

Results: A total of 66 transplant recipients with 75 episodes of IVIg treated (0.5g/kg for 5 doses) CRVs were included. The most common CRVs were Parainfluenza virus (n=20). The mean baseline Forced Expiratory Volume(L) in 1 second (n=59) compared with 3 months post-IVIg was 2.2±0.78 L and 2.15±0.78 L (p=ns) respectively. While mean baseline Forced Vital Capacity (n=58) and post-IVIg were 2.92±0.85 L and 2.85±0.90 L (p=ns) respectively. Six patients developed organising pneumonia, seven patients died within the three months post-IVIg, most of which had CLAD and/or acute rejection before CRVs infection. Adverse effect included hypertension (n=6), vomiting and tachycardia (n=1), no discontinuation of treatment.

Conclusions: IVIg appears to be effective and well tolerated in treating CARVs in lung and heart-lung transplant recipients, but further studies are needed. The potential long-term benefits of IVIg in preventing CLAD are yet to be determined.

EP_547 LIVING KIDNEY DONATION IN THE PRESENCE OF RENAL COMPLEX CYSTS: CASE SERIES

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Background: According to the mains guidelines,the detection of renal lesions in potential living kidney donors(LKD) requires the best therapeutic approach for the donor and a precise transmission's risk estimation to the recipient.Nephrological,surgical,radiological and oncological evaluation is the cornerstone of this process must be followed by exhaustive information for the couple on the procedure's risk-benefit balance.

Methods: We've considered LKD in our center from 2019 to 2024. The screening (Figure1)includes chest-abdomen CT angiography add subsequent abdomen's MRI in case of suspect renal lesions.Each case was multidisciplinary discussed taking into account Bosniak classification, size and location of the lesion,as well as the donor's anamnesis and absolute/relative renal function,as for the usual pre-donation screening.Donations were done just in small lesions easy to enucleate,after patients's informed consent.

Results: Of 45 donors, renal complex lesions were in 4(8.9%).One was suspicious for an angiomyolipomatous nature,two were classified Bosniak IIF and one Bosniak III.In the first case, we've done an intraoperative biopsy that support the diagnosis, confirmed by histopathology after backtable enucleation.In one's Bosniak IIF and Bosniak III cases,only backtable enucleation was performed, with diagnosis of clear cell carcinoma G1.In the remaining case, the donation was deemed feasible,but not yet planned(Table 1;Figure 2). All transplanted patients showed immediate functional recovery without urinary fistulas in post-transplant.Donors and recipients continued follow-up with MRI 3-6 months post-surgery,annual ultrasound and chest X-ray.No recurrence was found.

Conclusions:A multidisciplinary approach allows LKD even in the presence of renal lesions,with excellent results.To ensure the donor-recipient's safe,clear information and long-term follow-up are essentials.

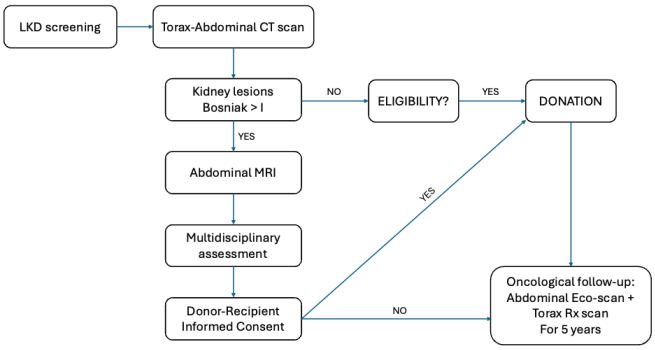

Figure 1.

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	Age	Sex	Serum Creatinine	Micro-Hematuria Yes/No	Urinary Citology Pos/Neg	Bosniak Class	MRI	Surgery
N°1	72	F	0,61	YES	NEG	III	15x17 mm sepimented	Backtable enucleation
N°2	46	M	1,03	NO	NEG	IIF	15 mm	Backtable enucleation
N°3	46	F	0,91	NO	NEG	\	\	Intraoperative enucleation
N°4	56	F	0,7	YES	NEG	IIF	11x13 mm sepimented	Pending

Table 1.

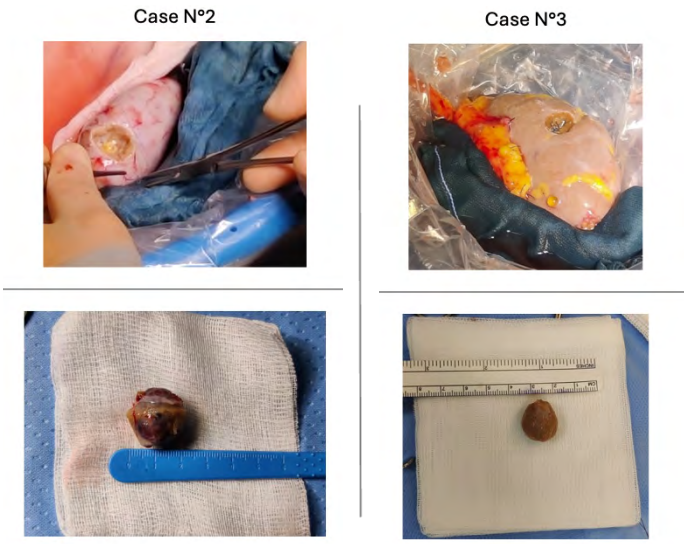

Figure 2.

EP_548 RENAL TRANSPLANT PERFUSION ASSESSMENT USING LASER SPECKLE IMAGING AND DEEP LEARNING FOR PREDICTING EARLY GRAFT FUNCTION

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Background: Kidney transplantation is the gold standard for treating end-stage kidney disease (ESKD), with early graft function being crucial for long-term graft survival. Despite advancements in transplant techniques, some kidney grafts experience early dysfunction or even failure. Laser speckle contrast imaging (LSCI), a non-invasive and real-time imaging technique, measures microvascular circulation by tracking erythrocyte motion. Given the strong correlation between renal function and cortical circulation, LSCI holds significant promise for evaluating graft function post-transplant. This study aims to integrate convolutional neural network (CNN) with LSCI data to automatically and accurately identify kidney grafts at risk of early dysfunction in real time.

Methods: We included 97 living donor kidney transplant cases, collecting intraoperative LSCI time-lapse data during the reperfusion phase. Graft function at one week post-transplant was used to classify these cases into two groups: “stable graft” (eGFR > 30 mL/min/1.73m^2, n=84) and “at-risk graft” (eGFR ≤ 30 mL/min/1.73m^2, n=13). A CNN model was developed and trained as a binary classifier to predict graft stability based on LSCI images. Given a set of LSCI images, the model outputs whether the case is classified as a “stable” or “at-risk” kidney graft.

Results: After manually selecting regions of interest and augmenting the LSCI dataset, we generated 840 frames for the “stable graft” group and 130 frames for the “at-risk graft” group. Preliminary results indicate that the CNN model achieved a high F1-score of 0.91, effectively balancing true positives, false positives, and false negatives in predicting stable grafts.

Conclusions: This study demonstrates the potential of integrating LSCI with deep learning to predict early graft function in real time, enabling timely interventions to mitigate early graft loss and improve long-term outcomes. Future work will focus on incorporating additional LSCI data and pre-transplant clinical parameters to further enhance predictive performance.

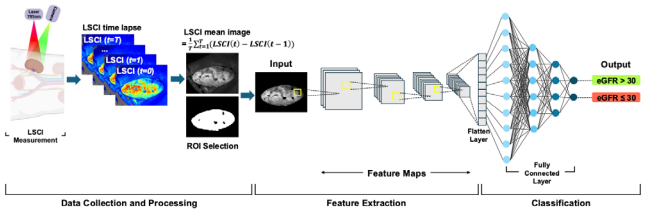

Figure 1. Proposed Convolutional Neural Network (CNN) model. eGFR, estimated glomerular filtration rate; LSCI, laser speckle contrast imaging; ROI, region of interest.

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EP_549 BIOLOGICALLY-DRIVEN MULTISTEP APPROACH FOR RECURRENT CHOLANGIOCARCINOMA LEADING TO LIVER TRANSPLANTATION

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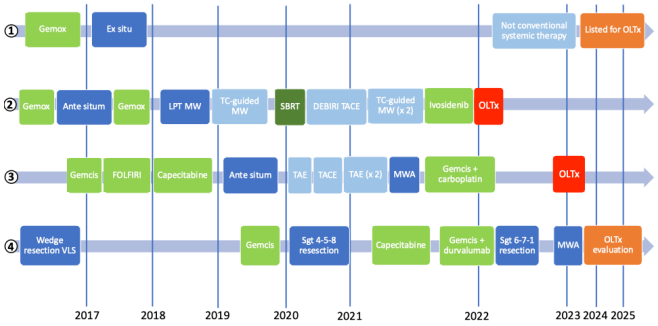
Background: Management of liver tumors relies on three principles: selecting favorable biology, prioritizing radical yet minimally invasive strategies (therapeutic hierarchy), and adopting a longitudinal approach to preserve liver parenchyma (iterative/combined treatments). This approach integrates systemic, surgical, and locoregional therapies within a multistep, iterative framework designed to optimize outcomes. The modern paradigm of transplant oncology has revolutionized cancer treatment by shifting the focus from achieving a cure to prioritizing meaningful gains in life expectancy, adding liver transplantation (LT) to the equation. Differentiating between favorable and unfavorable biology is often challenging. Indicators such as a positive response to chemotherapy, prolonged disease control despite recurrences, and a slow natural progression are crucial for assessing biological behavior.

Methods: We present four cases of patients who underwent multiple treatments for recurrent cholangiocarcinoma (CCA). An aggressive iterative, potentially curative, approach was guided by the favorable biological characteristics of their disease, aiming at long-term disease control.

Results: Patient 1 achieved a prolonged disease-free survival after ex situ liver surgery. Following disease recurrence 6 years later, she was listed for LT due to the slow progression of the disease. Patients 2 and 3 underwent ante situm liver resection, followed by systemic therapy and locoregional treatments (TAE, TACE) or microwave ablation. This iterative strategy provided extended disease control, leading to LT to improve control. Patient 4 underwent multiple surgical resections for CCAs; distinct histopathological features supported the hypothesis of de novo occurrence instead of recurrence. Given the prolonged disease control and suspected widespread biliary dysplasia contributing to new tumor development, the patient was also listed for LT.

Conclusions: Although CCA is typically aggressive, iterative treatments can achieve effective control in selected patients with favorable biology, such as slow progression or prolonged interval between recurrences. Identifying these patients is essential, as they may benefit from more aggressive treatment strategies, including liver transplantation.



EP_550 LEGACY EFFECT OF PRETRANSPLANT IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT RECIPIENTS WITH CRESCENTIC GLOMERULONEPHRITIS

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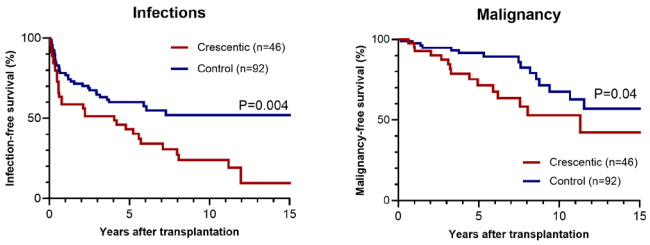
Background: Kidney transplant recipients with crescentic glomerulonephritis, including ANCA-associated vasculitis (AAV-GN) and anti-glomerular basement disease (GBM-GN), have often received an important burden of immunosuppression before transplantation. It is unclear what effect this pretransplant immunosuppression has on immunological outcomes, such as rejection or relapse, and the risk of infection or malignancy.

Methods: In a single-center cohort study of 2978 transplantations that were performed between 2000 and 2023, post-transplant outcomes of transplant recipients with underlying AAV-GN or GBM-GN were compared with a matched control group, adjusting for recipient age and gender, transplant year, previous kidney transplantation and dialysis vintage.

Results: During the study period, 21 recipients with AAV-GN and 25 recipients with GBM-GN received a kidney transplant. Compared to the matched control group (n=92), no differences were found in the incidence of graft loss (hazard ratio for graft loss 1.6, 95% CI 0.80-3.25) or rejection. Relapse after transplantation occurred in 3/21 patients with AAV-GN and none of the patients with GBM-GN. Severe infections requiring hospitalization occurred more frequently in the AAV-GN and GBM-GN group (HR 1.98 compared to the control group, 95% CI 1.18-3.30, Figure). Similarly, an increased risk for malignancy was found (HR 2.17, 95% CI 1.04-4.55, Figure).

Conclusions: Kidney transplant recipients with underlying crescentic glomerulonephritis are at an increased risk for infection and malignancy. These data suggest that pretransplant immunosuppression exerts an important legacy effect after transplantation, highlighting the need for immunosurveillance and personalized treatment in these patients.



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EP_551 BEST PRACTICES IN THE MANAGEMENT OF CMV IN TRANSPLANTATION

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Background: Kidney donation and transplantation face unique challenges in dealing with infectious disease prevention. This study explored current clinical practices in CMV management and how they align with best-practice recommendations.

Methods: A survey tool was designed and validated to collect data on the management of CMV prevention. Survey respondents included patients, donors, transplant surgeons, nephrologists, transplant coordinators, and hospital administrators from transplantation centres across France, Germany, Italy, and Spain. Qualitative data was collected in semi-structured focus group interviews conducted in each country, guided by survey findings. Ethics approval was obtained as per country-specific requirements.

Results: Among 253 survey participants, CMV did not have a substantial impact on providers decision making regarding donor selection (4%). 93% respondents noted CMV serology of both transplant recipients and donors to be a screening requirement at their centres, when compared to molecular testing (37%). CMV prevention protocols varied across institutions, with most utilising a patient specific approach based on the risk profile (43%), whereas some combined prophylactic and pre-emptive strategies (33%). In terms of patient education, the impact of CMV and other infections post-transplantation was not identified as a main concern.

Conclusions: These findings highlight the need for standardised patient education regarding infectious disease prevention, in general, and CMV, in particular, and for standardized prevention protocols.

EP_552 LIRICA AND LITALHICA: A MULTIDISCIPLINARY APPROACH TO LIVER TRANSPLANTATION FOR CHOLANGIOCARCINOMA

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Background: Liver transplantation (LT) for perihilar cholangiocarcinoma (pCCA) provides outstanding outcomes within the Mayo Clinic protocol (MP). However, an Italian survey revealed that, since 2015, 39% of pCCA patients undergoing LT deviated from the MP due to recurrent cholangitis, untreatable hyperbilirubinemia, or logistical obstacles. Major concerns include diagnostic difficulties, effect of radiotherapy, and the need to change chemotherapy from standard of care (SOC). Intrahepatic cholangiocarcinoma (iCCA) has traditionally been a contraindication for LT, but recent studies have explored its potential as a novel transplant oncology indication.

Methods: We developed two similar protocols proposing LT for unresectable iCCA (LIRICA) and pCCA (LITALHICA) after SOC neoadjuvant chemotherapy, serving as a test of time and to asses tumor biology. A multidisciplinary board (comprising hepatobiliary surgeons, transplant surgeons, oncologists, and radiologists) assesses tumor unresectability and confirms adherence to inclusion criteria, providing endorsements for approval by the Italian National Transplantation Center (CNT). Eligible patients undergo six months of SOC chemotherapy and are then restaged by CT, PET-MRI, and diagnostic laparoscopy. Those with stable disease or partial response proceed to transplantation, while patients with disease progression receive second-line chemotherapy.

Results: Since January 2024, 34 patients from 9 Italian centers have been evaluated (10 LITALHICA, 24 LIRICA). Of these, 5 were rejected based on exclusion criteria, and 18 were deemed eligible but could not be enrolled in the prospective protocols due to prior chemotherapy initiation. The first per-protocol LITALHICA case was aborted due to peritoneal carcinomatosis at exploratory laparotomy. The first LIRICA patient was successfully transplanted in August 2024 and is alive and recurrence-free after six months. Nine patients are awaiting LT.

Conclusions: Expanding the indications for LT requires robust scientific evidence from prospective trials. A multidisciplinary expert board provides the most effective framework for ensuring rigorous, case-by-case evaluation and strict adherence to criteria, efficiently balancing the principles of resectability and radicality.

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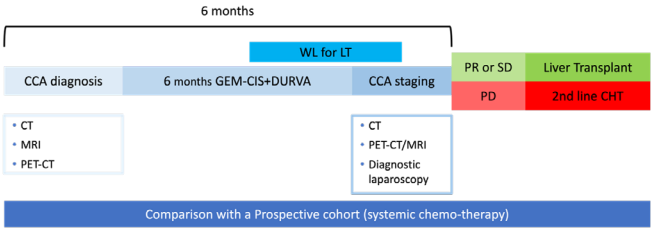

Figure 1: LIRICA and LITALHICA protocols. CCA: cholangiocarcinoma; CT computed tomography; MRI: magentic resonance imaging; PET: positron emission tomography; GEM: gemcitabine; CIS: cisplatin; DURVA: durvalumab; PR: partial response; SD: stable disease; PD: progression of disease; CHT: chemotherapy

Liver Transplantation for Non-Resectable Intrahepatic CholAngiocarcinoma (LIRICA)	Liver TrAnspLantation for Non-resectable Peri-Hilar cholangioCArcinoma (LITALHICA)
Inclusion Criteria	
• Histologically confirmed diagnosis of iCCA • First diagnosis or recurrence after R0 hepatic resection, N0, M0 without macrovascular invasion • Unresectable based on location or underlying liver dysfunction • Absence of major vascular invasion, extrahepatic disease, or involvement of regional lymph nodes • No extrahepatic metastatic disease • At least six months between first diagnosis of iCCA (or recurrence) and date of inclusion • At least six months of SOC chemotherapy, achieving disease stability or partial response • ECOG PS ≤ 1 • BMI ≥ 18 and ≤ 30 kg/m2	• Diagnosis of pCCA (transcatheter biopsy or brush cytology, CA 19-9 > 100 mg/mL and/or a mass on cross-sectional imaging with a malignant appearing stricture on cholangiography, or biliary ploidy with a malignant appearing stricture on cholangiography) • Unresectable tumor above cystic duct (pancreatoduodenectomy for microscopic involvement of CBD) or resectable pCCA arising in PSC • Absence of major vascular invasion, extrahepatic disease, or involvement of regional lymph nodes • No extrahepatic metastatic disease • Radial tumor diameter <3 cm • At least six months between first diagnosis of pCCA and date of inclusion • At least six months of SOC chemotherapy, achieving disease stability or partial response
Exclusion Criteria	
• Tumor involving nearby extrahepatic structures (including major hepatic vessels) by direct invasion • Tumor penetrating the visceral peritoneum • Previous extrahepatic metastatic disease • Prior neoplasms, except those treated curatively for more than 5 years without recurrence • HIV infection • History of solid organ or bone marrow transplantation • Substance abuse and medical, psychological, or social conditions that may interfere with the patient's participation in the study • Pregnant or breastfeeding women • Medical-surgical contraindications for liver transplantation	• Uncontrollable infection • Prior radiotherapy or chemotherapy • Prior biliary surgical resection or attempted surgical resection • Diameter of tumor >3cm • Presence of intra-hepatic metastases or iCCA • Present or past evidence of extrahepatic metastatic disease • Transperitoneal biopsy (including percutaneous ecography-guided FNA) • Prior neoplasms, except those treated curatively for more than 5 years without recurrence • Substance abuse and medical, psychological, or social conditions that may interfere with the patient's participation in the study • Pregnant or breastfeeding women • Medical-surgical contraindications for liver transplantation

Table 1: Inclusion and Exclusion Criteria for LIRICA and LITALHICA protocols

EP_553 VACCINE HESITANCY AMONG SOLID ORGAN TRANSPLANTATION PATIENTS: A MYTH OR REALITY

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Background: Vaccine hesitancy refers to delay in acceptance or refusal of vaccination despite availability of vaccination services. However, little is known about vaccine hesitancy among solid organ transplantation and his drivers. Shingles immunization is one of the newest vaccine recommended among solid organ transplantation, so to discover its vaccine hesitancy is a challenge for immunization programmes.

Methods: A systematic recommendation since 2022 about shingles immunization was performed among solid organ transplantation or being into the waiting list patients attended in our hospital in Spain. The recommendation could have been done by the clinical specialty, by the Preventive Medicine doctor or both. Sociodemographic information, type of attendance and previous vaccinations have been considered as possible drivers for shingles immunization and a binomial logistic regression was performed to identify tthem.

Results: In total, 3,184 patients transplanted or into the waiting list (2,220 of kidney; 239 of heart; and 725 of liver) were evaluated with a mean age of 64.1 years (SD 12.4), 8.7% being immigrants and the global seroprevalence of shingles immunization was 51.9% (95%CI: 50.2-53.7%). The shingles coverage was statistically lower among females, being an immigrant, those patients that have not received a correct pneumococcal vaccination, those that have not received previous or current flu vaccine, three or more doses against SARS-CoV2 or the current one, hepatitis B or tetanus or papillomavirus vaccine, having been already transplanted or having been attended also by a Preventive medical doctor. Age was not related as a driver of vaccine hesitancy (p-value >0.05). According to the multivariate analysis main drivers of shingles vaccination among SOT patients, independently of gender was: age, to be an immigrant, previous vaccination (flu, COVID, pneumococcal, hepatitis B or Tetanus) and having been attended additionally by a Preventive medical doctor.

Conclusions: More than a half of SOT have been vaccinated against shingles but especial attention should be given to immigrants. They could benefit from a Preventive medical attendance to recieve health education and to discuss the complacency, confidence and convinience to be immunized.

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EP_554 KIDNEY TRANSPLANTATION IN PATIENT WITH MPN MYELOPROLIFERATIVE NEOPLASM TREATED WITH TYROSINE KINASE INHIBITOR

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Background: Myeloid neoplasms with PDGFRB rearrangements are genotypically and phenotypically diverse, typically presenting as myeloproliferative neoplasm (MPN) with eosinophilia. Common morphologic diagnosis is chronic myelomonocytic leukemia with eosinophilia, associated with t (5;12) (q33; p13), resulting an ETV6-PDGFRB fusion gene (formerly TEL-PDGFRB). Patients bearing PDGFRB fusion genes achieve durable long-term remissions with imatinib. Consensus regarding kidney transplantation feasibility in patients with chronic myeloid leukemia (CML) well controlled by tyrosine kinase inhibitors has not yet been achieved.

Methods: case report.

Results: Female patient, 42 years old, had arterial hypertension and diabetes mellitus type 2 for seven years and CKD. After total hysterectomy and adnexectomy, due to uterine fibroids, developed acute respiratory distress syndrome, acutisation of CKD, threatened by pancytopenia. After the stabilization of the condition, a diagnosis of myeloproliferative neoplasm was made after pathohistological analysis of bone marrow biopsies PDGFRB (TIER3). After imatinib introduction, the condition stabilized. Patient achieved molecular response in treatment after a year, but developed ESRD (end stage renal disease) and was on chronic hemodialysis program. Her mother was examined as a potential kidney donor and no contraindications for kidney donation were found. Patient underwent clinical examination according to the protocol for examining the suitability of treatment with the method of kidney transplantation. Clinical and hematological bone marrow molecular examinations suggested CML molecular remission. Transplantation was performed with basiliximab in induction therapy, and with a standard immunosuppressive protocol (TAC + MMF + steroid), without complications. Imatinib adjustment with immunosuppressive drugs was required. Graft function and patient are stable in follow up period.

Conclusions: Patients with low-risk chronic phase CML in good disease control and ESRD may be considered for a treatment with kidney transplantation.

EP_555 PRE-TRANSPLANT OBESITY IS KEY MODIFIABLE FACTOR FOR PTDM - COHORT ANALYSIS OVER 10 YEARS

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Background: Post-transplant diabetes mellitus (PTDM) is associated with reduced patient and death-censored graft survival and has been linked to steroid use and obesity. Steroid avoidance regimens have been associated with a reduction in PTDM without impacting on patient or graft survival followed up for 5 years following kidney transplantation; however acute rejection remains a concern.

Methods: The primary objective of this study was to assess death censored graft and patient survival outcomes and report on PTDM onset in steroid avoidance immunosuppressant regimens over 11 years. The extracted data set included records of 1053 individuals, 254 associated with patients who had opted out of their data being used for research and 272 excluded as per exclusion criteria, leaving 577 individuals with a first-time kidney transplant meeting criterion for the study.

Results: There was no difference of patient or graft survival between those with PTDM, pre-existing diabetes or no diabetes. 16% (n=55) developed PTDM over a median follow up of 7.1 years (range: 0.9-13.8 years). After adjusting for confounding factors, the odds of PTDM diagnosis were associated with increasing BMI (odds ratio (OR): 1.01; 95% CI:1.03-1.18) and white ethnicity was associated with reduced odds of PTDM (OR: 0.45; 95% CI:0.23-0.90).

Conclusions: Our findings support lower PTDM rates and safe longer-term outcome following steroid free regimen. Timely weight management interventions before transplantation, particularly in high-risk groups, may reduce PTDM in this population.

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (years)	1.02 (1.00-1.04)	1.02 (0.99-1.04)
Ethnicity (white vs. non white)	0.54* (0.30-0.99)	0.45* (0.23-0.90)
Sex (Male)	1.51 (0.84-2.85)	1.37 (0.72-2.73)
Hypertension	1.46 (0.77-2.96)	1.16 (0.58-2.50)
BMI (kg/m^2)	1.09* (1.02-1.16)	1.10* (1.03-1.18)
Steroid avoidance immunosuppression	0.60 (0.33-1.16)	0.48* (0.24-0.97)
12 month % weight gain	1.02 (0.98-1.07)	1.03 (0.99-1.08)

In review

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EP_556 URINARY TRACT INFECTION IN KIDNEY TRANSPLANT RECIPIENTS, WHICH ANTIBIOTIC SHOULD BE USED AS THE FIRST TREATMENT?

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Background: Post-transplant urinary tract infection significantly impacts the quality of life in kidney transplant recipients (KTRs) and often requires hospitalization. Kidney function changes limit antibiotic use for urinary tract infection in KTRs, and prophylactic antibiotic use in the early post-transplantation period may affect antibiotic susceptibility. We investigated the bacterial pathogens and their susceptibility to antibiotics in urinary tract infection in KTRs.

Methods: We retrospectively reviewed 104 KTRs who underwent kidney transplantation at a single center between May 2019 and June 2024. Finally, this study included 41 urinary tract infection episodes requiring hospitalization in 20 KTRs. Urinary tract infection was defined as positive urine culture (>100,000 CFU/ml) with urinary symptoms (fever, frequency, or dysuria). Identification of the pathogen and antibiotics sensitivity were performed prior to antibiotics administration. The attending physicians chose antibiotics at their discretion.

Results: The most prevalent isolated microorganism were Escherichia coli, followed by Citrobacter freundii. The most commonly prescribed antibiotics were Piperacillin-tazobactam and Carbapenem. We identified 12 (34.3%) UTI episodes with extended-spectrum beta-lactamases (ESBL)-producing pathogens, and they all were susceptible to piperacillin-tazobactam and carbapenems. There was no significant difference in antibiotics resistance according to previous TMP-SMX administration and recurrence of UTI.

Conclusions: This study found that Escherichia coli was the most prevalent isolated microorganism in UTI and piperacillin-tazobactam was the most commonly used antibiotic with low resistance rate. Antibiotics resistance was not significantly different according to previous TMP-SMX administration and recurrence of UTI.

EP_557 CIED IMPLANT AFTER HEART TRANSPLANTATION: INSIGHTS FROM AN ITALIAN SINGLE CENTRE COHORT

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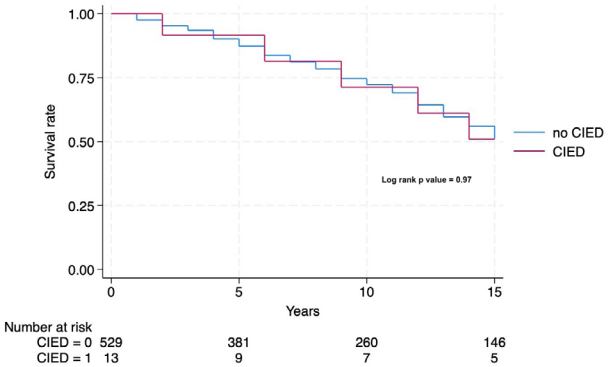
Background: With the advent of the bicaval anastomosis technique, the incidence of cardiac implantable electronic devices (CIED) after orthotropic heart transplantation (OHT) has significantly decreased. However, there remains limited knowledge regarding the current rate, indications, and predictors of CIED implantation associated with this approach. The purpose of this study was to evaluate the indications, patient characteristics, incidence, and survival related to CIED implantation after bicaval OHT

Methods: This was a retrospective, single centre, observational study which included all the adult patients who underwent OHT between Jan 2000 and Dec 2023 at our Institution. Retransplants were excluded. The primary end point was freedom from CIED implantation, and the secondary end point was all-cause mortality.

Results: We included 617 patients with a median follow-up of 8 years (IQR 2–18). The mean age of recipients was 52 ± 11 years, while the mean age of donors was 40 ± 13 years. CIEDs were implanted in 2% of patients (n 13). One patient had both an abdominal pacemaker with epicardial leads and a subcutaneous ICD (sICD). Among the CIEDs: 2 ICDs (14%) were implanted for secondary prevention of sudden cardiac death, 3 pacemakers (21%) for sinus node dysfunction, and 9 PM (64%) for high-grade atrioventricular block. Most PM were implanted after the first year (2 within 30 days *vs* 2 within the first year *vs* 8 beyond the first year). Overall survival rates were 97% at 1 year, 87% at 5 years, and 51% at 15 years. CIED implantation did not significantly impact survival (50% vs. 51%, p 0.97; see figure below). Recipients who required pacemakers were more likely to have received hearts from older donors (40 vs. 49 years, p 0.02) and used amiodarone pre-OHT (13 *vs* 33%, p 0.01).

Conclusions: Pacemaker implantation following OHT using the bicaval technique is uncommon and does not affect prognosis. Early sinus node dysfunction is rare. The primary risk factors appear to be donor age and amiodarone administration before heart transplantatation.



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EP_558 METABOLIC AND INFECTIOUS COMPLICATIONS RELATED TO DIABETES AFTER TRANSPLANTATION

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Background: Diabetes after renal transplantation is a serious metabolic complication either related to its degenerative complications or by the increase in deaths related to cardiovascular disease or following severe infections.

Methods: It is a descriptive and analytical retrospective study involving 169 renal transplant recipients in the nephrology department of the Sahloul Sousse University Hospital with a follow-up duration of more than one year. Results: Hospitalizations related to the diabetes after renal transplantation were noted in 5 patients (12.8%) including 3 patients for unbalanced diabetes and 2 patients for decompensation of diabetes on the ketotic mode. Diabeticis retinopathy was objectified in 2 patients (5.1%) with a delay of 2.5 years compared to renal transplantation. An ischemic heart disease was objectified in a single patient and this after a delay of 9 years after kidney transplantation. The prevalence of HTA and dyslipidemia in the diabetic group was significantly higher compared to non-diabetics (P=0.021 and p=0.001 respectively). Infectious complications were also more frequent in patients who developed the diabetes after renal renal transplantation with a statistically significant difference (p=0.05). The patient survival curve did not show a statistically significant difference between the two groups (p=0.65).

Conclusions: The diabetes after renal transplantation is a formidable complication. Its early diagnosis as well as its appropriate and early management could avoid the occurrence of its multiple complications on the renal transplant population.

EP_559 METABOLIC PROFILE AFTER KIDNEY TRANSPLANTATION: ABOUT 169 CASES

Zeinebou Dede[1], Narjes Ben Aicha[2], Wissal Sahtout[3], Raja Boukadida[3], Bouthaina Benabdallah[4], Asma Ben Abdelkrim[5], Awatef Azzabi[6], Sanda Mrabet[1], Dorsaf Zellama[7]

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Background: Kidney transplantation is currently the treatment of choice for end-stage chronic renal failure. Indeed, since the emergence of new immunosuppressants, the rejection problem has drastically decreased, thus giving way to other complications related to transplantation, including metabolic complications. Methods: This is a retrospective, descriptive study, including 169 patients with a kidney transplant at the Nephrology Department.

Results: Our series is composed of 123 men and 46 women, i.e. 72.8% and 27.2% respectively. The average age was 35.5 years ± 11 with extremes of 17 to 69 years. Obesity was noted in 16 patients and overweight in 48 patients, i.e. 9.4% and 28% respectively. Causal nephropathy was of interstitial origin in 42% of cases, glomerular in 31.4% of cases, vascular in 9.5% of cases and indeterminate in 17.2% of cases. We noted 12 cases of preemptive transplants and 157 cases of pre-transplant dialysis. Hemodialysis was the most widely used method of extra-renal clearance in pre-graft; it was noted in 123 patients, i.e. 72.8%. After renal transplantation, antithymocyte globulibne (ATG) was the most widely used in induction therapy (72.8% of cases) and tacrolimus was the most widely used in maintenance treatment (65.1% of cases). Regarding metabolic complications after renal transplantation, diabetes was noted in 39 patients (23.1%), hypertension in 105 patients (62.1%), dyslipidemia in 67 patients (39.6%) and hyperuricemia in 71 patients (42%).

Conclusions: The screening of metabolic diseases after kidney transplantation is essential given their frequency of occurrence and the severity of their impact on the survival of transplant patients vival of transplant patients.

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EP_560 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER PRESENTED WITH BOWEL PERFORATION: EMERGENCY IN KIDNEY TRANSPLANTATION

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Background: Posttransplant lymphoproliferative disorder (PTLD) is a rare but significant complication predominantly associated with Epstein-Barr virus (EBV) in immunosuppressed transplant recipients. We present an uncommon case of early-onset PTLD manifesting with small bowel perforation in a kidney transplant recipient.

Methods: A 31-year-old male, six months after an unrelated donor transplant (HLA 5 mm, PRA–, and Anti-T lymphocyte globulin induction), was on tacrolimus and mycophenolic acid maintenance without any sign of rejection. He was admitted with presumed gastroenteritis but rapidly developed an acute abdomen with pneumoperitoneum. Emergency laparotomy revealed multiple deep ulcers in the distal ileum, one of which had perforated (Figure 1), necessitating resection of the affected segment with double-barrel ileostomy. Immunohistochemical testing showed cytomegalovirus (CMV) positivity. While hospitalized for CMV treatment, the patient developed acute abdomen. Imaging confirmed a perforation in the remaining terminal ileum, leading to ileocecal resection and stoma formation. Pathological examination of the surgical specimen identified “Polymorphic PTLD.”

Results: At the time of transplantation, both the patient and donor were EBV IgM (–) and EBV IgG (+). Subsequent viral tests revealed EBV DNA (–), EBV VCA IgM (–), EBV VCA IgG (+), CMV DNA (+), and CMV IgM (–), with PET-CT showing no additional disease sites. Mycophenolic acid was discontinued, tacrolimus was dose-adjusted, and everolimus was added. The patient remains under close surveillance by oncology and transplantation services.

Conclusions: Fever (57%) and lymphadenopathy (38%) are the most frequent clinical findings in PTLD, followed by gastrointestinal involvement (27%), which can lead to serious morbidity and mortality under immunosuppressive therapy. While PTLD is often associated with EBV, this CMV positive case indicates that other viruses or multifactorial factors may also contribute to PTLD pathogenesis. Comprehensive follow-up, meticulous immunosuppression management, prevention of opportunistic infections are essential for early detection and effective management of severe complications, underscoring the importance of a multidisciplinary approach.

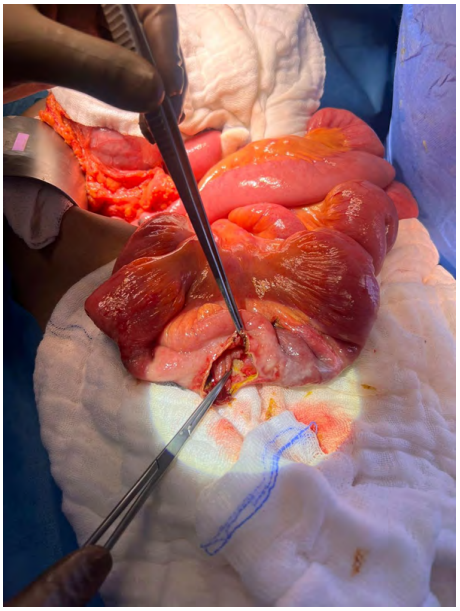

Figure 1. Deep ulcer extending to the serosa.

EP_561 TWO-FOLD RISE IN SPECIFIC ANTIBODIES IDENTIFIES SOLID ORGAN RECIPIENTS FREE OF REINFECTIONS IN AN IVIG CLINICAL TRIAL

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Background: Proven specific antibody failure is defined as failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines as part of the updated therapeutic indication of intravenous immunoglobulin in secondary antibody deficiencies by EMA in 2019. In a substudy performed in a randomized clinical trial of intravenous immunoglobulin (IVIG) for therapy of solid organ recipients with severe infections and moderate IgG hypogammaglobulinemia (IgG < 600 mg/dL) we evaluated the potential role of measurement of specific antibody titers as a potential profile to identify patients who were free of reinfections during the clinical trial.

Methods: The substudy of EudraCT: 2012-001327-12 included 10 patients that were randomized to standard of care therapy (SOC) and 9 patients to SOC + 5%-IVIG (2 dosis of 15 grams with interval between doses of 7-15 days followed by 3 dosis of 20 grams with interval of 15-30 days, total 90 grams). Specific antibody titers of anti-tetanus toxoid and anti pneumococcal polysaccharide antibodies performed by ELISA were evaluated at visit 1 (before randomization) and visit 7 (30-45 days after last IVIG dose or similar time in SOC-arm) of the clinical trial. Positive antibody response was defined as at least two-fold rise of specific antibodies (V7/V1).

Results: A 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and tetanus toxoid antigens was more frequent in IVIG-arm that in SOC-arm (77.8% vs 10%, p=0.003, 77.8% vs 20%, p=0.012, respectively). Two-fold rise to both antigens was more prevalent in IVIG arm (55.6% vs 0%, p=0.006). 2 fold rise to pneumococcal antigen and to both antigens identified patients who were free of reinfections during the clinical trial as compared with patients developing reinfections (80% vs 28,6%, p=0.046 and 60% vs 12.3% 0.046, respectively).

Conclusions: In a randomized clinical trial a 2-fold rise of specific antibodies that was more frequently observed with the use of IVIG, was associated with a protective effect against reinfection.

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EP_562 ACUTE PANCREATITIS IN KIDNEY TRANSPLANT RECIPIENT WITH CMV REACTIVATION

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Background: Acute pancreatitis is uncommon in kidney transplant recipients, and it is associated with a poor prognosis. Cytomegalovirus (CMV) in immunocompromised patients can cause significant disease. CMV pancreatitis is very rare condition and it is described in a few cases in immunocompetent patients. Acute pancreatitis in kidney transplant recipient with CMV infection is also reported only in a few cases.

Methods: case report.

Results: Female patient, 51 years old, diagnosed with membranous nephropathy at the age of 23, with progression to CKD, despite treatment with corticosteroids, cyclosporine and MMF. Among the comorbidities, he had arterial hypertension. She was treated with preemptive kidney transplantation at the age of 30, father was a donor of the kidney. She was CMV seropositive before transplantation, as well as her donor. She got valganciclovir as CMV prophylaxis for six months after kidney transplantation. In the follow up period, 9 years after kidney transplantation, she developed hepatitis C infection, with compensated liver function, F2 stage of fibrosis, genotype 1b, treated successfully with glecaprevir/pibrentasvir for 12 weeks, after she achieved viral load negativity, without complications and without viral reactivation in follow up period. By the time she developed CAN (chronic allograft nephropathy) followed by anemia and arterial hypertension. Twenty one year after kidney transplantation she got clinical presentation of nonobstructive acute pancreatitis followed by highly elevated serum amylase and lipase confirmed with CT (computed tomography) and MR (magnetic resonance) findings suggestive for acute pancreatitis and graft nephropathy progression. In the same time virological analyses confirmed CMV reactivation with viral load over 10.000 copies/ml. She was treated with adjusted dose of intravenous ganciclovir for three weeks, with broad spectrum antibiotics, adjusted immunosuppressive protocol, rehydration and polysymptomatic therapy, continued with oral valganciclovir. She achieved laboratory and clinical resolution of pancreatitis followed by CMV viral load negativization. Graf function recovered to parameters present prior to acute pancreatitis.

Conclusions: CMV reactivation could be cause of acute pancreatitis in kidney transplant recipients.

EP_563 CYTOMEGALOVIRUS-ASSOCIATED ACUTE CORONARY SYNDROME IN A KIDNEY TRANSPLANT RECIPIENT

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Background: Cardiovascular diseases remain a leading cause of mortality globally despite advancements in treatment. Cytomegalovirus (CMV) has emerged as a potential factor in the pathogenesis of atherosclerosis, linked to vascular endothelial injury and inflammatory cascades. In immunocompromised patients, CMV infections may significantly contribute to cardiovascular events. We present a unique case of acute coronary syndrome (ACS) triggered by CMV reactivation in a kidney transplant recipient.

Methods: Case report.

Results: A 38-year-old male with a kidney transplant (donor: mother, 8 years prior) presented with anemia, elevated nitrogenous waste products, and electrolyte imbalances. Initial diagnostic workup identified chronic graft dysfunction. CMV reactivation was confirmed by serological and molecular assays (IgM and IgG positive; serum PCR >10,000 copies/ml). Imaging studies and endoscopic evaluations corroborated the presence of CMV-related pathology. During hospitalization, the patient developed chest pain indicative of ACS, supported by EKG changes and elevated cardiac biomarkers. Urgent coronary angiography revealed significant stenosis in the left anterior descending artery (LAD), necessitating stent implantation. The patient responded to antiviral therapy (ganciclovir and immunoglobulins), along with standard ACS management, including dual antiplatelet therapy. Following stabilization, the patient exhibited improvement in graft function and cardiovascular symptoms. Notably, histopathology confirmed CMV involvement in colonic and vascular tissues, underscoring its systemic impact.

Conclusions: This case underscores the critical interplay between CMV reactivation and cardiovascular pathology in kidney transplant recipients. It highlights the importance of timely diagnosis and a multidisciplinary approach in managing such complex presentations. Further research into CMV-targeted therapies may mitigate similar complications in transplant populations.

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EP_564 CHARACTERISTICS OF LONG-TERM KIDNEY ALLOGRAFT SURVIVORS FOR MORE THAN 10 YEARS

Amgad El-Agroudy[1]
[1]*Arabian Gulf University; King Abdulla University City; Medicine Department*

Background: We studied the characteristics and predictors of survival in Bahraini renal transplant recipients with an allograft that functioned for more than 10 years.

Methods: Seventy-eight patients underwent renal transplantation between 1992 and 2010. Among them, 56 patients maintained functioning allografts for more than 10 years (range 10-30 years).

Results: Characteristics of the surviving patients, data on graft survival, and determinants of outcome were obtained by reviewing all medical records. The mean age at the time of renal transplantation was 33.6 ± 15.3 years. The source of the graft in 42 (75%) of recipients was from living-related donors with a mean age of 31.4 ± 7.7 years, and it was the first graft in 48 recipients. The primary immunosuppression regimen consisted of cyclosporine (CsA) and prednisolone. Azathioprine (AZA) was given to 52 (92.9%) recipients, while four patients received steroids and AZA only. Induction therapy was administered to 30 patients in the CsA group. Acute rejection episodes occurred in eight (14.3%) patients, of whom two experienced two episodes. During the last follow-up in January 2010, the mean serum creatinine was 118.3 ± 46.5 µmol/L. A history of cancer was noted in one patient, whereas hypertension was encountered in 54% and diabetes mellitus in 20.5%. We compared the graft functioning group with the graft failure group and found that the independent determinants of long-term graft survival included time of late acute rejection episodes and histopathologic findings of chronic allograft damage, post-transplant hypertension, and serum creatinine at one year.

Conclusions: We conclude that renal transplantation, even in its earliest years and despite the associated numerous complications, has provided a ten-year or more of near-normal life to patients with end-stage renal disease.

EP_565 QUALITY OF LIFE OF KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER IN BAHRAIN

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[1]*Arabian Gulf University; King Abdulla University City; Medicine Department*

Background: Although a positive effect of renal transplantation on quality of life (QOL) scores was demonstrated in numerous international studies, there are a few studies on renal transplant recipients in Arabic countries. This study aimed to assess the QOL in renal transplant recipients in Bahrain.

Methods: We used the standard QOL Index (QOLI) score instrument in Arabic languages. This study included 58 patients aged 26-71 years, and 63.8% of them were males. We excluded patients below 18 years old and failed renal transplants at the time of the study.

Results: The highest QOL score was in the psychological/spiritual domain (87.4 ± 12.2), followed by the family domain (85.5 ± 13.1), the health and functioning domain (82.7 ± 13.3), and the social and economic domain (80.5 ± 13.9). There was a highly significant high positive correlation between the QOLI and each of the tested domains ($P < 0.001$). Married participants had a significantly higher QOL score in the family domain than unmarried participants ($P = 0.025$). The QOL scores in the health and functioning domain were significantly affected by the patient's social status, residence, and coexisting diabetes mellitus. In addition, the QOLI scores were significantly greater among patients who did their transplants in Bahrain ($P = 0.045$).

Conclusions: We conclude that most renal transplant patients in Bahrain are satisfied with their QOL. Their QOL was also variably impacted by the different sociodemographic and clinical factors.

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EP_566 STEWARDSHIP OF CANDIDA AURIS DONOR-DERIVED TRANSMISSION DURING SOLID ORGAN TRANSPLANTATION; PRESENTATION OF 5 CASES

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Background: Candida Auris (C.auris) is considered an emerging multidrug-resistant fungal pathogen, which as of 2022 has been ranked by World Health organization as a critical priority pathogen. C. auris colonizes body sites and eradication is difficult. Consequently, C. auris infection is considered a highly feared infection by many transplant centers and is often considered one of the exclusion criteria for organ donation. Hereby we present our experience of a small series of donors with C. auris colonization or infection.

Methods: Medical records of five actual donors with C. auris colonization or infection during the period 04/2022-12/2024, provided by five different intensive care units, were reviewed. Donors' personal history, comorbidities, antecedent positive culture data, previous antimicrobials, C. auris source and days from admission to collection of C. auris isolate, C. auris treatment and organ procurement and allocation were analyzed.

Results: Out of five eligible donors (ED), 3 were diagnosed with cutaneous colonization (CC) and all of them became actual donors as the kidneys, liver (from 2 ED) and heart (from 1 ED) were procured. None of the recipients exhibited C. auris infection at any time of immediate or late post-transplant period. Only in one case there was a kidney graft loss due to acute thrombosis of the renal vein. One case of ED with C. auris urinary tract infection was observed, from whom kidneys and heart were retrieved and successfully transplanted. Kidney recipients were successfully treated with micafungin. Finally, one ED with candidemia was recorded and treated with antifungals until eradication of the fungus and kidneys successful transplantation.

Conclusions: Solid organ transplant recipients are in any case at high risk for developing C. auris invasive infections, which can be complicated by graft loss, morbidity and mortality. However, the organ shortage crisis demands the usage of non-standard risk donors; thus, organs from donors with C. auris infection or colonization may be considered for allocation, although the data are sparse. Our experience demonstrates that effective stewardship, rapid screening, diagnosis and treatment, are the best practice for prevention and management of donor-derived C. auris infection from the donor to the recipient.

Parameter					
	Case 1	Case 2	Case 3	Case 4	Case 5
Age (yr)	19	45	45	53	19
Sex	M	F	M	F	M
Comorbidities	NA	Hypertension; Obesity; Diabetes type 2;	Astrocytoma at the age of 16 years; Dyslipidemia; Hypertension	Psoriasis	NA
Antecedent treatment with steroids	NA	NA	NA	NA	NA
Clinically relevant antecedent positive culture data	Bronchial cultures: Acinetobacter baumannii complex; Klebsiella pneumonia; Proteus mirabilis	Bronchial cultures: Acinetobacter spp; Pseudomonas aeruginosa;	Bronchial cultures: Klebsiella pneumonia; Morganella morganii	Bronchial cultures: S. pneumoniae; Klebsiella pneumoniae	Blood: Acinetobacter Baumanii; Pseudomonas Aeruginosa
Previous antimicrobials	CTX; CLI; MER; AMK LZD	LZD; COL; MER	CTX; COL; IMI/REL; MET	COL; MET; LZD; CAZ-AVI	COL; MER; TIG; TEC; AMP/SUL
Days from admission to collection of *C. auris* isolate	17	45	3	3	23
C. auris Source	Skin Colonization	Urine >=100.000 CFU/mL	Skin Colonization	Skin Colonization	Blood
C. auris treatment	NA	MIC	NA	NA	ANI; AmB
Organ procurement	Kidneys, Liver	Kidneys, Heart	Kidneys, Liver, Heart	Kidneys	Kidneys

Abbreviations: M, male; F, female; Antimicrobials: CTX, ceftriaxone; COL, colistin; INN, Imipenem/relebactam IMI/REL; MET, metronidazole; LZD, linezolid; CAZ-AVI, Ceftazidime/avibactam; MER, meropenem; CLI, clindamycin; AMK amikacin; TIG, Tigecycline; TEC, Teicoplanin; AMP/SUL Ampicillin/Sulbactam; MIC, micafungin; ANI, anidulafungin; AmB, Amphotericin B (AmB), NA, not applicable

Table 1: Donor characteristics

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EP_567 MULTIDRUG-RESISTANT ENTEROBACERIACEAE ELICIT BOTH CMV INFECTION AND REJECTION IN KIDNEY TRANSPLANTS

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Background: The incidence of infections by extended-spectrum β-lactamase-producing (ESBL) and carbapenemase-resistant strains (CRE) is increasing in kidney transplant, but the full spectrum of clinical consequences has not been fully investigated.

Methods: We examined the relationship between ESBL and/or CRE colonization and/or infection and outcomes by retrospectively following, up over 24 months, a consecutive series of patients undergoing kidney transplantation at the Parma Hospital between Jan2016 and Feb2024. We identified 3 overlapping conditions namely, *Colonization*, *Infection*, and *Probable-MDR-Infection* (i.e., missed culture - usually because the patient was admitted through the emergency department on arrival at hospital - and clinical response to ESBL/CR-specific antibiotic therapy). We used logistic, and time-varying Cox proportion-hazard multiple regression models to analyze the adjusted association between each of the 3 conditions (indicator variates) and transplant complications (BKV viremia, CMV replication, biopsy-proven acute or borderline rejection [AR/BR]) or transplant failure (dialysis or death, whichever came first).

Results: We enrolled 521 de novo kidney transplants recipients: 40% had *Colonization*, 18% developed *Infection*, and 19% *Probable-MDR-Infection*. Major risk factors included female sex, dialysis vintage, antibiotic therapy, extended urinary catheterization, and ureteral fistulas for all the three conditions (P<0.05). ESBL/CRE colonization was associated with a higher risk of AR/BR (37% vs. 25%) and CMV replication (35% vs. 23%) (P<0.05, see **Figure 1** for crude and multivariable-adjusted risk for the condition *Infection*). Patients with *Probable-MDR-Infection* showed a trend toward and increased hazard of transplant failure (2.39-fold increase [95%CI; 0.98 to 5.85:P=0.056]).

Conclusions: ESBL/CRE colonization/infection is associated with increased risk of CMV proliferation, biopsy-proven acute/borderline rejection and of transplant failure.

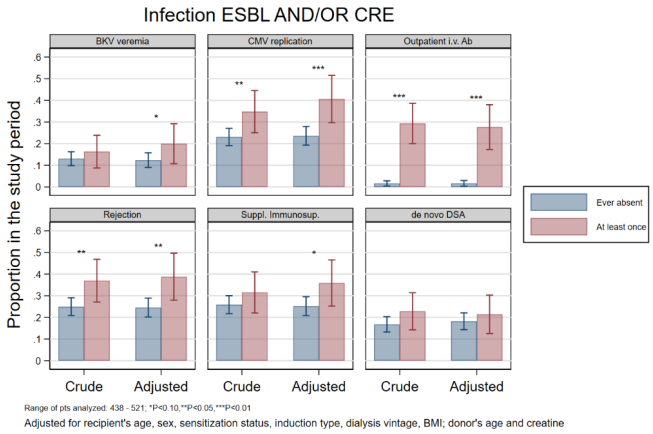

Figure 1

EP_568 VACCINATION AND PREDICTORS OF COVID-19 DEVELOPMENT IN HEART RECIPIENTS: A MULTICENTRE RETROSPECTIVE OBSERVATIONAL STUDY

Maria Simonenko[1], Petr Fedotov[2], Artem Kostomarov[3], Elena Kosmacheva[4], Margarita Kolodina[4], Irina Utmanova[5], Tatiana Golovina[6], Ilia Melnikov[7], Inna Zubareva[8], Natalia Gorbunova[9], Margarita Klimova[10], Mikhail Karpenko[11], Maria Sitnikova[2]

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Background: Infectious episodes are frequent after heart transplantation (HTx) and of the leading causes of death. Prevention of IE significantly improves recipients' survival. The aim of our study was to evaluate the efficacy and safety of vaccination against the COVID-19 in heart recipients.

Methods: We organized and registered multicentre study the "Database of patients after heart transplantation depending on the vaccination against the new coronavirus infection COVID-19" (№2022622422 from October 05th, 2022). Retrospectively results were analyzed that included 47 indicators and blinded results of observation of 367 heart recipients who were enrolled in the outpatient follow-up programme from February 2020 to May 2023.

Results: Majority of recipients included in the study were male (80%, n=294) and ischemic heart disease (40%, n=68) prevailed as a cause of heart failure. The average age of patients at the time of vaccination was 53±13-year-old and received the following immunosuppression: calcineurin inhibitors, mycophenolic acid (MPA) or everolimus were plus 82% of them induction early after HTx. 67% (n=245) of the recipients included in the analysis did not have COVID-19 before HTx, and another 33% (n=122) had COVID-19 after HTx without being vaccinated. Half of patients (47%; n=174) were fully vaccinated against COVID-19 and in 1 year 12% - received booster. Mild side effects were such as subfebrile (10%) or febrile fever (4%), general weakness (11%) or headache (2%) developed within 48 hours after a shot. Only 18% of patients from the vaccinated group were subsequently infected and survived. However, 5 individuals had a moderate disease and 2 of them developed post-COVID bronchial asthma (n=1) and alveolitis (n=1), which were cured by steroids. In the absence of vaccination, the relative risk of developing COVID-19 compared to vaccinated patients was 2.66 (CI 95%: 1.88; 3.75). Vaccination was associated with a 30.9% decrease in the absolute risk of COVID-19, and to prevent 1 case of it, 4 heart recipients need to be vaccinated (NNT = 3.2).

Conclusions: Vaccination against COVID-19 in heart recipients is safe and associated with a lower incidence of being infected and its milder course compared to unvaccinated ones. Predictors of COVID-19 infection were male sex, management with MPA and early-term induction.

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EP_569 PULMONARY ALVEOLAR MICROLITHIASIS: MANAGING COMPLEX CHALLENGES POST-LUNG TRANSPLANTATION

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Introduction: Pulmonary alveolar microlithiasis (PAM) is a rare genetic disorder involving calcium phosphate microlith deposition in alveoli, leading to progressive respiratory failure. Diagnosis is often incidental and typically made via chest imaging between the second and fourth decades of life. Lung transplantation is the only definitive treatment. This report explores the challenges of managing PAM post-lung transplantation.

Case Presentation: A 21-year-old female underwent double lung transplantation for severe PAM. Three weeks later, she developed acute pulmonary embolism in the right lower lobe, managed with low-dose heparin. Other findings included bilateral pleural effusions, pulmonary edema, and a stable pneumothorax, treated with furosemide. Imaging revealed an organized hematoma around the left pulmonary veins. Cardiological evaluation showed mild right ventricular dilation, pressure overload, and tricuspid regurgitation. Persistent Aspergillus infection required antifungal therapy and bacterial prophylaxis. Ventilation issues, including poor tracheostomy mask tolerance and panic attacks, were managed pharmacologically.

Discussion: PAM is a progressive disorder causing chronic respiratory failure, with lung transplantation as the only effective treatment. This case highlights the complexities of post-transplant care, including infection control, thromboembolic complications, and ventilation challenges. A multidisciplinary approach encompassing pharmacological management, immunosuppression monitoring, and mobilization strategies was essential for optimizing outcomes. Early identification and comprehensive management of complications are critical for improving post-transplant prognosis in PAM.

Conclusion: PAM, a rare disorder necessitating lung transplantation, presents significant post-operative management challenges. A multidisciplinary approach remains key to achieving better outcomes.

EP_570 OUTCOMES OF SEVERE CHRONIC KIDNEY DISEASE LONG-TERM AFTER HEART TRANSPLANTATION

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Objective: The aim of study was to estimate outcomes in recipients required renal replacement therapy (RRT) long-term after heart transplantation (HTx).

Methods: From January 2010 to December 2024 HTx was performed in 276 patients. Early-term RRT was prescribed to 18% due to acute kidney injury (AKI) but in long-term only 1 of them required it. In 2 other recipients RRT was initiated long-term after HTx due to progression of chronic kidney disease (CKD) to stage 5.

Results: In January 2022, 59-year-old man 9 years after HTx moved to another region and being included in our post-transplant follow-up. CKD stage 5 was diagnosed; RRT was initiated. On October 2022 he received kidney transplantation (KTx) and on March 2023 – RCA stent implantation. Since November 2024 there were serum creatinine and urea increase but heart transplant function was normal. Cellular rejection of kidney transplant was diagnosed and successfully treated by steroids. In 2022 51-year-old man underwent HTx due to dilated cardiomyopathy. Early post-transplant follow-up was complicated with renal dysfunction and he required RRT for 13 months until November 2023. Since May 2023 he was included in the KTx waiting list (KTx WL) but 14 months after RRT discontinuation he is no longer a candidate. While in KTx WL we gradually decreased the number of nephrotoxic medications: initiated Everolimus and gradually decreased until discontinuation steroids and Mycophenolic acid (MPA) that all lead to renal function improvement. Our 3rd clinical case was 66-year-old woman who have been heart transplanted 10 years prior due to IHD. Throughout the years there was a gradual progression of CKD associated with T2D, hypertension, tacrolimus and atherosclerosis to stage 5. In 2016 she was switched from MPA to Everolimus and in 2023 from Tacrolimus to Cyclosporine with positive outcomes. Since December 2024 the level of GFR decreased to 11 mL/min/1.73 m^2 and formation of dialysis fistula was created. While being on RRT she will be examined to be included as a candidate in the KTx WL.

Conclusions: Development of post-transplant CKD is associated with multiple factors. Recipients with severe renal function deterioration should be managed by multidisciplinary team, including cardiologist and nephrologist. Decrease of nephrotoxic medications is a key to postpone CKD progression.

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EP_571 INCREASED PATIENT ACTIVATION IS ASSOCIATED WITH REDUCED HEALTHCARE UTILISATION POST-TRANSPLANT

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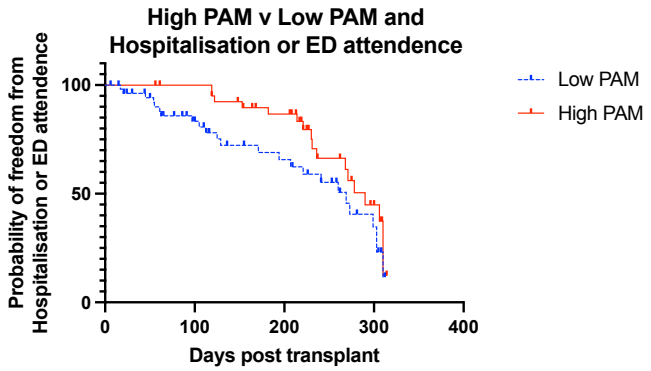
Background: The Patient Activation Measure (PAM) is a validated tool to assess a patient's knowledge, skills, and confidence in managing their health. Higher levels of patient activation have been shown to be associated with improved adherence to treatment regimens, reduced healthcare utilization and hospitalization and better health related outcomes in a variety of long-term conditions including advanced CKD. PAM has been used widely in the NHS. We aimed to determine if we could identify an association between PAM and adverse health related outcomes in our cohort of kidney transplant recipients and evaluate the utility of PAM to identify patients needing enhanced levels of monitoring, support and coaching to achieve optimal outcomes following a kidney transplant.

Methods: All transplant recipients completed the 13 question PAM as part of standard care during pharmacist delivered education after kidney transplantation and prior to discharge from hospital. PAM scores were retrospectively calculated. Un-paired t-test was used to compare the mean PAM score for English and non-English speakers. A Kaplan-Meir survival analysis was performed to determine the relationship between PAM score and hospital admission or attendance to the Emergency Department.

Results: A total of 98 transplant recipients had a PAM score calculated (Median score 53.2). The mean PAM score was lower if the recipient did not speak English, but not statistically significant (p=0.063). Median follow-up was 188 days. Recipients with higher levels of activation (level 3+4) were significantly less likely to be hospitalized or attend ED than those with lower activation (level 1+2), especially in the early months post-transplant (p=0.015).

Conclusions: Our study is limited by a relatively small size and short duration of follow-up. However, in common with other studies of PAM in long-term conditions, we have identified an inverse relationship between higher levels of patient activation and healthcare utilization. We believe that the PAM merits further study in a larger cohort with longer follow-up to determine the association between PAM clinically relevant and patient reported outcome measures (PROMs) with the aim of personalized interventions to improve post-transplant outcomes.



EP_572 IMMUNOGLOBULINS IN THE TREATMENT OF APLASTIC ANAEMIA AFTER KIDNEY TRANSPLANTATION

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Background: Anaemia is one of the most common complications after kidney transplantation (KT). Aplastic anaemia after KT can be caused by parvovirus B19 (ParvB19) infection, which shows tropism to the precursors of erythropoiesis, where the virus has a cytotoxic effect. After KT, pure red cell aplasia (PRCA), direct glomerular damage, activation of cytotoxic T-cells and cellular rejection (TCMR) are described. The diagnosis of ParvB19 infection is based on normocytic normochromic anaemia, severe reticulocytopenia and resistance to rhEPO. Evidence of viral DNA replication in the blood is crucial. In the case of proven ParvB19 infection, it is recommended reducing IS in order to improve the antiviral immune response. Intravenous immunoglobulins (IVIG) are used with regard to their immunomodulatory effect and ability to neutralize the virus.

Methods: We present 3 cases of PRCA caused by ParvB19 infection after KT (age: 28-39 yrs; men: 2). Normocytic and normochromic anaemia of moderate/severe grade not responding to rhEPO developed 30-45 days after KT. In all cases, repeated blood transf. was necessary. In a patient after secondary KT, ATG was used in induction, two patients received basilix. In one case, it was KT 2 years after a heart transplant. One patient was treated 2 times for biopsy proven TCMR. At the time of PRCA, the IS consisted of tacrolimus, mycophenolate acid and steroids. The diagnosis of PRCA was based on the reticulocytopenia and virus DNA in peripheral blood.

Results: Patients were treated with IVIG (0.4 g/kg/day) for 4 to 8 days (median: 5). Response to treatment was manifested by reticulocyte crisis and an increase in red blood cell without the need for rhEPO.

Conclusions: PRCA is a rare but serious complication after KT. Diagnosis is not complicated and IVIG treatment is effective. Recognition of PRCA makes it possible to eliminate the need for blood transf., reduce the hospitalizations, reduce the risk of TCMR and improve quality of life.

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EP_573 DIABETES SCREENING IN DIALYSIS POPULATION WITH A GLUCOSE CHALLENGE TEST AND CONTINUOUS GLUCOSE MONITORING - DIGEST STUDY

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Background: People on the kidney transplant waiting list have an increased risk of developing diabetes mellitus. An oral glucose tolerance test (OGTT) is the most reliable method to identify dysglycemia, but it is often impractical in this population. We investigated the effectiveness of the glucose challenge test (GCT) for identifying dysglycemia (defined as glycemia ≥ 140 mg/dL based on an OGTT) in a dialysis cohort. Additionally, we explored their glycemic profiles using continuous glucose monitoring (CGM).

Methods: This single-center prospective cohort study included adults on dialysis at the University Hospital of Antwerp. Exclusion criteria were infections, a history of diabetes or receiving glucose-lowering agents. The protocol involved a 50g-GCT followed by a 75g-OGTT 8-10 days later. Blinded continuous glucose monitoring (CGM) was performed in between the two tests.

Results: A total of 50 individuals met eligibility criteria, but 27 declined participation due to the OGTT burden, leaving 23 participants. Dysglycemia (2-hour post-OGTT glucose ≥140 mg/dL) was found in 13 participants, including one with diabetes (glucose ≥200 mg/dL). Those with dysglycemia had higher BMI (26.2±3.9 vs 22.8±3.3 kg/m², p=0.039), longer dialysis vintage (4.5±2.9 vs 1.6±1.4 years, p=0.009), and fewer transplant listings (8/13 vs 0/10, p=0.005). Fasting glycemia was not elevated in dysglycemia. They also had a lower insulinogenic index (4.3±2.1 vs 7.0±3.6, p=0.04) and similar HOMA-IR. Dysglycemia was more common in hemodialysis than peritoneal dialysis (12/14 vs 1/9, p<0.001). CGM revealed a lower coefficient of variation in peritoneal dialysis (23.6% vs 15.7%, p=0.002). The GCT showed 85% sensitivity and 70% specificity for dysglycemia. A two-step approach using GCT ≥130 mg/dL to guide OGTT could avoid 40% of OGTTs while missing only 15% of dysglycemia cases.

Conclusions: The GCT has a sensitivity of 85% to diagnose dysglycaemia. Using a two-step approach of GCT and OGTT, up to 40% of OGTTs can be omitted, facilitating screening procedures for diabetes mellitus in kidney transplant candidates.

EP_574 EFFECT OF BONE MINERAL METABOLISM ON ANTIHYPERTENSIVE DRUG CONSUMPTION IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION

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Background: The prevalence of arterial hypertension (AH) after kidney transplantation (KT) is 55-90%. Optimal control of blood pressure after KT affects graft and patient survival. Persistent secondary hyperparathyroidism (sHPT) is described in 40-60% of patients in the first year after KT and can negatively affect the course of blood pressure after KT.

Methods: A multicentre prospective study of effect of bone mineral metabolism on AH drug consumption in the first year after KT. The cohort consisted of 148 patients after KT in 3 Slovak transplant centres, average age: 49.9 ± 13.4 years, men: 66.4%, secondary/tertiary KT: 12.5%, KT from a living donor: 10.5%. We monitored the length of dialysis, sensitization, donor type, length of cold ischemia, type of induction and IS, intact parathormone (iPTH), calcaemia (Ca), phosphathaemia (P) and magnesaemia (Mg), graft function and number of AH drugs at D0, M1, M3, M6, M12. In uni- and multivariate analysis, we correlated iPTH, Ca, P, blood pressure, graft function, post-transplant diabetes mellitus (PTDM) with the consumption of AH drugs.

Results: In our cohort, the prevalence of AH on the day of transplantation was 87.5%, the average number of AH drugs was 2.5 ± 1.6 (max. 4.1). In a univariate analysis, independent predictors of a higher combination of AH before KT were higher recipient age (p=0.0383), duration of dialysis (p=0.0068), higher iPTH concentration (p=0.0480), and higher Mg (p=0.0052). The multivariate analysis confirmed as an independent predictor of a number of AH drugs the higher age of the recipient at the time of KT (p=0.0486), the baseline concentration of iPTH and the time in dialysis. At 1 and 3 months after KT, the number of AH continued to be affected by time on dialysis and the onset of graft function. The relationship between increased iPTH and higher AH counts during the 1. year after KT was a constant factor, as was the persistent prospective relationship of iPTH to AH counts. In M3, we identified Mg supplementation as a protective factor for the number of AH drugs (p=0.0408).

Conclusion: Early KT, consistent treatment of sHPT before and after KT, and Mg supplementation are important mechanisms for improving blood pressure control and reducing the consumption of antihypertensive drugs after KT.

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EP_575 QUALITY OF LIFE ASSESSMENT IN LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS: A SCOPING REVIEW OF TOOLS AND OUTCOMES

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Background: The assessment of quality of life (QoL) in patients undergoing living-donor kidney transplantation (LDRT) is essential to understanding the long-term impact on health and well-being. In this study, we conducted a scoping review to examine the use of QoL assessment tools in kidney transplant recipients.

Methods: We extracted all articles related to QoL and LDRT available in MEDLINE Ovid, EMBASE Ovid, CENTRAL, and PSYCINFO. All articles explicitly reporting QoL measures in the context of LDRT, written in English and available in full-text, were included.

Results: The search identified 29 articles describing 18 different tools used to assess QoL. All the tools were adapted from various clinical settings to fit the context of living-donor kidney transplantation. The majority of the selected studies (72%) utilized the SF-36 questionnaire. The main themes explored included physical and emotional well-being and general health conditions. To a lesser extent, social integration, pain, and sleep were also investigated. However, areas such as professional life, sexual health, and the practical and emotional management of chronic therapy were not covered by these tools. Ten studies (34%) directly compared QoL outcomes between recipients of living-donor and deceased-donor transplants. A meta-analysis of four of these studies, involving a total of 770 transplant recipients (315 living-donor and 455 deceased-donor), highlighted superior QoL outcomes in living-donor kidney recipients across all assessed domains. Fourteen studies (48%) compared QoL outcomes before and after transplantation. The results showed a significant improvement in QoL after transplantation, regardless of the transplant type, although LDRT was associated with better outcomes.

Conclusions: LDRT is associated with superior QoL outcomes compared to all other available replacement therapies. The studies reviewed highlight the lack of QoL assessment tools specifically designed for the living-donor kidney transplantation context, as well as the need to investigate additional psychological domains relevant to this population.

EP_576 OUTCOMES OF BK VIRUS INFECTION IN KIDNEY AND KIDNEY/PANCREAS TRANSPLANTATION - RESULTS FROM A SCREENING PROGRAMME

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Background: Outcomes from routine screening for BKV viraemia in kidney and kidney/pancreas recipients have not been widely reported. Here, we present the outcomes of BKV infection detected during a screening programme started in December 2020.

Methods: Screening involved blood BKV PCR testing monthly for the first 6-months post-transplantation, and then every 3-months until 1-year, with immunosuppression (IS) reduction undertaken according to a protocol. Induction was with Alemtuzumab or anti-thymocyte globulin, with tacrolimus and mycophenolate maintenance. In this retrospective study, viraemia trends and graft outcomes are reported for 42 of 283 recipients who became viraemic and had a minimum of 12 months follow-up.

Results: Mean recipient age was 53±13 years. The overall incidence of BKV viraemia was 14%. First BKV positivity occurred after a median time from transplantation of 2.5 months (range 1.5-9 months). Viraemia at initial diagnosis was <4 log10copies/ml in 24 recipients, 4-5 log10copies/ml in 11 and >5 log10copies/ml in 7 recipients. Mean log10copies/ml at diagnosis was 4.06±0.93 and the mean peak level was 4.5±0.93. IS reduction was done in 31 recipients - 27 with a peak log10copies/ml of >4 and 4 with a log10copies/ml of <4. Four patients received Leflunomide. Clearance of viraemia occurred in 39/42 (93%) recipients after a median duration of 2.4 months (range 0.5-6.3), including in 11 patients in whom IS was unchanged. Mean S. creatinine level at diagnosis of BK viraemia was 131±68 µmol/l, 12-months post-transplantation was 115±44 and the latest value after a median follow-up of 32 months was 120±44 µmol/l. Nine recipients underwent a graft biopsy – 4 showed BKV nephropathy, 1 acute tubular necrosis, 3 acute cell-mediated rejection and 1 combined BKVN and rejection. All rejection episodes were steroid responsive. No grafts were lost in the follow-up period.

Conclusions: Despite the high incidence of BKV viraemia during screening, early immunosuppression reduction or observation alone undertaken according to a defined protocol resulted in clearance of viraemia in most recipients with preservation of graft function.

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EP_579 HEPATOCYTE GROWTH FACTOR DYNAMICS AS A PROGNOSTIC MARKER FOR SALVAGE LIVER TRANSPLANTATION

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Background: Hepatocellular carcinoma (HCC) is a challenging disease, and the choice between hepatectomy and primary liver transplantation (LT) remains a complex issue. Hepatectomy is being performed more often due to problems associated with liver transplantation, such as donor shortage, living donor risk, and economic cost. However, HCC recurrence after hepatectomy remains a significant problem. Identifying a reliable biomarker that can predict which patients require early salvage LT could help optimize treatment strategies and outcomes. Recent research suggests the potential role of hepatocyte growth factor (HGF) in forecasting HCC recurrence after hepatectomy.

Methods: This prospective study evaluated the clinical relevance of HGF recovery in predicting early recurrence of HCC after hepatectomy. HCC patients were categorized into two groups: those with recovered HGF levels (n=32) and those without HGF recovery (n=16). Detailed data was collected on patient demographics, tumor characteristics, operative details, and follow-up outcomes. The primary endpoints were recurrence-free survival (RFS) and overall survival (OS) up to 24 months post-hepatectomy. Univariable and multivariable analyses were conducted to assess the impact of HGF recovery on HCC recurrence.

Results: Significant differences were observed between the HGF-recovered and HGF-non-recovered groups. The non-recovered group showed a notably higher recurrence rate (43.8% vs. 9.4%, p=0.006) and lower 24-month RFS (14.1% vs. 46.4%, p=0.055). Vascular invasion and larger tumor size were also associated with higher recurrence rates. Multivariable analysis confirmed non-recovery of HGF as an independent predictor of early HCC recurrence (p=0.032 for 12 months; p=0.020 for 24 months).

Conclusions: This study emphasizes that HGF recovery serves as a crucial prognostic indicator for early HCC recurrence following hepatectomy. Patients who show poor HGF recovery post-hepatectomy may face an increased risk of early HCC recurrence. Monitoring HGF levels could help identify high-risk patients who might benefit from early salvage LT as a curative option. Further studies could establish HGF as a standardized prognostic marker to improve patient management and guide treatment decisions, particularly in salvage LT.

EP_580 HUMAN PARVOVIRUS B19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS: THERAPEUTIC STRATEGIES AND OUTCOMES

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Background: Human parvovirus B19 infection (PV-B19) is known to occur in the early post-transplant period causing pure red cell aplasia, refractory anemia, and persistent infection in solid organ transplant recipients (SOTR). Due to tissue tropism, PV-B19 occurs more commonly in kidney transplant recipients (KTR) than other SOTRs. The Centers for Disease Control and Prevention recommends implementing standard and droplet precautions in hospitalized SOTRs with suspected PV-B19. However, uniform therapeutic strategies against PV-B19 are lacking.

Methods: A total of Eight KTRs with allograft dysfunction and severe anemia were detected by RTPCR to have PV-B19 in the 30-72 days of post-transplant period. KTRs baseline characteristics, therapeutic approaches, graft and patient outcomes were studied

Results: All Eight KTRs presented with allograft dysfunction, fever and generalized weakness (Table-1). All KTRs had clinically significant disease (refractory anemia with Reticulocytopenia requiring multiple blood transfusions) and were treated with IVIG therapy, one of them with persistent graft dysfunction was resistant to IVIG therapy (with pure red cell aplasia on bone marrow aspiration biopsy), developed allograft rejection, and received off-label foscarnet therapy (60mg/kg/bd) for 5 days, to recover from PV-B19. One KTR succumbed to the tubercular cerebral abscess during PV-B19 illness.

Conclusions: Severe anemia due to PV-B19 requiring multiple blood transfusions can trigger rejection. Infected KTR should be segregated to prevent nosocomial transmission. IVIG is the cornerstone therapy in PV-B19, and foscarnet may play an essential role in IVIG-resistant PVB19.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age (years)	47	25	30	32	43	26	29	33
Sex	Male	Male	Male	Female	Male	Male	Male	Male
Type of transplant	Live	Deceased donor	Live	Deceased donor	Deceased donor	Live	Live	Live
Induction	ATG	ATG	No induction	ATG	ATG	No induction	ATG	ATG
Immunosuppression	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone	Tac, MMF, Prednisolone
Time of PVB19 Detection and transplant	40 days	45 days	15 days	42 days	35 days	32 days	35 days	72 days
Anaemia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lowest HB	4.2	4.0	4.1	5.1	4.8	6.0	4.2	4.8
No of PRBC transfusion	12 units	2 units	3 units	2 units	2 units	2 units	2 units	6 units
Leukopenia	Yes (1200)	No	No	No	No	No	No	No
Thrombocytopenia	No	No	No	No	No	No	No	No
Clinical Symptoms	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Interruption of immunosuppression	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Specific Treatment	IVIG, foscarnet,	IVIG	IVIG and Tac changed to Cyclosporine	IVIG	IVIG	IVIG and Tac changed to Cyclosporine	IVIG	IVIG
Graft dysfunction	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
LOHS (days)	60	22	25	12	25	11	7 days	15 days
Renal biopsy	TCMR	Not done	Not done	Not done	Not done	Not done	Not done	Not done

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EP_581 EARLY, VERY HIGH-TITRE CONVALESCENT PLASMA THERAPY IN CLINICALLY VULNERABLE INDIVIDUALS WITH MILD COVID-19

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Background: COVID-19 convalescent plasma (CCP) is a treatment option for COVID-19. The COVIC-19 trial evaluates the safety and efficacy of early, very high-titre CCP in immunocompromised individuals with mild COVID-19.

Methods: This randomized, controlled, open-label trial assessed CCP in immunocompromised patients (n=120) with mild COVID-19 in 10 clinical trial centres across Germany, France and the Netherlands (EudraCT 2021-006621-22; NCT05271929). Patients were randomized 1:1 to receive either standard of care (SoC) alone (SoC group) or SoC and two units of CCP. The majority of patients (n=88, 75%) had received organ transplantation. The majority of patients had received ≥ 2 SARS-CoV-2 vaccinations (n=108, 92.3%). The primary endpoint was hospitalization for progressive COVID-19 symptoms or death by day 28 after randomization, analyzed on a modified intention-to-treat basis (117 patients).

Results: Between April 11, 2022, and November 27, 2023, 120 patients were enrolled. Patients in the CCP group received a median of 559 ml CCP from convalescent, vaccinated donors with very high levels of SARS-CoV-2 antibodies (median 81,810 IU/ml) at a median 4 days after symptom onset. The primary outcome occurred in 5/58 patients (8.6 %) in the SoC group and in 0/59 patients (0 %) in the CCP group, difference -8.6% (95 % confidence interval of difference -19% to -0.80%; p-value 0.027; Fisher's exact test). The course of SARS-CoV-2 antibodies in the patients demonstrated a passive transfer of antibodies by the CCP, in particular neutralizing effects against new SARS-CoV-2 variants. Whole genome sequencing of SARS-CoV-2 in patients during follow-up showed significant intra-host viral evolution, but without differences between groups. CCP was well tolerated. Twelve patients (20%) in the CCP group experienced 14 serious adverse events and 21 patients (36%) in the SoC group experienced 33 serious adverse events, none were considered to be related to the study intervention.

Conclusions: Early administration of high-titre CCP can prevent hospitalization or death in immunocompromised patients with mild COVID-19.

EP_582 ANTIBODY MEDIATED REJECTION AND BKV NEPHROPATHY: ONE CAUSES THE OTHER. EXPERIENCE OF A TRANSPLANT CENTER

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Background: Antibody-mediated rejection (AMR) and BKV nephropathy (BKVN) cause graft loss. Treatment of both complications is not always effective. In hyperimmune patients or with a history of rejection the action that takes place is the increase in immunosuppression which causes viral infections such as BKV. In patients with BKV viral replication, the action taken is the reduction of immunosuppression, which can lead to an increased risk of rejection, as AMR. The literature on the co-existence of AMR and BKVN is scarce.

Methods: We analyzed the cases of 4 kidney transplant patients with a coexisting BKVN with AMR at IRCSS ISMETT, a multi organ transplant center in Palermo.

Results: In two patients' minimization of immunosuppressive therapy controlled viral replication, which prevented the development of overt BKVN but both patients developed donor-specific antibodies with antibody-mediated rejection and slowly graft loss. The other two patients with a history of AMR developed BKVN and were treated with mTOR and pulse intravenous immunoglobulin (IVIg) after the start of viral replication. With the start of mTOR and maintenance of adequate doses of immunosuppressive therapy, both patients maintained a stable GFR, despite lower for their transplant age. At the same time, therapy with IVIg allowed to control viral replication and the presence of donor-specific antibodies

Conclusions: The coexistence of BKVN and RA, although rare, when it occurs can be a diagnostic and therapeutic dilemma, as they are at opposite ends of the immune spectrum. In our experience, the use of mTOR inhibitors in hyperimmune patients may protect against the risk of BKVN and should be more widely used. The use of immunoglobulins for their immunomodulatory properties as therapy for BKVN without excessively reducing immunosuppression may protect against the risk of AMR. In the future, cell therapy using ex vivo expanded virus-specific T cells and specific vaccinations could represent a breakthrough in the prophylaxis of the most immunosuppressed patients.

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Infectious diseases, malignancies & long term challenges

EP_583 SMALL INTESTINE NEUROENDOCRINE TUMOR IN A DUAL KIDNEY-HEART TRANSPLANT RECIPIENT- A CASE REPORT

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Background: Cancer is an important cause of mortality in solid organ transplant (SOT) recipients. Patients under immunosuppression are at a higher risk of tumor formation, tumor progression or tumor recurrence. The risk of malignant transformation depends on type of immunosuppressive medication, its load and duration. Neuroendocrine neoplasms (NENs) are relatively rare malignancies that most frequently occur in the intestines, pancreas and lungs. Little is known about their incidence, behavior and prognosis in SOT recipients. There is evidence of indolent course of NENs under transplant-related immunosuppression and of small volume, locally metastasized disease in transplant recipients not being a contraindication to organ transplant.

Methods: We report a clinical case of an small intestine NEN in a dual combined kidney-heart transplant recipient

Results: A 50-year-old female patient with systemic lupus erythematosus (SLE), lupus nephritis class III and severe ischemic cardiopathy received dual combined kidney-heart transplantation 25 and 8 years ago. She presented to the emergency department with hematochezia and hemorrhagic shock. An abdominal CT-scan objectivated an active bleeding from a branch of the ileocolic artery. Angiography and coiling were not successful in stopping the bleeding and a laparotomy was performed. A tumor in the small bowel was identified and resected in toto. The histologic analysis showed a highly differentiated NEN of the ileum with a maximal diameter of 1.2cm (pT2, pN0, L1, V0, G1, mitose rate <1/2mm2, Ki-67<1%). The resection margins were free of tumor and there wasn't any evidence of metastases in the abdominal CT-scan. Hemoglobin stabilized in the postoperative setting and the patient could be discharged. A Gallium-DOTATOC-PET to complete the staging is pending. The immunosuppressive therapy, consisting of tacrolimus and everolimus, was maintained as everolimus is known for its negative effect on angiogenesis and tumor growth.

Conclusions: NENs is a rare and mostly indolent entity of tumors with an unclear incidence in SOT recipients. This case should incentivate the transplant community to find out more about their behavior, prognosis, management and follow-up in retrospective analyses and longitudinally observation in transplant cohort registries.

Transplant immunology & immunosuppression

EP_584 IMMUNOLOGIC RISK STRATIFICATION BY COMBINING HLA-EPLET AND PREDICTED INDIRECTLY RECOGNIZABLE EPITOPE

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Background: Although limiting the number of HLA mismatches between donor and recipient effectively reduce the risk of kidney allograft rejection, this approach has some limitations.Several algorithms have been developed, aiming to predict alloimmune reactivity. HLA matchmaker (HLA-EPMM) and PIRCHE-II (Predicted Indirectly Recognizable HLA Epitopes) algorithms are promising solutions to estimate the risk for alloreactivity after kidney transplantation.

Methods: We examined 200 kidney transplant recipients from 2001 to 2023. The primary purpose of our study was to verify whether a combination of HLA-EPMM and PIRCHE-II algorithms can improve risk stratification of kidney transplantation. The 2nd purpose was to evaluate whether a nadir of Tacrolimus concentration or intrapatient variability is associated with the development of de novo DSA, acute rejection, chronic ABMR, and graft failure regarding high HLA-EP MM or high PIRCHE-II.

Results: PIRCHE-II or Total EP MM alone was insufficient to predict graft failure. When each of them was combined with IPV or a nadir of tacrolimus concentration, the high/high group had a statistically significantly higher risk of allograft failure than that of the low/low group respectively. High- PIRCHE / high-EPMM group had significantly the highest risk of graft failure compared with the other 3 groups. Independent predictors of graft failure on multivariate analysis were Chronic ABMR, and the low nadir of tacrolimus trough level.

Conclusions: HLA-Total EP MM cut-offs alone did not predict the risk of graft failure, however, if used in combination with PIRCHE-II. We demonstrated that High- PIRCHE and Total EP MM group is significantly the worst graft outcome compared with high-/low-, low-/high-, and low-/low- PIRCHE and EP MMs, respectively. Together with HLA EP MM, The PIRCHE-II algorithm can provide a better estimated alloreactive risk for individual patients and eventually an improved allograft kidney survival.

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Transplant immunology & immunosuppression

EP_585 CANCER AFTER ADULT LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Cancer after KT can cause death with functioning graft (DWFG) and shorten the long-term graft survival. The impact of immunosuppressive (IS) medications on cancer before graft failure has not been investigated meticulously including the blood levels of IS medications.

Methods: This single-center, retrospective cohort study included 1274 adult living donor KTs between January 2008 and December 2021. Cancer before graft failure was identified in 141 recipients. Mortality and DWFG free survival was compared between recipients with and without cancer before graft failure. The risk factor of cancer before graft failure was investigated using multivariate Cox regression analysis. In each IS regimen with steroids, calcineurin inhibitors (CNIs: cyclosporine, tacrolimus, and extended release tacrolimus), and mycophenolate mofetil (MMF), trough levels of CNIs and MMF and exposure to CNIs and MMF were compared between recipients with and without cancer before graft failure. The impact of cancer screening examinations on the DWFG was compared among recipients with cancers incidentally or symptomatically detected, recipients with cancer detected by screening examinations, and recipients without cancer.

Results: Mortality was significantly higher in the recipients with cancer ($P < 0.001$, Hazard ratio (HR) 7.97, 95% confidence interval (CI) 4.99-12.72). DWFG was identified more frequently in the recipients with cancer ($P < 0.001$, HR 9.72, 95% CI 5.69-16.59). The risk factors of cancer before graft failure were recipient age and Brinkman index. Trough levels of IS medications and exposure to IS medications did not demonstrate any significant differences in every immunosuppressive regimen. DWFG was significantly more identified in recipients with cancers incidentally or symptomatically detected than in those with cancer detected by screening examinations (P = 0.040, HR 2.20, 95%CI 1.04-4.65).

Conclusions: The administered IS medications and blood levels of IS medications were not the significant risk factors of cancer before graft failure. Administration of immunosuppressive medications itself can be the risk of cancer. Cancer screening examinations might be useful to prevent DWFG due to cancer.

EP_586 DONOR-DERIVED CFDNA: FEASABILITY ASSESSMENT OF A NOVEL INDEL-BASED NGS BIOMARKER IN RENAL TRANSPLANT

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Background: Renal transplant is the optimal treatment for end-stage kidney disease (ESKD). Antibody-mediated rejection (ABMR) remains a leading cause of graft failure, with up to 20% of transplants failing within five years. Monitoring *de novo* donor-specific antibodies (DSAs) and early detection of ABMR are crucial for timely treatment and graft survival. Donor-derived cell-free DNA (dd-cfDNA) is a promising emerging non-invasive biomarker for detecting allograft injury. Although dd-cfDNA assays are increasingly implemented, further validation, particularly in high-immunological risk recipients is required. Building on our prior HLA-specific antibody research, the HLA-AB study (ClinicalTrials.gov NCT06025240) evaluates a novel next-generation sequencing (NGS) indel-based assay for detecting dd-cfDNA as a non-invasive biomarker of allograft injury.

Methods: Twenty-four 'high-immunological risk' renal transplant recipients (cRF >20%, level IV HLA mismatch, or re-transplant) were recruited between October 2023 and July 2024 in Liverpool University Hospitals. Ethics approval was obtained (REC 23/WA/0260). Blood samples were collected at 6- and 12-months post-kidney transplant. dd-cfDNA was extracted and analysed using the OneLambda Devyser Accept cfDNA kit and Illumina MiSeq system, with correlations to renal function, virology, existing biopsies, ultrasound and DSA results.

Results: Preliminary data from 14 recipients show dd-cfDNA levels ≥1% correlation with allograft injury and possible calcineurin inhibitor toxicity. Intermediate dd-cfDNA levels (0.5-1%) link with emerging DSAs, supporting early immunological injury detection. Levels ≤0.5% correlate with stable graft function. dd-cfDNA levels <0.5% are observed in viral replication without graft injury. Full data for 24 recipients at 6- and 12- months timepoints will be presented.

Conclusions: This *proof-of-concept* study demonstrates the feasibility of using indel-based NGS assay to detect dd-cfDNA as a non-invasive biomarker in renal transplant recipients. We are the first UK centre to pilot the Accept assay which is a promising avenue for monitoring high-risk transplant recipients and potentially reducing the need for invasive biopsy. Further research will refine its integration into a pragmatic clinical algorithm.

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Transplant immunology & immunosuppression

EP_587 THE RELATIONSHIP BETWEEN REBOUND THYMIC HYPERPLASIA AND REJECTION RISK IN RENAL TRANSPLANTATION

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Background: The thymus gland is a lymphoid organ located in the anterior mediastinum, especially associated with T cell proliferation. Rebound thymic hyperplasia may develop in the thymus after stressful situations for the body, such as immunosuppression, chemotherapy, major surgery or burns. Purpose of the study; To determine the incidence of rebound thymic hyperplasia in the clinical follow-up of these patients by retrospectively scanning the thorax CT scans of renal transplantation patients performed in our hospital. Additionally, our study aimed to evaluate the relationship between thymic hyperplasia and allograft rejection.

Methods: 346 patients who underwent renal transplantation surgery in our hospital between January 2012 and August 2024 were evaluated. All control CT scans between the ninth and fifty-fourth months after the operation were retrospectively scanned. A total of 630 CT images were evaluated.

Results: 112 of the 346 patients evaluated were excluded from the study for various reasons.Thymic hyperplasia was detected in 10 (4.71%) of the remaining 234 patients. Pathology-proven rejection was detected in 4 of these 10 patients (40%).In these patients, acute T cell-mediated rejection was detected in 3 of them and acute humoral rejection was detected in 1 of them, on the basis of chronic rejection.

Conclusions: We think that the possible immune stimulation that may develop due to hyperplasia in the thymus in patients receiving immunosuppression therapy after transplantation surgery may cause an increase in the risk of rejection.

EP_588 ENTERIC COATED BUDESONIDE FOR RECURRENT IGA NEPHROPATHY: CASE SERIES

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Background: IgA nephropathy is a common glomerular disease. The exact incidence of recurrence of IgA nephropathy after kidney transplantation is not known, but varies from 20-30%. Few risk factors such as related living donors, the presence of donor-specific antibodies, and formation of denovo donor-specific antibodies are implicated. Not many clinical trials are evaluating the treatment regimens for the recurrence of IgA nephropathy in transplant, although multiple trials are in progress for native disease. In this case series, we treated four patients with recurrence of IgA nephropathy in renal transplant with enteric-coated Budesonide.

Cases: **Patient 1:** -a 53-year-old Caucasian man underwent an LRKT in 2021. In March 2023, the patient had recurrence of IgA nephropathy and started Budesonide and SGLT2i. 4 months later eGFR improved to 38mls/min from 30mls/min and Proteinuria dropped to <50 from 123. At one-year follow, eGFR remains at 35mls/min and proteinuria remains <50. **Patient 2**: A 40-year-old Indian man underwent a LUKT in 2018. In September 2023, the patient had recurrence of IgA nephropathy and was started on Budesonide and SGLT2i. At 4 months there was no improvement of eGFR, but uPCR improved to 180 from 380. At one year proteinuria has improved to 77, and eGFR remains at 34mls/min. **Patient 3:** A 42-year-old Caucasian man underwent LRKT in 2011. The patient had a recurrence of IgA nephropathy in 2018. Budesonide and SGLT2i were started in April 2024 for worsening uPCR 380 from 150 and eGFR drop to 25mls/min. 4 months post-initiation eGFR improved to 28mls/min, but there was no improvement in uPCR. Now at 8 months, eGFR remains at 25mls/min and uPCR remains at 463. **Patient 4:** A 43-year-old Caucasian man with ESRD secondary to collapsing FSGS and IgA nephropathy underwent an LRKT in 2022. In March 2023, the patient was found to have recurrence of IgA nephropathy without evidence of FSGS for which he started Budesonide and SGLT2i. 4 months later, proteinuria improved to 180 from 350 and eGFR stabilized at 28mls/min. A year later eGFR was worse at 26mls/min, and uPCR crept up to nephrotic range.

Conclusions: Although it is a small number, enteric-coated Budesonide appear to benefit in circumstances where there is non-nephrotic range proteinuria and early initiation at onset of proteinuria, and in patients with single diagnosis.

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EP_589 PHARMACOGENETIC PROFILING TO OPTIMISE TACROLIMUS DOSING: A SINGLE TRANSPLANT CENTER EXPERIENCE

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Background: Pharmacogenetics (PGx) is the study of genetic factors contributing to the variability of drug response. Evidence cites up to 45% of tacrolimus interpatient variability may be attributed to genetic differences in cytochrome (CYP) 3A5. CYP3A5 expressors display enhanced tacrolimus clearance, lower drug levels and increased risk of rejection. We explore the utility of pre-emptive PGx profiling on tacrolimus targets in our single Australian transplanting center.

Methods: PGx testing for CYP3A5 genotypes was conducted for wait-listed patients during a 10-month period. CYP3A5 expressors identified received genotype guided dosing (GGD) with 1.5 times the standard weight-based dose according to Clinical Pharmacogenetic Implementation Consortium guidelines.

Results: PGx testing was done in 81 wait-listed patients with 17 (21%) identified as CYP3A5 expressors with enhanced tacrolimus clearance. A total of 25 proceeded to receive a kidney transplant, of which 7 were CYP3A5 expressors. The tacrolimus dose needed for target attainment for CYP3A5 expressors was 3 times higher compared to non-expressors (0.184mg/kg vs 0.06mg/kg; p value=0.0017). It took approximately 2.5 times longer for CYP3A5 expressors without GGD to reach therapeutic levels (8 days vs 3 days). This is in contrast to CYP3A5 expressors who did receive GGD (n=5). This cohort achieved target levels within 2 days, comparable to non-expressors and required less dose changes 1-month post-transplant (6.45 vs 4 per patient).

Conclusions: Pre-emptive PGx profiling had utility in the identification of at-risk metabolic phenotypes as well as in the implementation of personalised tacrolimus dosing for kidney transplant recipients. Despite small numbers, there was an observed benefit in optimising tacrolimus dosage requirements, shortening length of time to target attainment and reducing the number of dose changes required post-transplant.

EP_590 GUARDIAN IN KIDNEY TRANSPLANTATION: ORCHESTRATING IMMUNE BALANCE WHILE GUARDING AGAINST REJECTION

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Background: CD47 plays a pivotal role in renal immunomodulation by preventing macrophage-mediated phagocytosis and maintaining immune balance. Its presence across renal and immune cells ensures homeostasis, dynamically adapting to inflammation and immune stimuli. However, dysregulation of CD47 expression can disrupt this balance, promoting immune-mediated damage and increasing the risk of allograft rejection (AR). This study investigates CD47's renal expression to evaluate the immune environment and identify potential risks for rejection.

Methods: We analyzed CD47 expression in the renal allografts of 126 patients, focusing on antibody-mediated rejection (ABMR) and mixed rejection involving T-cell-mediated and ABMR. CD47 was assessed in key renal compartments—peritubular capillaries (PTCs), endothelial cells (ECs), interstitial cells (ICs), tubules, and glomeruli—and its correlation with interstitial fibrosis (IF), transplant glomerulopathy (TG), and arteriosclerosis (TA) in follow-up biopsies was evaluated.

Results: CD47 expression in ECs and ICs significantly correlated with AR type ($p<.05$). CD47 expression in tubules, mesangium, ECs, and ICs was negatively associated with tubulitis, glomerulitis, PTCitis, interstitial macrophage and lymphocyte infiltration ($p<.01$). Reduced CD47 levels in ECs and other renal compartments were linked to vascular rejection, proteinuria, PTC destruction, and higher C4d grades ($p<.001$). Furthermore, decreased CD47 expression in ECs, ICs, tubules, and interstitium increased the risk of IF, TG, TA, and proteinuria development, and graft loss ($p<.001$).

Conclusions: CD47 plays a key role in maintaining renal immune balance through its expression in intrinsic renal and infiltrating immune cells. Its downregulation can disrupt this balance, promoting immune-mediated damage and AR. Studying CD47 expression patterns in renal biopsies offers critical insights into graft immune status and helps predict risks of rejection, injury, and graft loss.

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EP_591 SCLERODERMA RENAL CRISIS IN RENAL TRANSPLANT PATIENT

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Background: Systemic sclerosis is an autoimmune condition causing fibrosis of the skin and adjacent tissues. Sclerosis of medium and small-sized arteries is also a hallmark of this condition. Scleroderma renal crisis is rare and occurs in only 5-10% of patients with diffuse scleroderma. The incidence or prevalence of scleroderma renal crisis in transplant patients is not known. Here we present a rare scenario where a patient developed scleroderma post-transplant and then progressed to develop scleroderma renal crisis.

Case presentation A: 79-year-old lady with a background of renal transplant, and cutaneous scleroderma, was admitted with extreme fatigue, bluish discoloration of fingers, and digital ulceration. Blood pressure was 160/90mmHg. Tests showed creatinine of 300µmol/L from the previous result of 180µmol/L. Two months prior, the patient suffered with UTI, where creatinine increased to 180 from a three-year baseline of 100µmol/L. Transplant ultrasound showed reduced perfusion throughout with possible transplant artery stenosis. Biopsy showed mucoid changes in arteries and arterioles (Figures 1 and 2). Glomerular changes showed capillary crenation (Figure 2). Features on biopsy were consistent with scleroderma renal crisis. Treatment comprised of iloprost infusion for five days. Mycophenolate dose was increased to 750mg twice a day. Tacrolimus and oral Prednisolone were stopped. Her medical history included a renal transplant in December 2020 for ESRD secondary to type 2 diabetes and hypertension, and hereditary hemorrhagic telangiectasia. Cutaneous scleroderma was diagnosed in 2021, one year post renal transplant.

Conclusions: Scleroderma renal crisis in renal transplant is a rare complication. Treatment strategies are unclear. In our case, treatment with ACEi, stopping Tacrolimus stabilized renal transplant function. Although it is tempting to use IV methylprednisolone for possible rejection, while waiting for biopsy results, caution need to be exercised due to potential nature of intravenous steroids making scleroderma renal crisis worse.

Figures

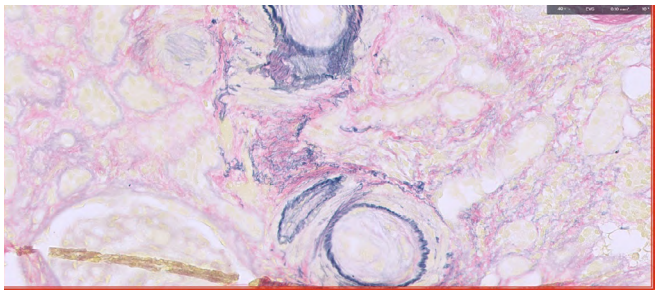

Figure 1: Mucoid changes in the arterioles along with duplication of elastic lamina

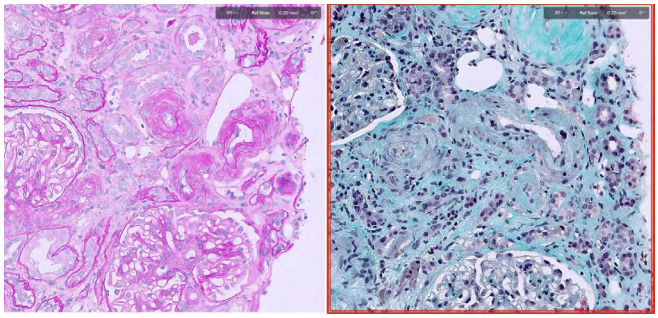

Figure 2:PAS and trichrome stain showed arteriolar mucoid changes.

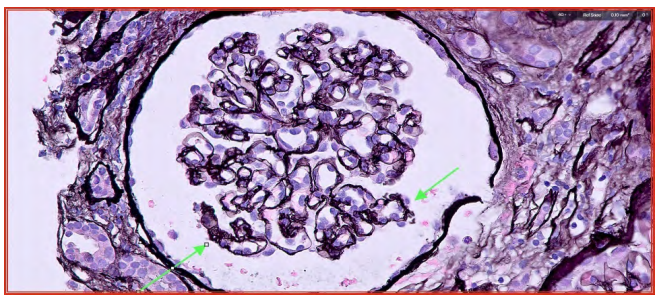

Figure 3: Silver stain showing glomerular capillary loop crenation.

EP_592 DE NOVO HLA ANTIBODY PREDICTORS IN KIDNEY TRANSPLANTATION: LIMITED SUCCESS WITH MACHINE LEARNING

Abhishek Sharma[1], **Ajay Madhusuthanan**[2], *Hemant Sharma*[3]

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Background: Despite technological advances in machine learning algorithms (MLA) and artificial intelligence, predicting de novo HLA antibody development post-kidney transplantation remains challenging. A critical review examined whether modern computational approaches have advanced our understanding beyond traditional statistical methods.

Methods: We analysed recent studies (2020-2024) employing machine learning techniques to predict De Novo HLA antibody formation in kidney transplant recipients, focusing on model performance, novel predictors identified, and clinical applicability.

Results: Machine learning models consistently identify pre-transplant sensitization as the dominant predictor, with reported feature importance ranging from 30-60% across studies. Other significant predictors mirror well-established risk factors: female gender (OR 1.5-2.0), previous transplantation (HR 2.1-3.2), and HLA mismatching. Despite sophisticated methodologies including neural networks, gradient boosting, and explainable AI techniques, models demonstrate poor predictive performance in unsensitized recipients (AUC 0.55-0.65). Complex relationships suggested for factors like cold ischemia time often lack biological plausibility or clinical validation.

Conclusions: Current machine learning approaches, while methodologically sophisticated, have failed to identify hidden factors influencing de novo HLA antibody development. The consistent reliance on established clinical predictors suggests that either crucial biological markers remain unmeasured or that antibody development involves stochastic processes beyond current detection methods.

Study	Key ML Finding
Ravindhran et al.	Hybrid ML models showed best performance for graft survival prediction
Cornaby & Weimer	PCA identified HLA antibody patterns
Bae et al.	ML not superior to traditional methods
Paquette et al.	ML-based decision support tool development

Table 1:

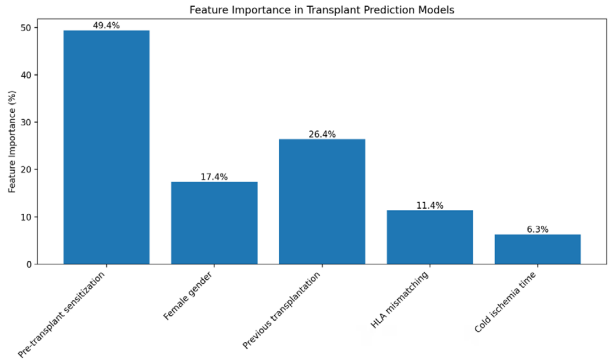

Fig 1:

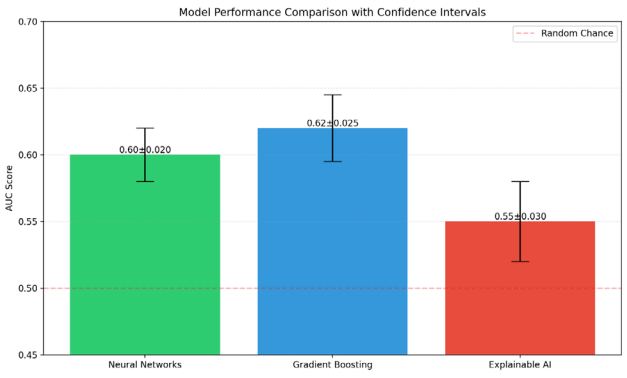

Fig 2:

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EP_593 DOES BK VIRAEMIA AND MANAGEMENT IMPACT GRAFT FUNCTION IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS?

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Background: BK does not cause disease in the immunocompetent population. In kidney transplant (KT) recipients it can result in poor graft function (GF), and ultimately graft loss. Although advances in post-KT immunosuppression benefit GF by reducing early rejection risk. This increases BK viraemia (BKV) and BK-virus associated nephropathy (BKVN) episodes. BK's ubiquitous nature makes screening for BK pre-transplant futile. The 2009 KDIGO adult guidelines focus on monthly BKV screening for the first-year post-KT via serum polymerase chain reaction. Following detection, prompt immunosuppression reduction is recommended. BK infection typically occurs pre-adolescence. Therefore, pre-school age children are likely to be seronegative pre-transplant, increasing BKV risk and its sequalae following KT. There are no guidelines for detecting and managing BKV in paediatric renal transplant recipients (pRTR).

Methods: A retrospective study, involving 40 pRTR who received a KT in Leeds Children's Hospital's between 2018-2022, was completed. This allowed for a 12-month minimum follow up period post-KT, from starting data collection. BKV and BKVN episodes and immunosuppression changes were recorded, alongside baseline and transplant characteristics. Chi squared and multivariate analyses were conducted, looking at associations between BKV/BKVN management, clinical sequalae and potential contributing factors.

Results: 17.5% (22/40) had an episode of BKV and 5% (2/40) BKVN. Although 46% of variation in BK viral load reduction can be explained by Figure 1, no significant association was found between immunosuppression reduction and change in BK viral load. There was no statistically significant association between immunosuppression changes and subsequent improvement in GF.

Conclusions: The BKV and BVKN prevalence is similar to existing literature (Hamasaki et al., 2019; Kwon et al, 2019). Whilst it is unclear from the results whether reducing immunosuppression after BKV detection improves GF; the assumption remains that not reducing immunosuppression increases the likelihood of developing BKVN and subsequent GF deterioration. BKV remains a barrier to successful transplantation in pRTR. Standardised BKV guidelines in pRTR are needed to evaluate the efficacy of current management and novel treatments.

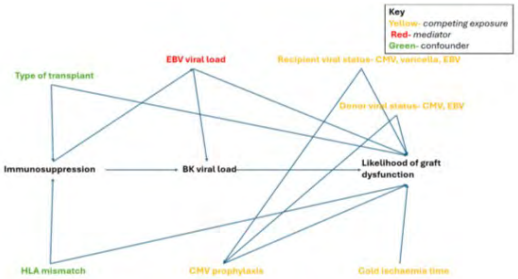

Figure 1- Direct Acyclic Graph showing the confounders, mediators and competing exposures considered during the study

Patient	CMV status		CMV Prophylaxis	EBV Status		CIT	BKV viremia post-transplant (months)	No. of BKV episodes	No. of biopsies	Biopsy Results	Was IS reduced after identification of BKV?	How long did BKV persist?	Did they have any other episodes?	eGFR (ml/min/1.73m²)		Graft Dysfunction		Hypertension 12 months post-transplant
	Donor	Recipient		Donor	Recipient									6 months	12 months	6 months	12 months	
1	Positive	Positive	Valgancyclovir	Positive	Positive	LRD	2	1	5	Antibody mediated rejection and T cell rejection	No- tacrolimus reduced by 0.5mg just over 4 weeks later and mycophenolate reduced by 50mg 6 weeks later	3 months	EBV	52	73	Yes- Stage 3a	No- Stage 2	Yes
2	Negative	Negative	Valgancyclovir	Positive	Positive	6hrs 41mins	5	1	2	Acute cellular rejection BANFF Grade 1B	no	1 month	EBV	78	130	No- Stage 2	No- Stage 1	No
3	Indeterminate	Negative	Valgancyclovir	Positive	Negative	2hrs 56mins	3	1	1	BKN	No- azathioprine stopped after 3 months	17 months	EBV	Not available- refuse d/COVID	76	N/A	No- Stage 2	No
4	Negative	Negative	None	Positive	Positive	12hrs 48mins	<1	1	0	N/A	Yes- mycophenolate stopped	1 month	No	64	88	No- Stage 2	No- Stage 2	No
5	Positive	Negative	Valgancyclovir	Positive	Positive	2hrs 35mins	23	2	1	BANFF Class 3 Borderline rejection	Yes- mycophenolate and prednisolone reduced on day of detection	1st episode- 4 months	EBV	79	98	No- Stage 2	No- Stage 1	No
6	Positive	Positive	None	Negative	Negative	5hrs 21mins	1.5	2	3	Borderline T cell rejection and BKN	Yes- prednisolone reduced within 2 weeks, mycophenolate stopped after 3 months	1st episode- 12 months	EBV	46	48	Yes- Stage 3a	Yes- Stage 3a	No
7	Positive	Positive	None	Positive	Negative	2hrs 50mins	5	1	2	No signs of rejection	No data	3 months	EBV	140	128	No- Stage 1	No- Stage 1 but there is 2+ haematuria	No

Table 1- Summary of the transplant characteristics, BK characteristics and transplant outcomes in patients with a detected episode of BKV. Graft dysfunction was defined based on the categorisation of chronic kidney disease (CKD). This is described as Stage 3 CKD and above, eGFR less than 60 ml/min/1.73m2, or the presence of haematuria or proteinuria in Stage 1 CKD and above. Patients 4,5 and 6 had a reduction in immunosuppression and patients 3 and 6 developed BKN.

EP_594 THE SYSTEMCHANGE INTERVENTION IMPROVES MADICATION-TAKING HABIT: SECONDARY ANALYSIS OF THE MAGICSTUDY

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Background: Change Habits by Applying New Goals and Experience (SystemCHANGE™), which harnesses patients' established, reoccurring, reliable personal systems to support medication taking to become a dependable routine, has previously been shown to improve medication adherence in adult kidney transplant recipients. The goal was to perform a secondary data analysis from two previous trials, the Medication Adherence Given Individual Change (MAGIC) and the MAGIC Turkish studies, investigating the effect of SystemCHANGE™ on medication-taking habit and medication adherence.

Methods: Electronic medication adherence data from the 126 participants in the two trials was retrieved. A recently developed habit index, quantifying week-by-week consistency in the pattern of medication intakes, was computed for each participant during screening, during each of the 6 months of intervention, and during each of the 6 months of maintenance. The habit index ranges between 0 and 1. Medication adherence was measured using the Medication Event Monitoring System (MEMS®).

Results: Data from 126 participants were analyzed. Habit strength and medication adherence were lower for United States participants ($p < 0.001$ for both variables). During the intervention phase, adherence was higher for both groups ($p = 0.008$) and habit was higher only for the SystemCHANGE™ group ($p = 0.007$). For United States participants, the effect of intervention on adherence and habit was stronger and remained during the maintenance phase ($p < 0.001$ and $p = 0.044$).

Conclusions: The SystemCHANGE™ intervention, focused on linking medication taking to habits, reflects numerically in the habit index with a positive effect on the habit index and, consequently, on medication adherence.

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EP_595 INCIDENCE OF AR USING ICI TO DOWNSTAGE HCC PRIOR TO LT - A SINGLE CENTER STUDY

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Background: Hepatocellular carcinoma (HCC) is a primary indication for liver transplantation in China, with evolving inclusion criteria, particularly concerning tumor downstaging beyond Milan criteria before transplantation. Immune checkpoint inhibitors (ICIs), targeted therapies, and their combination have become pivotal in pretransplant treatment, showing promising oncological benefits. However, these therapies are associated with a higher incidence of acute rejection (AR). This prospective analysis evaluated one-year outcomes, focusing on AR, recurrence-free survival (RFS), and overall survival (OS).

Methods: Between October 2018 and December 2023, 69 patients underwent LT for HCC, with 59 receiving tumor downstaging prior to LT. The cohort was divided into three groups based on downstaging therapies: • **Group 1 (n=41):** TACE, RF ablation, or resection. • **Group 2 (n=6):** Targeted therapy alone. • **Group 3 (n=12):** Combination of targeted therapy and ICIs. The median age of the cohort was 50.5 years, comprising 56 male and 3 female patients. Immunosuppression followed a standardized protocol involving Basiliximab, Tacrolimus (Tac), initial Mycophenolate Mofetil (MMF) later switched to Sirolimus, and steroids.

Results: The median interval between the conclusion of ICI therapy and LT was 41.2 days with a range of 10-87 days. At one year post-transplant, no cases of AR were reported. RFS rates for Groups 1, 2, and 3 were **93%, 84%, and 84%**, respectively, while OS rates were **85%, 100%, and 75%**. The TNM staging at transplantation was as follows: • **Group 1:** 13 patients with T2-T4 and 28 with Tx-T1. • **Group 2:** 3 patients with T2 and 3 with Tx-T1. • **Group 3:** 4 patients with T2-T3 and 8 with Tx-T1.

Conclusions: The prospective evaluation of LT recipients with prior ICI therapy revealed no increased incidence of AR compared to those without ICI therapy. This outcome may be attributed to our standardized protocol and meticulous postoperative monitoring, including immunosuppression management. RFS and OS at one year were comparable across all three groups.

EP_596 PHENOTYPES OF INFLAMMATORY PANCREATIC ENDOTHELIAL CELLS SUGGEST MECHANISMS OF IMMUNOTHROMBOSIS

Christophe Masset[1], Nathalie Gerard[2], Richard Danger[3], Sarah Bruneau[4], Gaelle Tilly[5], Manuel Laslandes[2], Sophie Brouard[6], Magali Giral[7], Gilles Blancho[8], Julien Branchereau[9], Benoit Mesnard[2], Diego Cantarovich[10], Nicolas Degauque[11], Jacques Dantal[12]

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Background: The pathophysiology of immunothrombosis following pancreas transplantation remains insufficiently understood. In this study, we analyzed the phenotype of pancreatic endothelial cells (hPAEC) in response to various inflammatory stimuli to assess their response compared to glomerular endothelial cells (hGENC).

Methods: We compared hPAEC and hGENC at the basal state using single-cell RNA sequencing and flow cytometry analysis. We further investigated their responses to inflammatory cytokines in an in-vitro model of cultured endothelial cells. Finally, we explored donor-derived molecules that could contribute to the activation of hPAEC.

Results: At the basal state, hPAEC exhibited a more inflammatory and thrombotic phenotype than hGENC. Their responses to inflammatory cytokines were broadly comparable, except for IL6 + sIL6r, which led to significantly higher activation of hPAEC. Furthermore, no specific effects of Angiotensin II or Resistin were observed. When cultured with donor sera, hPAEC exhibited a heterogeneous response. Notably, donors whose sera induced activation of hPAEC had significantly higher levels of sCD40L and MMP-9. Kidneys transplanted from these donors had significantly worse allograft outcomes compared to others.

Conclusion: The pancreatic endothelium appears more susceptible to activation both at the basal state and in response to inflammatory stimuli. The combination of donor-derived molecules and cytokines released during ischemia/reperfusion likely accumulates, ultimately leading to a highly inflammatory state of the pancreatic endothelium.

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EP_597 ANTI AT1R AUTOANTIBODIES IN PANCREAS TRANSPLANTATION

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Background: Auto-antibodies targeting the angiotensin-II receptor (AT1R-AA) have been identified as drivers of the immune response in kidney transplantation and contribute to allograft vascular inflammation. We investigated the role of AT1-AA in pancreas transplantation with a special focus on rejection and thrombosis.

Methods: We included all pancreas transplant recipients followed in our center with available pre-transplant sera (D0). AT1R-AA levels were assessed using a standardized ELISA immunoassay. A multivariate cause-specific Cox model was used to examine the association between AT1R-AA and pancreas rejection and survival. Additionally, discarded pancreatic tissues from deceased donors were analyzed for AT1R expression.

Results: Among 305 patients, 34 experienced pancreatic rejection at one-year. In multivariate analysis, AT1R-AA positivity (≥10U/ml) was significantly associated with occurrence of pancreatic rejection (HR= 2.63, 95%CI = 1.166; 5.947, p= 0.020). Additionally, patients for whom the AT1R-AA titer was superior to the median expression of the cohort (≥ 6.26U/ml) had a trend for a higher risk of allograft failure (HR = 1.748, 95%CI = 0.988; 3.095, p= 0.05). AT1R-AA levels were significantly higher in patients with early thrombosis compared to others (10.1 U/ml vs 6.3 U/ml, p< 0.0001). The analysis of discarded tissues from deceased donors (n= 26) revealed a significant reduction in pancreatic AT1R expression among those receiving beta-blocker therapy (52% decrease, p= 0.04).

Conclusion: The presence of AT1R-AA was found to be significantly associated with a higher risk of pancreatic rejection and allograft failure resulting from complete thrombosis. Variations in pancreatic AT1R expression may contribute to different outcomes observed among patients with pre-transplant AT1R-AA.

EP_598 DELISTING THE RISK: OUTCOMES IN HIGHLY SENSITISED PATIENTS AND ROLE OF DE-LISTING IN TRANSPLANTATION

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[1]Northern General Hospital; Sheffield Kidney Institute; Nephrology, [2]Northern General Hospital; Sheffield Kidney Institute; Renal Transplant Surgery, [3]NHS Blood and Transplant; Histocompatibility and Immunogenetics, [4]NHS Blood and Transplant; Histopcompatibility and Immunogenicity, [5]NHS Blood and Transplant; Histocompability and Immunogenetics

Background: Highly sensitised patients (HSP) represent 12% of the UK kidney transplant list, often facing prolonged waiting times, higher rejection rates, and graft failure. Re-transplants are further complicated by vasculopathy, cardiovascular co-morbidity, and long dialysis vintage. Depleting induction agents (e.g., Thymoglobulin, Alemtuzumab) are widely used but increase infection risk. “De-listing” strategies aim to improve transplant opportunities by removing unacceptable antigens but may heighten immunologic risks.

Methods: This retrospective study analysed kidney transplants performed at a single centre (May 2013–June 2024) in sensitised patients receiving depleting agents or undergoing de-listing. Data from local systems and NHS Blood and Transplant were reviewed. Outcomes included patient and graft survival. De-listing decisions were MDT-led, aiming for a negative or weakly positive B Cell Flow Cytometric Crossmatch.

Results: Of 744 transplants, 44 sensitised patients (22 female, 22 male) were included, with a median follow-up of 3.16 years (IQR 1.1–4.8). Median age was 44 years (IQR 31–55), dialysis vintage was 7.3 years (SD 5.2), and mean cRF was 89% (SD 18). Among 15 de-listed patients, mean cRF decreased from 94.6% (SD 19) pre-de-listing to 89.2% (SD 25) post-de-listing. Thirty-five patients (80%) were regrafts, including six receiving a third graft. Transplant types included DBD (25), DCD (12), and LD (7), with Alemtuzumab used in 36 patients, Thymoglobulin in seven, and Basiliximab in one. Patient survival was 100% at 1 and 3 years. Graft survival was 93% at 1 year and 84% at 3 years. Mean eGFR at 6 months was 47.8 ml/min/1.73m² (IQR 35–61), and mean uPCR was 33.8 mg/mmol (IQR 24.58). Acute rejection occurred in nine patients (20.5%), including four antibody-mediated cases. Surgical complications affected 27% of patients, and 43.18% experienced infections requiring admission. De-listing reduced median time to transplant to 251 days.

Conclusions: With detailed planning and intelligent de-listing strategies, HSP can achieve successful kidney transplantation with favourable outcomes despite co-morbidities. De-listing reduces wait times to transplantation, supporting sustainable treatment option and significantly reducing the health-related carbon footprint.

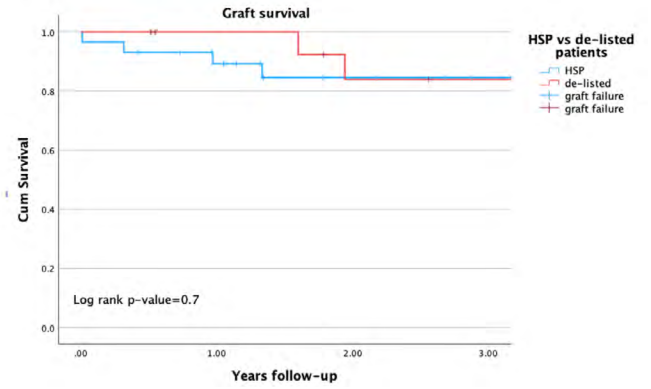
Table 1

Office on the web Frame

Before De-list		After de-list		
Mean cRF (%)	Mean NHSBT Match Score*	Mean cRF (%)	Mean NHSBT Match Score*	Mean de-list to transplant (days)
94.64	7 (6.87)	89.23	25 (25.4)	251

*Potential suitable UK donors per 10,000 (N/10,000)

Figure 1



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EP_599 SUCCESSFUL RENAL TRANSPLANTATION IN AN 11-YEAR -OLD FEMALE WITH SCHIMKE IMMUNE-OSSEOUS DYSPLASIA

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Background: Schimke Immuno-Osseous Dysplasia (SIOD) is a rare, autosomal recessive disorder caused by mutations in the *SMARCAL1* gene. It presents with disproportionate growth restriction, nephrotic syndrome with focal segmental glomerulosclerosis (FSGS), progressive renal failure, severe atherosclerosis, and immune dysfunction. End-stage kidney disease (ESKD) is a common and life-threatening complication. Renal transplantation is considered a viable therapeutic option for ESKD in SIOD, though immunological challenges necessitate careful management.

Methods: We report the case of an 11-year-old female diagnosed with SIOD and ESKD, on chronic hemodialysis since 2015. The patient underwent live-related renal transplantation in May 2017, with her 40-year-old mother as the donor. The surgical procedure involved right lumbar allotransplantation with vascular anastomosis to the iliac vessels. Post-operative immunosuppression consisted of low-dose tacrolimus and mycophenolate mofetil (MMF), adjusted based on tolerance and efficacy.

Results: The surgery was uneventful, with immediate graft function observed. The patient's serum creatinine stabilized at 0.5 mg/dL at discharge, and graft perfusion was excellent (resistance index: 0.67). One-week post-discharge, MMF was discontinued due to intolerance, and low-dose steroids were added. At the last follow-up, the patient exhibited stable renal function (serum creatinine: 0.8 mg/dL) and manageable immunosuppressive therapy without recurrence of nephrotic syndrome or signs of chronic allograft nephropathy.

Conclusions: Renal transplantation represents a viable and effective treatment for ESKD in SIOD patients. Despite the complexities of immunological and clinical management, careful planning and monitoring can result in favorable outcomes, providing improved quality of life for affected patients.

EP_600 TACROLIMUS-INDUCED DE NOVO ALLERGY AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: In recent years, there have been occasional reports on the onset of allergies and exacerbations caused by tacrolimus after transplantation. In children, who are more prone to allergies than adults, this significantly impacts their quality of life, including diet, skin care, and post-transplant course. We report cases of postoperative tacrolimus-induced de novo allergies in our hospital and investigate the underlying mechanisms.

Methods: Among the patients who underwent liver transplantation and who are currently undergoing follow-up in our outpatient department, we retrospectively examined 9 patients who developed new allergies after liver transplantation.

Results: The average age at transplantation was 13 months and the male-to-female ratio was 5:4. One patient had an ABO-incompatible transplant, and 1 was a DSA-positive case. The average time from transplantation to the onset of allergy was 6.3 months, and symptoms included rash, diarrhea, itching, nasal discharge, and asthma. One patient required hospitalization for convulsions. At the time of onset, IgE, eosinophil fraction, thymus and activation-regulated chemokine (TARC) levels were all significantly higher than in non-onset cases, but there was no significant difference in EB virus count or tacrolimus trough value. Three patients required a switch from tacrolimus to cyclosporine. All patients required antihistamines, and treatment was continued with dietary restrictions and consultation with the allergy department of our hospital. All the patients survived, and the post-transplant course was generally good without rejection. The onset of allergy after pediatric liver transplantation due to tacrolimus is hypothesized to be due to a type 1/2 Helper T cell (Th1/2) imbalance, but this has yet to be proven. TARC is a Th2-related chemokine, and we demonstrated that it was significantly higher in the allergic group than in the control group.

Conclusions: Tacrolimus-induced allergies have a significant impact on the quality of life of children; therefore, comprehensive management, including the adjustment of immunosuppressants, is necessary while paying close attention to the onset and progression of the disease, and also continuing to research the mechanism of such allergies.

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EP_601 HYPERACUTE REJECTION AFTER DESENSITIZATION OF ABOI ROBOTIC LDKT

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Background: Hyperacute rejection in transplantation is mediated by preformed antibodies and can be avoided by confirming ABO compatibility, crossmatching(CXM), and detecting donor-specific antibodies(DSA). Advances in technology and development of desensitization protocols, it is now acceptable for transplantation across this barrier, such as ABO incompatible(ABOi) living donor kidney transplantation(LDKT).

Methods: The recipient was a 51 years old male patient with hypertension nephropathy and blood type ABO-O+. The donor was the spouse and 51 years old female patient with ABO-B+. Immunologic tests showed four mismatch of human leukocyte antigen(HLA), negative CXM, DSAs results. Initial anti-B IgG and IgM titers were 1:521 and 1:512. For desensitization, we applied 500mg of rituximab and 8 cycles of plasma exchange and IVIGs. The final titer was decreased to 1:16 and decided to proceed the operation.

Results: The right kidney was used for the graft and had two arteries with one ligated and single vein and weighed 163g. During the ureter anastomosis, the graft's color was minimally changed to purple, but intra-operative doppler sonography showed intact inflow and outflow and completed the surgery. Postoperative urine output was 50ml per hour, and uncontrollable high blood pressure was checked. Doppler sonography was re-checked and the main artery flow was still intact, but the graft showed diffused ischemia. Suspicious of artery anastomosis stricture, we decided to go under re-operation. When opened, the artery and vein anastomosis were intact, but total infarction of the graft. And graft nephrectomy due to hyperacute rejection was done. The final pathology showed definite antibody mediated rejections. Studies of single antigen antibody assays, DQ-DSAs, Non-HLA, and minor-HLA antibodies, there were no explainable results. We have concluded that the cause of the hyperacute rejection might be ABO antibodies.

Conclusions: In ABOi LDKTs, even after desensitization and successfully decreasing the titer of anti-ABO antibodies, hyperacute rejection can occur.

EP_602 SAFETY AND EFFICACY OF BELATACEPT IN PANCREAS TRANSPLANTATION

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Background: Calcineurin inhibitors (CNIs) are the cornerstone of immunosuppressive regimens in solid organ transplantation but are associated with nephrotoxicity and diabetogenic effects. Belatacept, a costimulation blocker with a favorable renal and glycemic profile, has gained traction in kidney transplantation but remains rarely utilized in pancreas transplantation due to concerns about acute rejection. This study evaluates outcomes in five pancreas transplant recipients switched to belatacept for various indications, with follow-up spanning 2 to 8 years.

Methods: Five patients (four simultaneous pancreas-kidney [SPK] and one pancreas transplant alone [PTA]) were converted to belatacept for CNI toxicity (n=2), recurrent rejection (n=2), or erratic drug absorption (n=1). All patients received alemtuzumab induction followed by CNI-based maintenance therapy. Belatacept was administered monthly, with stepwise CNI reduction. Clinical outcomes, including glycemic control, renal function, graft survival, and rejection episodes, were assessed over a mean follow-up of 55.2 months.

Results: Belatacept conversion preserved excellent pancreatic endocrine function in all patients (mean HbA1c 5.3±0.2%, detectable C-peptide levels, no insulin requirements). Renal function improved in three SPK recipients (mean eGFR increased from 36±19 to 56±20 mL/min/1.73m²) but worsened in one due to nonadherence. The PTA recipient maintained stable renal function (eGFR >90 mL/min/1.73m²). Rejection episodes were observed in three patients: one borderline rejection and two acute rejections in a patient with non-adherence profile and during belatacept interruption due to insurance issue for another one, none resulting in graft loss. No viral infections or discontinuation of belatacept were noted.

Conclusions: Belatacept conversion is effective in preserving pancreatic endocrine function and stabilizing or improving renal function post-pancreas transplantation. Rejection episodes were manageable and occurred predominantly in patients with nonadherence or interrupted belatacept therapy. These findings highlight belatacept's potential when used in conjunction with low-dose CNIs, underscoring the need for adherence and further studies to optimize its role in pancreas transplantation.

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Transplant immunology & immunosuppression

EP_603 DONOR SPECIFIC HLA ANTIBODIES IN HEART TRANSPLANTATION COMPARING DCD AND DBD ALLOGRAFTS

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Background: The development of donor specific HLA antibodies (DSA) is associated with increased rates of rejection in heart transplant (HT) recipients. We examine the development of DSA in recipients of allografts from donation after circulatory death (DCD) and donation after brainstem death (DBD) donors.

Methods: Retrospective chart review of all patients who underwent HT at our institute between January 2020 and July 2023 (n=129). Patients (n=11) who died in hospital early after HT, specifically during the same admission for the procedure, were excluded. DSA data were collected at approximately 6 months, 1 year, 2 years, 3 years, and 4 years post-transplant.

Results: 118 patients were included (83 DBD, 35 DCD). All DCD transplants were retrieved by direct procurement and perfusion. 1-year survival conditional to discharge from hospital after transplant was 98.3% (116/118). There were no statistically significant differences in the development of DSA between the DBD and DCD groups. Furthermore, there were no significant differences between groups when examining HLA class, median fluorescence index (MFI) level, persistence, and timing (developed within 6 months or later) of DSA development (Table 1). We did not observe any differences in rejection rates within our cohort.

Conclusions: In our study, the development of DSA did not differ between DBD and DCD heart transplant recipients. A larger cohort is required to examine this finding and its relationship with rejection.

	DBD (n = 83)	DCD (n= 35)	*P value*
Pre-transplant calculated reaction frequency (cRF) >10%	13 (16%)	3 (8%)	0.463
Donor specific antibodies (DSA)	14 (17%)	6 (17%)	1
Class I	12 (86%)	5 (83%)	1
Class II	5 (36%)	2 (33%)	1
High level (MFI >5000)	5 (36%)	1 (17%)	0.798
Low to intermediate level (MFI <5000)	9 (64%)	5 (83%)	0.829
Persistence of DSA (>1 year)	4 (29%)	0 (0%)	0.445
Transient DSA	10 (71%)	6 (100%)	0.657
Early DSA (present before 6 months post-HTx)	7 (50%)	4 (67%)	0.869
Late DSA (present or persist more than 6 months post-HTx)	7 (50%)	2 (33%)	0.898
Acute cellular rejection	33 (40%)	11 (31%)	0.518
Antibody mediated rejection	2 (2%)	1 (3%)	1
1-year survival conditional to discharge from hospital after transplant	81 (98%)	35 (100%)	1

EP_604 OUTCOMES OF HIGH IMMUNOLOGIC RISK PATIENTS DESENSITIZED PRIOR TO KIDNEY TRANSPLANTATION

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Background: There are no accepted guidelines in doing desensitization therapy for of high immunologic risk patients prior to kidney transplantation. Also, local evidence on the benefit of this regimen is lacking.

Methods: We performed a retrospective study at National Kidney and Transplant Institute. Those with high immunologic risk and underwent desensitization prior to kidney transplant January 1, 2018 up to December 31, 2023 were included. The following were collected: creatinine levels, estimated glomerular filtration, incidence of renal allograft function, incidence of acute rejection, and mortality.

Results: A total of 115 patients were included and 28.44% had no detectable donor-specific antibodies (DSA), 40.37% had an Mean Fluorescence Index (MF) ≤5000. Median serum creatinine ranged from 0.91 mg/dL at 1 year to 1.16 mg/dL at 3 years, returning to 0.94 mg/dL by 5 years (p=0.097), while mean eGFR declined from 82.26 to 69.77 mL/min/1.73 m² over the same period (p=0.850). Graft survival decreased from 88% at 6 months to 60% at 5 years, with graft failure rising from 12% to 40%. Patient survival without complications dropped from 84.35% at 6 months to 62.86% at 5 years, while survival with complications peaked at 17.53% at 1 year and fell to 5.71% by 5 years.

Conclusions: High immunologic risk patients undergoing desensitization therapy prior to kidney transplantation face notable declines in graft and patient survival rates over five years.

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Transplant immunology & immunosuppression

EP_605 NMP AND INFLAMMATORY MEDIATORS ADSORPTION IN EXTENDED CRITERIA KIDNEY TRANSPLANTATION

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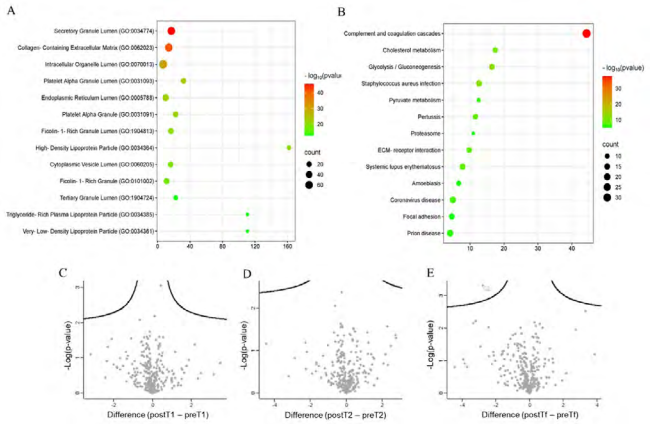
Background: Kidney transplantation faces challenges due to the shortage of donor organs, leading to the increased use of Extended Criteria Donor (ECD) organs, including those from elderly donors, donors with comorbidities, and those after circulatory death (DCD). This study focuses on the application of the PerLife system, integrated with the PerSorb device, to modulate inflammatory mediators during normothermic machine perfusion (NMP) of an ECD kidney. The PerSorb device, designed to adsorb inflammatory molecules, demonstrated effective removal of cytokines during the perfusion process.

Methods: An ECD donor kidney underwent 320 minutes of normothermic perfusion, allowing detailed organ viability assessments and cytokine modulation, after a total static cold storage time of 715 minutes. To characterize the effectiveness and efficiency of adsorption, perfusate samples were collected, after perfusion parameters stabilization, pre-and post the adsorption cartridge at the following time points: 60 minutes after the perfusion start (T1), 120 minutes after the perfusion start (T2), 320 minutes after the perfusion start (T_end), for perfusion dynamics (pressures, flows, vascular resistances, temperature); perfusion solution composition stability for biomolecular and proteomic examination; oxygenation parameters, and lactate levels; urine output.

Results: A significant volume of urine output and successful post-transplantation outcomes, with no delayed graft function, highlight the efficacy of this approach. Additionally, the adsorption of inflammatory cytokines was characterized by concentration-dependent removal, suggesting a balanced modulation of both pro- and anti-inflammatory responses. Figure 1, Bubble plot of Gene Ontology - Cellular Component (GOCC) analysis:

Conclusions: The integration of PerSorb into the perfusion process might offer a promising option for evaluating organ viability, and theoretically mitigating ischemia-reperfusion injury. Further studies are needed to validate these findings and explore the long-term clinical impact of this approach on graft survival and function.



EP_606 BORTEZOMIB MAY BE EFFECTIVE FOR RECURRENT AUTOIMMUNE HEPATITIS AFTER PEDIATRIC LIVER TRANSPLANT

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Background: Autoimmune hepatitis (AIH) is a chronic inflammatory liver condition that can lead to cirrhosis and end-stage liver disease, often requiring liver transplantation (LT). While pediatric LT has significantly enhanced survival rates, challenges such as acute steroid-resistant rejection and AIH recurrence remain substantial obstacles.

Methods: This report describes the first pediatric liver transplantation performed in Uzbekistan on a 14-year-old boy with AIH-induced liver cirrhosis. The patient underwent standard immunosuppressive therapy post-transplantation. When steroid-resistant rejection and AIH recurrence were detected, conventional therapies, including pulse methylprednisolone and anti-thymocyte globulin (ATG), were administered without success. Bortezomib, a proteasome inhibitor, was subsequently introduced as salvage therapy.

Results: After the initial dose of bortezomib, the patient demonstrated significant improvement in bilirubin levels and liver synthetic function. A second dose, administered seven days later, led to normalization of liver function markers and serological antibodies by postoperative day 30. The patient was discharged in stable condition under a triple immunosuppressive regimen.

Conclusions: This case highlights the effective use of bortezomib as a rescue therapy for steroid-resistant rejection and recurrent AIH following pediatric LT. It emphasizes the importance of alternative therapeutic strategies in managing complex post-transplant immune complications and advocates for further research into the role of bortezomib in post-transplant care.

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EP_607 SPECIFIC IMMUNOADSORPTION USING SECORIM (DIAMED) ADSORBER FOR PRECONDITIONING IN AB0I KTX

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Background: AB0-incompatible kidney transplantation (AB0i KTx) is a promising strategy to expand the living donor pool. Desensitization with blood group antigen-specific immunoadsorption (IA) combined with rituximab enables excellent graft survival rates and results despite a higher immunological risk in a mortality advantage compared to remaining on the waiting list. Specific IA of blood group antibodies was introduced in Germany in 2004. The Charité uses the SECORIM© adsorber from Diamed, marketed in Germany since 2021.

Methods: To record the performance characteristics of the SECORIM© adsorber in the preconditioning of recipients before AB0i KTx, we have been conducting a prospective observational study in our transplant center since December 2023. We have analyzed the number of necessary IA treatments, decrease in isoagglutinin titers and kinetics of total protein, albumin, coagulation parameters including fibrinogen, IgM, IgG, IgA.

Results: The median age of the 17 patients we have examined so far is 54 years, of whom four are female and 76% male. The median baseline anti-A/B titer for IgG was 1:164 (1:16-1:512), for IgM 1:16 (1:4-1:64). The median number of treatments required to reduce the blood group antibody titer to < 1:8 for IgG was 3. After the first IA with the SECORIM© adsorber, the anti-A/-B IgG titer was reduced by a median of 2.7 titer levels and the IgM titer by 2.4 titer levels. Over 3 pre-KTx IA, the blood group antibody titers were reduced by 2.6 levels for IgG and by 1.5 levels for IgM. After each of three IA procedures we saw an average decrease of 22% for IgA, 23% for IgG and 24% for IgM. Albumin and protein decreased by 19% and 22% respectively compared to baseline after three IA procedures. Fibrinogen was reduced by 51% after three IA, Albumin by 19%. In two cases a change of procedure (plasmapheresis) was necessary, both patients had high titers and rebound. No patient had infectious or bleeding complications.

Conclusions: The preliminary results of our small series so far support a high efficiency and safety of desensitization using blood group antigen-specific IA with the SECORIM© adsorber. Nevertheless, there is a decrease in other proteins such as fibrinogen and albumin without clinical relevance.

EP_608 UNRAVELLING THE CAUSE-A CASE OF PERIOPERATIVE ANAPHYLAXIS AND IMPLICATIONS FOR TRANSPLANT RELISTING

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Background: 38year old male admitted for simultaneous kidney-pancreas (SPK) transplant. No known medication allergies. Type 1 diabetes mellitus (28year history), on haemodialysis (3 years). No surgical history. Physically fit and active. Active on waiting list 2 years, 1 previous SPK offer. DBD organs confirmed transplantable, proceeded to theatre and developed peri-operative anaphylaxis.

Methods: Stepwise case review, and diagnostic drug challenges to enable transplant relisting, highlighting this case's uniqueness. Events timeline:- 05:30 anaesthetic induction with remifentanil, propofol and atracurium, 05:34 uneventful intubation, 06:10 skin preparation with chlorhexidine, insertion of chlorhexidine-coated CVC line, 06:15 meropenem slow bolus, methylprednisolone (sodium succinate) infusion-run over 30minutes, 06:38 caspofungin infusion, 06:40 approx. 10mg caspofungin received, BP 55/32, difficulty in ventilation, angioedema, haemodynamically compromised. In-theatre discussions not safe to proceed, transplant abandoned (organs offered back to NHS Blood and Transplant Hub), patient stabilised and transferred to intensive care unit. Clear tryptase rise (peaked 09:46 – onset of anaphylaxis 06:40). Discharged home day 5 with adrenaline autoinjector (EpiPen®). Suspended from transplant list pending allergy testing. Clinical incident reported as per anaesthetic anaphylaxis protocols (local/national). Local nephrologist and GP notified of presumed caspofungin anaphylaxis.

Results: Patient underwent skin testing for perioperative drugs received, and additional steroid testing (Table 1). Methylprednisolone sodium succinate identified as index drug, but timeline raised strong suspicion caspofungin also involved. Agreed to proceed with drug challenges (Table 2) to mitigate risks and support transplant relisting. Patient consented.

Conclusions: Patient reactivated on transplant list, after reassessment, with a tailored immunosuppression plan (Table 2) documented in electronic patient records. Immunology skin testing has limitations, such as irritation causing positive intradermal test and unvalidated concentrations (e.g. caspofungin). Methylprednisolone sodium succinate or caspofungin are rare anaphylaxis triggers, warranting clinician awareness.

Table 1. Immunology Skin Tests

Drug	Skin Prick Test	Isolated Intradermal Test	Advice
Drugs received at time of surgery			
Methylprednisolone sodium succinate	negative	**POSITIVE**	Avoid all future use
Caspofungin	negative	negative	N/A
Chlorhexidine 0.05%	negative	negative	N/A
Meropenem	negative	negative	N/A
Latex	negative	negative	N/A
Propofol	negative	negative	N/A
Remifentanil	negative	negative	N/A
Lidocaine 2%	negative	negative	N/A
Atracurium	negative	negative	N/A
Rocuronium	negative	negative	N/A
Additional steroid testing			
Hydrocortisone	negative	**POSITIVE**	Avoid all future use
Methylprednisolone acetate	negative	negative	N/A
Triamcinolone	negative	negative	N/A
Dexamethasone	negative	negative	N/A

Table 2: Drug challenges & tailored perioperative dosing for SPK Transplant

Drug	Challenge Dose	Result	Individualised dose for SPK Transplant (perioperative)
Dexamethasone (base) IV	3.3mg	No reaction	77.4mg IV (≡ 93.8mg dexamethasone sodium phosphate ≡ 500mg methylprednisolone sodium succinate)
Liposomal amphotericin IV	100mg	No reaction	300mg IV (3mg/kg)
Oral prednisolone	30mg	No reaction	N/A

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EP_609 TACROLIMUS ASSOCIATED NEUTROPENIA POST-TRANSPLANTATION - CASE SERIES

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Background: Tacrolimus associated neutropenia is rarely observed in solid organ transplant recipients, despite being a recognised adverse event. It is poorly described in the literature. We reviewed 5 patient cases where tacrolimus was deemed the probable cause of late onset neutropenia (absolute neutrophil count, ANC <1.8x10^9L), with a median onset time of 217 days post-transplant (mean 1297days [125-4367days]). In all cases leucopenia causing medicines were reviewed, other viral and malignancy causes for neutropenia were excluded, before considering a therapeutic ciclosporin switch (target level 50-150ng/ml).

Methods: A retrospective review was conducted using a renal pharmacy database to identify patients who had undergone a therapeutic ciclosporin switch due to tacrolimus related side effects over an 11-year period [01/01/2014-30/09/2024]. Patients' electronic records were then interrogated. Data was input into Microsoft Excel for descriptive statistical analysis.

Results: Patient data is described in Table 1 (pre-ciclosporin switch) and Table 2 (post-ciclosporin switch). 4/5 patients had a bone marrow examination which revealed no abnormalities and described drug related myeloid maturation suppression. In all 5 cases, after tacrolimus discontinuation and therapeutic switch to ciclosporin, neutropenia resolved with a mean time to resolution (ANC>1.8) 65days [40-88days].

Conclusions: These 5 cases, from a single centre over an 11-year period, highlight that whilst this adverse event remains uncommon, it warrants consideration when other potential causes have been excluded. The exact mechanisms underlying tacrolimus associated neutropenia have yet to be elucidated. However, these cases suggest an association, with resolution observed only after replacing immunosuppressive treatment. In select patients, anti-proliferative immunosuppressants were reintroduced when clinically indicated. Increased awareness of tacrolimus associated neutropenia could facilitate earlier discontinuation of the drug, thereby mitigating the risks of infection and other complications arising with over immunosuppression.

Table 1: Pre-ciclosporin [CyA] switch data

Case number	Type of transplant, Induction agent & dose, CMV status Donor/Recipient	Transplant date	Neutropenia onset (ANC <1.8) days post transplant	Days neutropenic prior to CyA switch	Mean tacrolimus trough level (ng/mL) 12months prior to neutropenia onset	Mycophenolate Mofetil (MMF) dose at onset of neutropenia	Prednisolone given whilst off MMF	Concurrent CMV infection	Bone marrow biopsy	G-CSF given	sCr (umol/L) 3 months pre CyA
1 (M, 71 y/o)	DCD Kidney, Alemtuzumab 30mg SC, CMV -/-	21/10/2016	125	174	8.7	750mg BD	5mg OD	Yes	No	No	153
2 (M, 57 y/o)	DCD Kidney, Alemtuzumab 60mg IV, CMV +/-	02/03/2013	183	373	8.5	750mg BD	No	No	Yes	No	167
3 (F,36 y/o)	DCD SPK, Alemtuzumab 30mg SC, CMV -/+	03/03/2022	217	369	7.1	500mg BD	5mg od	No	Yes	No	152
4 (F, 70 y/o)	DBD Kidney, Basiliximab 40mg IV, CMV -/-	30/12/2018	1591	380	8.3	500mg BD	5mg OD	No	Yes	Yes	82
5 (M, 32 y/o)	DBD SPK, Alemtuzumab 60mg IV, CMV +/-	18/02/2012	4367	164	8.4	500mg BD	5mg OD	No	Yes	No	122

Table 2: Post-ciclosporin [CyA] switch data

Case number	Mean CyA trough level (ng/ml) 6 months post switch	Days post CyA switch ANC > 1.8 on 2 occasions.	sCr (umol/L) 3 months post CyA	Prednisolone stopped post recovery of neutrophils	MMF or Azathioprine (AZA) reintroduced
1 (M, 71 y/o)	78.3	54	142	No	MMF
2 (M, 57 y/o)	158	79	154	N/A	AZA
3 (F,36 y/o)	94.3	40	143	No	AZA
4 (F, 70 y/o)	82	88	75	No	No
5 (M, 32 y/o)	136.3	ongoing	109	No	No

EP_610 A ONE-DAY PROTOCOL FOR DONOR-DERIVED CELL-FREE DNA MONITORING IN KIDNEY ALLOGRAFTS

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Background: Donor-derived cell-free DNA (ddcfDNA) is a promising minimally-invasive biomarker for the detection of kidney allograft injury. However, the added clinical value of ddcfDNA remains unclear. The current expensive and time-consuming NGS methods for the detection of ddcfDNA are inconvenient for clinical monitoring. Here, we use a personalized digital (d)PCR-based method that allows quantification of ddcfDNA within a single day.

Methods: Blood plasma was collected at the time of a for-cause biopsy, stable day 7 (D7) and stable month 6 (M6) of in total 142 kidney transplant recipients. Using HoloGRAFT™ (Omixon), donor-specific copy number variant (CNV) markers were selected for every recipient. DPCR was used to measure at least two donor-specific assays.

Results: At the time of a for-cause biopsy, the median (range) ddcfDNA concentration was significantly higher (82 [5-3571] copies/ml) compared to stable M6 (16 [0-335] copies/ml, $p < 0.0001$), but comparable to stable D7 (91 [10-742] copies/ml). At the time of biopsy-proven acute rejection (BPAR) the ddcfDNA concentration was 165 (19-3571) copies/ml, which was significantly higher compared to the samples accompanying biopsies without acute rejection (non-AR, 43 [5-188] copies/ml, $p < 0.0001$). Both the concentration of ddcfDNA in copies/ml as well as the percentage of ddcfDNA of total cfDNA discriminated BPAR from non-AR biopsies (BPAR: 0.7 [0.2-9.5]% vs non-AR: 0.3 [0.04 -1.4]%, $p < 0.001$). ROC analysis to discriminate BPAR from non-AR showed an AUC of 0.86 with a sensitivity of 71%, specificity of 86%, PPV of 56% and a NPV of 92%.

Conclusions: Personalized dPCR specifically targeting ddcfDNA is a convenient and rapid tool for monitoring ddcfDNA values after kidney transplantation. DdcfDNA has the potential to augment clinical decision making by excluding the presence of allograft rejection, potentially avoiding unnecessary biopsies.

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Transplant immunology & immunosuppression

EP_611 GDNA CONTAMINATION ON DONOR-DERIVED CFDNA TESTING IN TRANSPLANTATION: UNMASKING THE HIDDEN THREAT

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Background: Accurate cell-free DNA (cfDNA) testing is critical in transplantation, where precise donor-derived cfDNA (dd-cfDNA) quantification informs key clinical decisions. Sufficient cfDNA yield and concentration are essential, but genomic DNA (gDNA) contamination poses a significant challenge to accurate downstream analysis. Robust cfDNA isolation protocols are needed to mitigate gDNA interference and preserve dd-cfDNA test accuracy.

Methods: Blood samples from transplant patients were collected in tubes containing either cfDNA stabilization preservatives (BCT, Streck) or anticoagulants (EDTA). Plasma was processed per manufacturer guidelines and stored frozen prior to cfDNA extraction. Purified cfDNA quality was characterized using capillary electrophoresis (TapeStation, Agilent). Operational and analytical parameters were compared between the two protocols, with dd-cfDNA quantified as a percentage (%) using the AlloSeq cfDNA assay (CareDx).

Results: Plasma-EDTA samples had gDNA contamination, requiring additional purification steps to ensure cfDNA purity. This extended processing took significantly longer (5.5 vs. 2.5 hours for plasma-Streck), reducing daily sample throughput (16 vs. 48) and batch productivity per full-time employee (1 vs. 2). QC metrics revealed lower NGS passing rates for cfDNA-EDTA (76.1%) compared to cfDNA-Streck (96.6%), driven by lower yields (13.4–27.5 ng for cfDNA-EDTA vs. 91.7–125.9 ng for cfDNA-Streck). More critically, cfDNA from plasma-EDTA without extra purification yielded significantly lower dd-cfDNA values than cfDNA-Streck or other gDNA-free samples.

Conclusions: These findings highlight the importance of cfDNA preservative or extra purification to prevent or remove gDNA contamination and ensure accurate dd-cfDNA analysis. Non-validated alternative pre-analytical processes can increase the risk of false negative dd-cfDNA results, with potentially severe consequences in clinical applications.

EP_612 SEX DIFFERENCES AND KIDNEY TRANSPLANTATION OURCOMES IN SOUTH KOREA: A PSW STUDY

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Background: Immunological factors predominantly drive transplant failures, with immune responses varying by sex and age, potentially influencing graft outcomes. This study assessed the impact of sex differences on both short-term and long-term kidney transplantation outcomes.

Methods: We analyzed data from kidney transplant recipients at a South Korean university hospital between January 2000 and December 2023. Short-term outcomes included serum creatinine levels at discharge, delayed graft function, acute rejection episodes, and early readmissions. The long-term outcome focused on all-cause mortality. A total of 470 recipients were evaluated, with propensity score matching applied to balance covariates through nearest-neighbor matching.

Results: Among the 470 identified patients, the average age was 46.14 (15.29) years. There were 246 males (52.34%) and 224 females (47.65%). In the 45–60 age group, males exhibited significantly lower serum creatinine levels at discharge after kidney transplantation compared to females, indicating a notable sex-based difference in short-term renal function. For recipients over 60years, kidneys from female donors correlated with a reduced mortality risk, suggesting a beneficial effect on long-term survival.

Conclusions: These findings align with existing literature indicating that, although males generally have higher baseline glomerular filtration rates (GFR), the decline rate with age can be more pronounced in females, affecting serum creatinine levels. Additionally, previous studies have shown that donor age and sex can influence transplant outcomes, with older female donors often providing grafts with favorable survival rates. Therefore, considering both donor and recipient demographics is crucial in kidney transplantation to enhance patient outcomes.

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EP_613 REDUCED CALCINEURIN INHIBITORS WITH EVEROLIMUS IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION

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Background: ABO-incompatible kidney transplantation (ABO-IKT) has proven to be a feasible strategy for increasing the living donor pool, with results comparable to those of ABO-compatible KT. Everolimus (EVR) has demonstrated potential in lowering calcineurin inhibitor (CNI) exposure while maintaining sufficient immunological control. The use of EVR in combination with reduced CNI in de novo ABO-IKT may offer significant benefits in optimizing clinical outcomes and minimizing complications.

Methods: This observational retrospective study compared the outcomes of reduced CNI with EVR with those of standard Tac with mycophenolate mofetil (MMF) in de novo ABO-IKT recipients at our institution, between January 2014 and December 2023. A total of 80 patients were initially enrolled in this study. The participants were categorized into an MMF group (n=54) and an EVR group (n=26). The primary endpoints were graft survival and patient survival rates, while the secondary endpoints included EVR/MMF continuation rates, cytomegalovirus (CMV) incidence, the rates of acute cellular rejection frequency, and antibody-mediated rejection. To mitigate confounding factors, propensity score matching was implemented based on age, sex, HLA mismatch, flow cytometry crossmatch positivity, and calcineurin inhibitor type, resulting in a 1:1 matched cohort of 42 patients.

Results: After propensity score matching, no significant differences were observed between the EVR and MMF groups in graft survival or patient survival, the primary endpoints. Secondary endpoints, including drug continuation rates, acute cellular rejection, and antibody-mediated rejection rates, were comparable. Moreover, no notable differences in CMV incidence were detected between the two groups.

Conclusions: Our findings suggest that EVR with reduced CNI achieves comparable graft and patient survival outcomes to MMF with standard CNI in de novo ABO-IKT. Secondary endpoints, including rejection rates and drug continuation, were similar. A lower trend in CMV incidence with EVR has been reported before. More extensive studies are necessary to determine its optimal use and benefits in combination with reduced CNI for ABO-IKT.

EP_614 SWITCH TO AZATHIOPRINE FOLLOWING THE DIGESTIVE TOXICITY INDUCED BY MYCOPHENOLATE MOFETIL IN KIDNEY TRANSPLANT PATIENTS

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Background: Mycophenolate mofetil (MMF) is an anti-metabolite that inhibits the proliferation of lymphocytes. It is used in combination with anticalcineurins in post-renal transplant maintenance treatment. It can cause digestive toxicity that sometimes requires discontinuation of treatment. We report our experience.

Methods: We analyzed the effect of switching to azathioprine from mycophenolate on amelioration of diarrhea and graft survival. We report our experience.

Results: Among the 329 kidney transplants in our department, 11 patients (3.34%) were switched to azathioprine, Their average age was 26 years with a slight male predominance (6 men and 5 women). The dominant initial nephropathy was chronic interstitial nephropathy, two patients had a cadaveric kidney, The median delay after transplantation was 1 year with an extreme of 10 months to 11 years, The most common symptoms were chronic diarrhea and vomiting, one patient was asymptomatic, the average dose of MMF was 1.5 g/d with a median MMF AUC of 80.5, the infectious investigation and celiac serology were negative, all patients had signs of chronic gastritis at the upper digestive endoscopy with A villos atrophy in 3 patients including the patient who was asymptomatic, at total colonoscopy 4 patients had signs of acute ileocolitis with rarefied and atrophic Crypts. The median response time to MMF change was 20 days with a favourable evolution noticed in most patients

Conclusions: MMF is an excellent immunosuppressant that thanks to it reduces acute rejection, but we sometimes have to stop it because of digestive toxicity. In the face of chronic diarrhea in a kidney transplant, it is necessary to know how to eliminate infectious, neoplastic and celiac disease causes to retain the drug origin.

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EP_615 EXPLORING IMMUNE-RELATED PROTEOMIC CHANGES PRE- AND POST- KIDNEY TRANSPLANTATION

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Background: Understanding immune-related proteomic changes following kidney transplantation is an essential first step to elucidating underlying mechanisms of transplant success or failure. This pilot study aimed to investigate shifts in immune proteomic profiles in patients pre- and post- kidney transplantation

Methods: Serum samples of 28 patients pre- and post-kidney transplantation were analysed using OLINK inflammation panel I & II (total of 737 proteins analysed). Data underwent rigorous quality control, including normalisation and batch effect correction. Differential protein expression analysis compared pre- and post-transplant samples. Principal component analysis (PCA) and hierarchical clustering were employed to explore proteomic shifts and identify patterns indicative of post-transplant changes.

Results: Differential analysis identified 23 proteins with significant changes between pre- and post-transplant samples. PCA revealed distinct clustering of pre- and post-transplant groups, with the first two components explaining 15.7% and 14.1% of the variance. Hierarchical clustering further highlighted proteomic shifts, with one cluster exclusively comprising post-transplant samples. Observed changes pre- and post- transplantation likely reflect the systemic effects of kidney transplantation and immunosuppressive medications. Results suggested alterations in immune regulation, reduced inflammation, and shifts in metabolic and structural proteins. Notably, proteins such as CXCL17, CCL23, and PRR4 ($p < 0.01$), associated with immune responses exhibited significantly lower levels post-transplant.

Conclusions: This study provides a preliminary exploration of immune-related proteomic changes following kidney transplantation. The results highlight potential avenues for further investigation in larger cohorts. These findings lay the groundwork for future work aimed at biomarker discovery and improved transplant monitoring.

EP_616 URINARY MITOCHONDRIAL DNA IS RELATED TO ALLOGRAFT FUNCTION IN LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Ischemia reperfusion injury (IRI) is the main harmful process in kidney transplantation and increases the risk of complications and impaired graft function. Mitochondrial DNA (mtDNA), implicated in organ damage caused by IRI, has shown promise as a biomarker for assessing and predicting graft function. The aim of this study is to explore the presence, dynamics, and prognostic value of urinary mtDNA.

Methods: This study is a post-hoc analysis of the VAPOR-1 trial with a cohort of 57 living donor kidney transplantation (LDKT) recipients in the University Medical Center in Groningen (UMCG). The mtDNA amount is measured using quantitative polymerase chain reaction (qPCR) of three genes; ND1, ND6 and D-loop.

Results: In the first urine after transplantation, the mtDNA gene amount is associated with graft function after transplantation. Higher mtDNA in the first urine was associated with higher estimated glomerular filtration rate (eGFR) at 12 and 24 months after transplantation and an increase in eGFR between month 1 and 24 months after transplantation, suggesting that the amount of mtDNA in the first urine reflects renal function rather than renal injury.

Conclusions: This study underscores the potential of urinary mtDNA as a prognostic tool for renal allograft function and advocates a re-evaluation of the way early post-transplantation renal damage markers are interpreted.

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EP_617 PATHOLOGISTS' EXPERIENCE AND ROUTINE PRACTICE IN HIGH-VOLUME LUNG TRANSPLANT CENTERS: AN INTERNATIONAL SURVEY

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Background: Lung allograft pathology encompasses a broad spectrum of disorders. Recently, new entities, challenging lesions and advanced technologies have emerged.

Methods: The study aimed to assess pathologists' experience and current practice in their centers. A 24 item-survey was designed by leaders of the Lung Allograft Pathology Working Classification (WC), which is currently under revision. The survey was sent to lung pathologists of transplant centers with recognized experience in the field.

Results: Responses were received from 35 professionals: 51% Europeans and 43% Americans/Canadians who were primarily from high-volume centers performing >50 transplants annually. Regarding post-transplant monitoring, 77% reported a combination of surveillance protocol and clinically-driven assessments, primarily using transbronchial biopsy (TB) (86%) and bronchoalveolar lavage (83%). Nearly all respondents (94%) supported the reintroduction of grade AX, which had been included in the 1996 WC, for cases where lung parenchyma is inadequately sampled. Acute and chronic rejection were cited as challenging to grade in TB due to various factors highlighted in the survey. Consequently, 60% of specialists endorsed introducing an "indeterminate" category in both acute and chronic rejection. A topic deemed important was large airway sampling with 54% advocating for further investigation using bronchial biopsies, with 82% recommending independent evaluation of bronchial lesions. Digital pathology was routinely used for clinical and research purposes for nearly half of the respondents. Artificial intelligence algorithms were considered useful by a minority for the diagnosis of immunological disorders especially for acute rejection. 49% of professionals viewed dd-cfDNA potentially useful as a complementary tool to a biopsy, while 14% considered it a useful tool to predict the need for a biopsy. Additionally, 86% emphasized the importance of a synoptic template for uniform reporting of biopsies.

Conclusions: This survey highlights current practices of pathological post-transplant monitoring and underscores key challenges and advancements in the field. These findings will be important for the ongoing update of the Lung Allograft Pathology WC ensuring it aligns with clinical needs and practices.

EP_618 EMULATED TARGET TRIAL OF EVEROLIMUS IN LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) is a major indication for liver transplantation (LT). However, recurrence of HCC remains a significant challenge. Everolimus (EVR), an mTOR inhibitor used for immunosuppression, has potential anticancer properties. This study aimed to emulate target trials (ETT) that investigated the effect of EVR initiation on HCC recurrence, using electronic health records from the French National Health Data System.

Methods: Our study included 3670 adult liver transplant recipients with HCC between 2009 and. The ETT randomly assigned individuals to initiation of EVR or no initiation of EVR. The primary endpoint was HCC recurrence-free survival (RFS). The causal estimand of interest was the average treatment effect of initiating EVR, estimated by the difference in RFS and OS probabilities at 5 and 10 years after inclusion.

Results: Most LT recipients were male with a high prevalence of arterial hypertension, diabetes mellitus, tobacco use, and obesity. The 10-year cumulative incidence of HCC recurrence was 20.1%. EVR treatment for at least 24 months before HCC recurrence was associated with a protective effect on 5-year RFS [hazard ratio (HR) of 0.67 (95% CI 0.58 to 0.83)] and 5- year OS (HR 0.66, 95% CI 0.60 to 0.74). This effect diminished over a 10-year period for both RFS and OS. A longer time lag was associated with a more pronounced protective effect of EVR on the RFS. A consistent protective effect on RFS and OS was observed in sensitivity analyses in alcohol users and HCV patients. In diabetic patients, EVR demonstrated a protective effect against HCC recurrence yet exhibited a detrimental role in terms of overall survival. G-computation demonstrated that when patients are exposed to EVR for at least two years, there is a protective effect on OS in case where they develop HCC recurrence (HR: 0.56 (95% CI 0.35 to 0.90)) .

Conclusions: Our emulated trial data suggest that EVR significantly contributes to reducing HCC recurrence within the first five years post-LT and consistently improves OS in patients transplanted for HCC, underscoring its potential as a valuable therapeutic strategy in this patient population.

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EP_619 SPATIAL TRANSCRIPTOMICS IN PAEDIATRIC KIDNEY TRANSPLANT REJECTION

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Background: Unfortunately, many children suffer kidney failure for a variety of reasons. Kidney transplantation provides the best outcomes for these children. However, kidney transplants are a finite resource and are unlikely to last beyond 25 years, meaning most children will need re-transplanting in the future. We aim to identify biomarkers that may help diagnose transplant rejection earlier and with greater sensitivity than monitoring serum creatinine.

Methods: First, we de-paraffinised and then stained five kidney transplant biopsy samples with allograft dysfunction with haematoxylin and eosin (H&E). We then used a proteinase digestion protocol to remove barriers that will impede RNA collection. The degraded samples were then stained using immunofluorescence techniques with a variety of antigen markers. The samples were then imaged using confocal microscopy.

Results: We confirmed a diagnosis of acute T-cell-mediated rejection (aTMR) with H&E and identified areas of borderline rejection (BR) in the same sample. We optimised our immunofluorescence staining protocol and decided on using CD45, Pan-CK, and Syto-13 stains for identifying leucocytes, tubular epithelial cells, and nuclei, respectively. We are now able to segment areas around leucocyte involvement in BR and aTMR.

Conclusions: We now plan on proceeding with spatial transcriptomics and measuring RNA transcripts in areas of BR and comparing it with areas of aTMR using Bruker GeoMx technology.

EP_620 TORQUE TENO VIRUS LOADS AND IMMUNOSUPPRESSION INTENSITY IN STABLE OUTPATIENT SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Torque teno virus (TTV) is a promising biomarker for immune function in solid organ transplant recipients. It is not known whether immunosuppressive drug trough concentrations are associated with plasma TTV concentrations in the maintenance phase after solid organ transplantation. In this study, we aimed to investigate associations of trough concentrations of tacrolimus and mycophenolic acid with TTV load in kidney transplant recipients (KTR) and lung transplant recipients (LuTR) through a cross-sectional analysis at one-year post-transplantation.

Methods: A total of 290 KTR and 68 LuTR enrolled in the TransplantLines Biobank and Cohort Study at one year after transplantation were included. Whole blood tacrolimus and plasma mycophenolic acid (MPA) concentrations were measured using liquid chromatography-mass spectrometry (LC-MS/MS) and TTV load was measured using a real-time PCR assay (TTV R-GENE®, bioMérieux). Univariable and multivariable linear regression analyses were performed, adjusting for age, sex, smoking behavior and other immunosuppressive drugs.

Results: The KTR had a mean age of 55.3 ± 14.4 years, with 108 (37.2%) being female. The LuTR had a mean age of 55.7 ± 12.9 years, with 23 (33.8%) being female. TTV load was lower in KTR (4.49 ± 1.42 log10 copies/mL) than in LuTR (6.98 ± 1.39 log10 copies/mL). In KTR, tacrolimus concentration not associated with TTV load (st. $\beta = 0.05$, $p = 0.42$), while MPA concentration was positively associated with TTV load (st. $\beta = 0.25$, $p < 0.001$). Similarly, in LuTR, tacrolimus concentration was not associated with TTV load (st. $\beta = -0.15$, $p = 0.22$), while MPA concentration was positively associated with TTV load (st. $\beta = 0.37$, $p = 0.004$).

Conclusions: These findings indicate that MPA concentration at one year post transplantation is positively associated with TTV load, independent of tacrolimus concentration in both KTR and LuTR. Tacrolimus concentration showed no association with TTV load. These findings could shape future strategies for tailoring immunosuppression based on TTV load in solid organ transplant recipients.

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EP_621 MODULATION OF EXTRACELLULAR VESICLE RELEASE FROM ACTIVATED ENDOTHELIAL CELLS

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Background: Endothelial activation is a critical event during transplantation, influencing graft outcomes and immune responses. Extracellular vesicles (EVs) – lipid membrane-bound particles released by all cell types with unique biosignatures and immunomodulatory potential – function as intermediaries of cell signalling. However, the role of EVs released by activated endothelial cells during transplantation remains poorly understood. We hypothesise EVs derived from endothelial cells under inflammatory or normal conditions will have distinct cargo and induce different functional responses. This study aimed to investigate the characteristics and functional roles of EVs derived from activated endothelium.

Methods: The endothelial cell line HMEC-1 was activated with 20ng/ml IFNγ or left untreated for 72 hours, as assessed by flow cytometry for HLA-DR and ICAM-1 expression. EVs were isolated by size exclusion chromatography and characterised by nanoparticle tracking analysis (NTA), transmission electron microscopy (TEM), and western blot. EV surface marker expression was analysed with the MACSPlex EV flow cytometry kit (Miltenyi Biotec). Analysis of EV contents was conducted by mass spectrometry and Nanostring miRNA panel. Functional assays for endothelial proliferation and wound healing in response to these EVs was conducted by XTT and scratch assays respectively.

Results: HMEC-1 cells stimulated with IFNγ upregulated expression of HLA-DR ($p<0.05$) and ICAM-1 ($p<0.001$) indicating activation of the cells. Isolated EVs were 50-250nm in diameter with EV morphology and markers CD9, CD63 and TSG101 as assessed by NTA, TEM and western blot respectively. EV release following IFNγ stimulation decreased 70% as compared to untreated cells ($p<0.001$) (figure 1A-B). EV surface marker profile was altered, notably with the increased expression of HLA-class II ($p<0.001$) on EVs from IFNγ stimulated cells (figure 1C), confirmed by proteomics to be HLA-DR and HLA-DP specifically. These EVs did not result in any change to endothelial proliferation or wound healing. Work is underway to analyse the miRNA content.

Conclusions: The EV profile from endothelium activated by IFNγ is distinct from untreated endothelium. The presence of HLA-class II suggests these EVs have potential role in modulating immune responses.

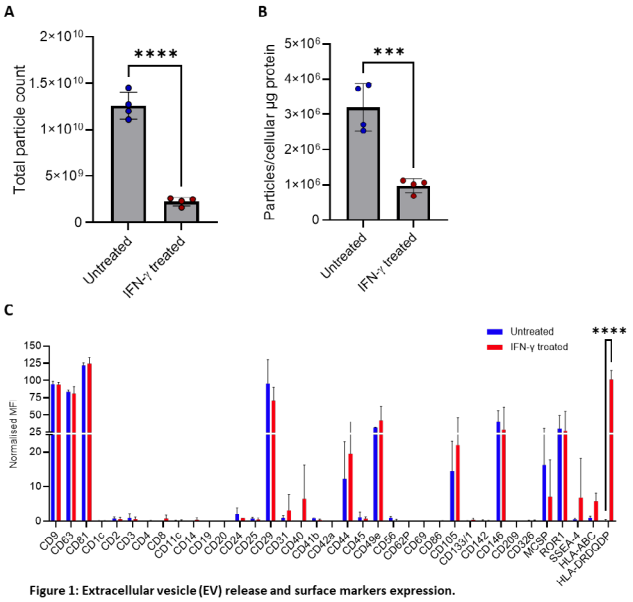

Figure 1: Extracellular vesicle (EV) release and surface markers expression.
HMEC-1 cells were treated with IFNγ or left untreated for 72 hours and EVs were isolated from the conditioned cell culture media by size exclusion chromatography. Particle counts were established by nanoparticle tracking analysis (A), and normalised to cellular content at the point for conditioned culture media collection (B). Surface marker expression was assessed by MACSPlex EV flow cytometry kit (C). Data shown represents mean ± SD of n=4. Statistical analysis was performed using a one-way ANOVA.

EP_622 NK ALLORECOGNITION REGULATES DONOR-SPECIFIC ANTIBODY PRODUCTION VIA THE INVERTED DIRECT PATHWAY

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Background: Two pathways of allorecognition lead to the production of donor specific antibodies (DSA) after transplantation: the indirect pathway (involving recipient CD4+ T and B cells), and the inverted direct pathway (involving donor CD4+ T cells originating from the graft and recipient B cells). The inverted direct pathway results in an early and transient wave of DSA, which can be observed in some patients transplanted with a T cell-rich graft (such as lung and intestine). This inter-individual heterogeneity led us to investigate the mechanisms involved in controlling the inverted direct pathway of DSA generation.

Methods and Results: Reproducing the clinical inter-individual heterogeneity of DSA generation through the inverted direct pathway, a cardiac graft from CBA (H-2k) mice induces an early DSA response in a CD3εKO C57BL/6 (H-2b) recipient mouse, whereas a Balb/c (H-2d) heart graft does not. Using adoptive transfer of T cells, we observed that CD4+ T cells from CBA donor survive longer than their Balb/c counterparts in C57BL/6 recipient mice. This difference was explained by the fact that C57BL/6 NK cells promptly eliminate T cells from Balb/c, thus preventing their interaction with recipient's B cells. Depletion of NK cells in CD3εKO C57BL/6 recipient mice prolonged the survival of transferred allogeneic Balb/c CD4+ T cells, resulting in DSA production through the restored inverted direct pathway. The clinical validity of these original experimental findings is currently being investigated in a large cohort of lung transplant patients.

Conclusions: In the context of transplantation, NK cell-mediated allorecognition is a double-edged sword. While the present study demonstrate that this mechanism protects against the microvascular lesions resulting from the generation of DSA through the inverted direct pathway, our group has previously reported that these same alloreactive NK can directly cause missing self-induced chronic microvascular rejection.

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EP_623 EVALUATION OF EARLY MYCOPHENOLATE LOADING WITH GENERIC MMF IN THAI KIDNEY TRANSPLANT PATIENTS

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Background: Mycophenolate mofetil (MMF) dosing for kidney transplantation (KT) in the Asian population is typically lower than in Western patients. An early loading protocol with higher dose achieves early target AUC more effectively that the standard fixed dose. Our previous study showed that a 2 g/day loading protocol achieved MPA AUC > 30 in 71% of the Thai population. However, the long-term outcomes of this loading protocol remain unexamined.

Methods: We conducted a retrospective study of KT patients at our center. A loading protocol using generic MMF (Immucept; Intas Pharmaceutical Ltd., India) at 2 g/day for one week, followed by a reduction to 1–1.5 g/day, was implemented in 2018. Patients who underwent KT between April 2018 and December 2021 were included in the loading group and compared to a historical cohort (2014–2016) receiving a fixed standard Asian dose of original MMF. Primary outcomes were acute rejection rates, graft outcomes, and infection complications.

Results: A total of 174 patients in the loading group and 136 in the historical cohort were included. Mean age was 44 ± 10 years. The historical cohort had more living donor KTs (50.7% vs 21.8%; p < 0.001) but fewer re-transplantations (1.5% vs 9.8%; p = 0.003). The loading group received more IL2-RA (81.6% vs 54.4%; p < 0.001) and anti-thymocyte globulin (14.4% vs 1.5%; p < 0.001). Rates of delayed graft function were similar (45.6% vs 46.6%; p = 0.866). Acute rejection within two years was lower in the loading group (10.3% vs 18.4%; p = 0.042), particularly for acute cellular rejection (2.9% vs 8.1%; p = 0.039) and mixed rejection (0.6% vs 3.7%; p = 0.049). Antibody-mediated rejection rates were comparable (6.6% vs 6.9%; p = 0.923). Kaplan-Meier analysis showed higher rejection-free survival in the loading group (log-rank p = 0.032) (Figure 1). eGFR at two years was similar (58 ± 22.4 vs 60.3 ± 23 mL/min; p = 0.38). Graft loss within two years was comparable (1.7% vs 1.5%; p = 0.86). No differences were observed in serious infections or CMV syndrome.

Conclusions: The MMF loading protocol, followed by standard Asian dosing, reduced acute rejection rates, particularly acute cellular rejection, without increasing adverse outcomes. Use of generic MMF showed no negative impact on transplant outcomes.

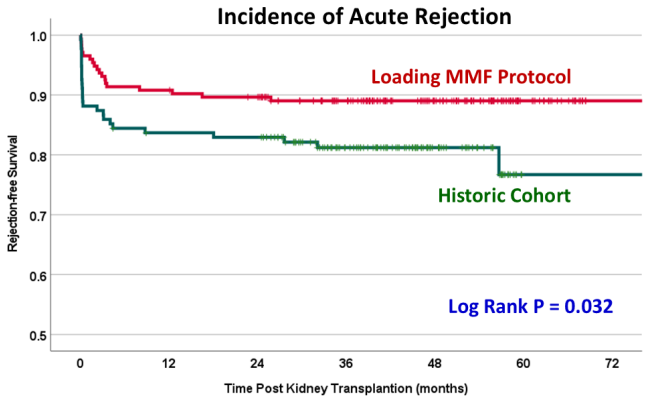

Figure 1: Kaplan-Meier Analysis for Incidence of Acute Rejection

EP_624 IMMUNOSUPPRESSIVE TREATMENT WITH TACROLIMUS AND PREDNISONE IN OLDER ADULT KIDNEY TRANSPLANT RECIPIENTS

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Background: The immunosuppressive regimen in kidney transplant (KT) that has shown the greatest efficacy consists of triple therapy with tacrolimus + mycophenolate + prednisone or tacrolimus + everolimus + prednisone, with no major changes made to adapt to the new profile of kidney transplant recipients (KTR). Often, it is necessary to suspend the third immunosuppressive drug, either due to intolerance or infectious/neoplastic events. Our objective was to analyze KTR on dual therapy and compare their baseline characteristics and post-transplant outcomes with those on triple therapy.

Methods: A retrospective study analyzing 552 KTRs (January 2017–March 2022). Data were collected on donor, recipient, and post-transplant outcomes. The median follow-up was 49.5 [32–66] months.

Results: The mean recipient age was 59 years, 41.9% female. 41.9% were on dual therapy with tacrolimus + prednisone at 11 (IQR 3–35) months post-transplant (56.3% initially started with tacrolimus + mycophenolate; 43.7% with tacrolimus + everolimus). The reason for the suspension was infectious events in 64.3%. Analyzing by age, 19.3% of KTRs <65 years suspended the third drug at 14 months post-transplant compared to 54.7% of those ≥65 years who did so at 7.5 months. Only 21.6% had the third drug reintroduced. Patients requiring suspension of the third drug were older, had grafts from older donors, and had worse renal function outcomes. Additionally, patients on dual therapy had more infectious and neoplastic events, with no increase in acute rejection or development of DSA. Multivariate analysis showed that age ≥65 years (OR 2.01 [1.2–3.2]) and having been readmitted ≥3 times for post-transplant infection (OR 3.2 [1.8–5.6]) were factors associated with suspension of an immunosuppressive drug post-transplant.

Conclusions: The suspension of the third immunosuppressive drug is a common phenomenon, especially in older adults KTRs, and usually occurs after infectious/neoplastic events. Anticipating these events and designing more individualized immunosuppression schemes should be a focus of our efforts in the upcoming years

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EP_625 THYMOGLOBULIN VS GRAFALON, INDUCTION TREATMENT IN KIDNEY TRASPLANT WITH MAASTRICHT TYPE III DONOR

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Background: Organ donation after controlled cardiac death has been crucial to increase the number of kidney transplants (KT); however, it is associated with a higher risk of delayed graft function. To palliate this risk, various strategies have been developed, such as reducing cold ischemia time, preservation with ECMO, and delaying the calcineurin inhibitors with the use of antithymocyte agents as induction treatment. The two most commonly used drugs are Thymoglobulin® and Grafalon®, both rabbit antithymocyte globulins, although they have different antigenic profiles and antibody concentrations. The equivalence between both is unknown, though it is postulated that Thymoglobulin® is three times more potent than Grafalon®. The aim of this project is to analyse the evolution of renal graft function, severe infectious complications, and graft survival, in relation to the induction treatment received with Thymoglobulin® (Genzyme) or Grafalon® (Neovii Biotech) in KT patients with controlled cardiac death donors.

Methods: We have carried out a retrospective, longitudinal, single-centre cohort study. The analysis includes 205 low immunological risk KT patients with Maastricht type III DCD donor performed at our hospital from January 2015 to December 2022. These patients received induction with Thymoglobulin® and Grafalon® according to the clinical practice of our centre, due to the risk of DGF. A comparative analysis was conducted regarding DGF, acute rejection, survival, infections, and bone marrow toxicity.

Results: Of the 205 KT patients, 165 received induction with Thymoglobulin® and 40 with Grafalon®. No significant differences were found in the characteristics of donor and recipient. There were also no differences in renal function nor in acute rejection (AR). There was a trend towards higher CMV infection in the Thymoglobulin® group, with no differences in other infections. A significantly higher lymphopenia was observed during the first year in the Thymoglobulin® group.

Conclusions: These results suggest that Grafalon® and Thymoglobulin® are comparable in terms of efficacy and safety, with a more favourable haematological profile for Grafalon® in low-immunological-risk KT recipients. However, further studies are needed to confirm these findings.

Figure:

	Thymoglobulin	Grafalon	P
Donors			
Age (years, mean ± SD)	54,4±12,3	58,5±10,2	0.055
Male (n, %)	75,9	75	0,900
Hypertension (n, %)	45,6	57,5	0,179
DM (n, %)	17,5	15	0,707
Cold ischemia time (h)	10,5±3,9	13,1±4,3	<0,001
Recipients			
Age (years, mean ± SD)	54,4 ±13,6	56,7±9,8	0,325
Male sex (%)	69,4	71.8	0,768
Caucasian race (n, %)	86,9	87,5	0.285
Hypertension (%)	90,3	77,5	0.029
DM (%)	24,2	20	0.572
Cardiovascular disease (%)	26,3	35	0,270
Body mass index >30 (%)	35,4	32,5	0.730
Hemodialysis (%)	78,8	95	0,101
Postrasplant			
Acute rejection (%)	35,9	46,2	0,238
DGF (%)	45	46,2	0,469
Total dosage (mg/Kg)	4,7±1,8	7,7±1,6	<0,001
Creatinine day 7 (mg/dL)	5,2±	4,9±	0,78
Creatinine month 1 (mg/dL)	2,2±	2,1±	0,682
Creatinine month 6 (mg/dL)	1,8±	1,9±	0,510
Creatinine month 12 (mg/dL)	1,8±	1,6±	0,335
Lymphocytes day 7 (nº/µL)	329	846	<0,001
Lymphocytes month 1 (nº/µL)	546	1094	<0,001
Lymphocytes month 6(nº/µL)	798	1089	0,032
Lymphocytes month 9 (nº/µL)	1031	1331	0,034
Lymphocytes month 12 (nº/µL)	1184	1479	0,102
Surgery complications (%)	9,9	17,5	0,179
Recipient survival (%)	97,4	92,4	0,511
Graft survival (%)	94,9	82,1	0,060
PostTx DM (%)	39,1	45,9	0,453
CMV infection (%)	40,8	26,3	0,106
BK infection (%)	17,6	15,8	0,796

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EP_626 THE EFFECT OF DAILIPORT ON RENAL FUNCTION IN KIDNEY TRANSPLANT PATIENTS

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Background: This report evaluates the effects of “dailiport” on renal function in renal transplant patients, analyzing changes in Tacrolimus (TAC), Creatinine, eGFR, and UACR pre- and post treatment. Data were collected from patients with complete measurements at three and six months. The study aimed to assess changes in these renal parameters and examine the influence of age on treatment outcomes.

Methods: . Statistical methods included descriptive analyses (mean and standard deviation) and inferential tests such as paired-samples t-tests, Wilcoxon signed rank tests, and Chi-square tests for age-related impacts.

Results: The results showed no significant change in Tacrolimus levels three months post-treatment (mean pre: 6.08, post: 5.98; t = 0.25, p = 0.8060; Wilcoxon Pr ≥ |S| = 0.6936). Creatinine levels remained stable at three months (mean pre: 186.59, post: 199.05; t = -1.29, p = 0.2116) but significantly increased after six months (Wilcoxon Pr ≥ |S| = 0.0065). eGFR showed no significant change at three months (mean pre: 38.50, post: 37.59; t = 0.79, p = 0.4361) but demonstrated a significant decline after six months (mean pre: 39.67, post: 34.07; t = 3.44, p = 0.0040; Wilcoxon Pr ≥ |S| = 0.0020). UACR showed minimal variation, with results inconclusive due to sample size limitations. Age (over or below 65) had no significant effect on the studied parameters.

Conclusions: These findings suggest that prolonged use of “dailiport” is associated with significant changes in creatinine and eGFR, highlighting potential risks to renal function. While age does not appear to influence these changes, close monitoring of renal parameters is critical to manage adverse effects. Further research with larger samples and longer follow up is needed to confirm these results and optimize treatment strategies for renal transplant patients.

EP_627 TACROLIMUS-RESISTANT UNIVERSAL CAR-T CELLS MEDIATE ANTI-TUMOR IMMUNITY IN HEPATOCELLULAR CARCINOMA

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Background: Tumor recurrence remains a substantial problem in patients who underwent liver transplantation. Although chimeric antigen receptor (CAR)-T therapy has emerged as a promising immunotherapeutic approach to fight cancers, its preparation process is complicated and the killing ability of CAR-T cells can be largely abolished in the presence of immunosuppressants.

Methods: We generated a GPC3-specific CAR with a mutated calcineurin subunit B (CNB) and overexpressed this CAR in murine T cells, after which we knocked off the TCR/CD3 complex of these CAR-T cells to generate immunosuppressant-resistant universal (IRU) CAR-T cells.

Results: IRU-CAR-T cells display improved effector function in vitro, compared with CAR-T cells carrying wild-type CNB. Also, IRU CAR-T cells retain anti-tumor effector function in vivo in the presence of both allogeneic T cells and FK506. Furthermore, the function and survival of allogenic grafts were not affected by IRU-CAR-T.

Conclusions: These findings demonstrate the efficacy of IRU-CAR-T cells as a universal, ‘off-the-shelf’ treatment option, which holds great promise to treat patients who occurred tumor recurrence after liver transplantation.

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EP_628 IMPACT OF ANTIHUMORAL THERAPY ON HYPERCOAGULABILITY IN KIDNEY TRANSPLANT RECIPIENT

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Background: The development of de novo anti-HLA donor specific antibodies (DSAs) is associated with poor outcomes in kidney transplant recipients. Previously we have shown that the presence of DSAs is associated with hypercoagulability as measured by the thrombin generation assay (TGA), which may contribute to the pathomechanism of antibody-mediated rejection (ABMR). We present a 23-year-old female patient's case with end-stage renal failure due to ANCA vasculitis, who underwent a successful cadaver kidney transplant in 2013. She conceived a child with stable graft function 9 years after transplantation. After delivery, during routine DSA screening, elevated anti-HLA II DSA titers (anti-DQB: 36685 MFI) were found with normal renal function parameters. In 2024, a kidney graft biopsy proved active ABMR and acute T-cell rejection (1-g/ptc/v>0, +1-c4d>1, +1-g+ptc>1). Antirejection treatment was initiated, including plasmapheresis, i.v. immunglobulin, and tocilizumab (TZC) administered parenterally monthly for 6 months.

Methods: Hemostasis parameters were monitored, and TGA was performed, determining lag time, endogenous thrombin potential (ETP), peak thrombin, and time to peak parameters. In order to correlate the results with potential changes in DSA status over time during antirejection treatment, repeated samples were taken before treatment and monthly for 6 months.

Results: As a result of treatment, the DSA titer against HLA II showed a discrete decrease (29360 MFI). On the other hand, the degree of hypercoagulability showed considerable decrease during the course of treatment: D-dimer decreased from 0.83 mg/L to below threshold (0.26 mg/L), peak thrombin was reduced from 327.3 nM to 203.15 nM, and ETP decreased from 1604 nM*min to 1304 nM*min.

Conclusions: Our case illustrates that the presence of DSAs can lead to hypercoagulability, which may promote the development of ABMR, however, such hemostasis abnormalities may be reversed with appropriate antihumoral treatment.

EP_629 B-CELL FLOW CROSSMATCH POSITIVITY AND ACUTE REJECTION: CAUSE FOR ALARM?

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Background: The impact of B-cell positive cytometric flow crossmatch (B-cell cFCXM) on early kidney transplant outcomes remains unclear. This study aimed to evaluate whether a B-cell cFCXM positivity increases the risk of acute rejection within the first-year post-transplant.

Methods: A retrospective cohort study was conducted at our center, including kidney transplant recipients from 2020-2023. Only patients with local follow-up were included. Recipients were categorized based on B-cell cFCXM results (positive or negative). The primary outcome was the incidence of biopsy-proven acute rejection (BPAR) during the first-year post-transplant.

Results: 247 kidney-only transplants were done in our centre (63 LD, 102 DBD and 82 DCD). 207 patients had their 1st kidney transplant, 27 patients having a 2nd kidney transplant, and 9 who previously had 2 or more kidney transplants. 4 patients were excluded from the analysis as their crossmatch reports were unavailable. Of the patients evaluated, 43 had positive B-cell cFCXM, 191 had negative B-cell cFCXM results and 9 had historic B-cell cFCXM positive. As these 9 patients had current B-cell negative cFCXM results they were included in the B-cell negative group. Of those with a B-cell positive cFCXM; 5 were reported as intermediate immunological risk, and 1 in the historic B-cell positive and 1 in the B cell negative groups were reported as intermediate immunological risk. All others were reported as standard immunological risk. The incidence of BPAR in the first year was comparable between groups 13.95% (B-cell cFCXM positive) vs. 16.5% (B-cell cFCXM negative), p =0.68 (see table 1)

Conclusions: In this cohort of kidney transplant recipients, B-cell cFCXM positivity did not significantly increase the risk of acute rejection in the first-year post-transplant. These findings suggest that B-cell cFCXM positivity alone may not warrant heightened concern for early rejection risk. Further studies with larger sample sizes are needed to validate these results.

	B-cell Positive cFCXM			B-cell Negative cFCXM		
Tx	**Rejection (%)**	**No Rejection (%)**	**Total**	**Rejection (%)**	**No Rejection (%)**	**Total**
1	4 (12.9)	27 (87.1)	31	25 (14.2)	151 (85.8)	176
2	1 (12.5)	7 (87.5)	8	5 (26.3)	14 (73.7)	19
3	0	2 (100)	2	3 (60)	2 (40)	5
4	0	1 (100)	1	0	0	0
5	1 (100)	0	1	0	0	0
OVERALL	**6 (13.95)**	**37 (86.05)**	**43**	**33 (16.5)**	**167 (83.5)**	**200**

Table 1

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EP_630 SHORT-TERM FASTING BEFORE LIVING KIDNEY DONATION HAS AN IMMUNE-MODULATORY EFFECT

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Background: Short-Term Fasting (STF) is an intervention reducing the intake of calories, without causing undernutrition or micronutrient-related malnutrition. It aims to systemically improve resilience against acute stress. Several (pre-) clinical studies have suggested protective effects of STF, marking the systemic effects STF can induce in respect to surgery and ischemia-reperfusion injury. In addition, STF also affects the number of circulating immune cells. We aim to determine the effect of STF on the abundance and phenotype of different immune cell populations.

Methods: Thirty participants were randomly selected from the FAST clinical trial, including living kidney donors, randomised to an STF-diet or control arm. In an observational cohort sub-study we prospectively included 30 patients who donated blood samples repeatedly during study runtime. Using flow cytometry analyses, immune cell phenotyping was performed on peripheral blood mononuclear cells. Three panels were designed to investigate the presence and activation status of peripheral T cells, B cells, dendritic cells (DCs) and myeloid cells.

Results: Eight participants were excluded due to sample constraints. Baseline characteristics showed no significant differences, except for fasting duration. Weight changes were minimal and non-significant across different time intervals, with slight trends towards long-term weight loss pre-surgery. Glucose, insulin, and β-hydroxybutyrate levels differed significantly between groups, reflecting adherence to the fasting diet. Flow cytometry and RNA sequencing analysis revealed no baseline differences between groups, with high variability within each group. STF changes the levels and phenotype of immune cells, reducing the abundance and activation of T cells, including regulatory T cells, increased presence of (naïve) B cells, and elevation of type 1 conventional DCs (cDC1s). In addition, a decrease in central memory T cells was observed.

Conclusions: STF results in reduced numbers and activation status of T cells and Tregs, increased presence of (naïve) B cells, and elevation of cDC1s. Further research should focus on the clinical implications of changes in immune cells and significance of these observed immunological changes.

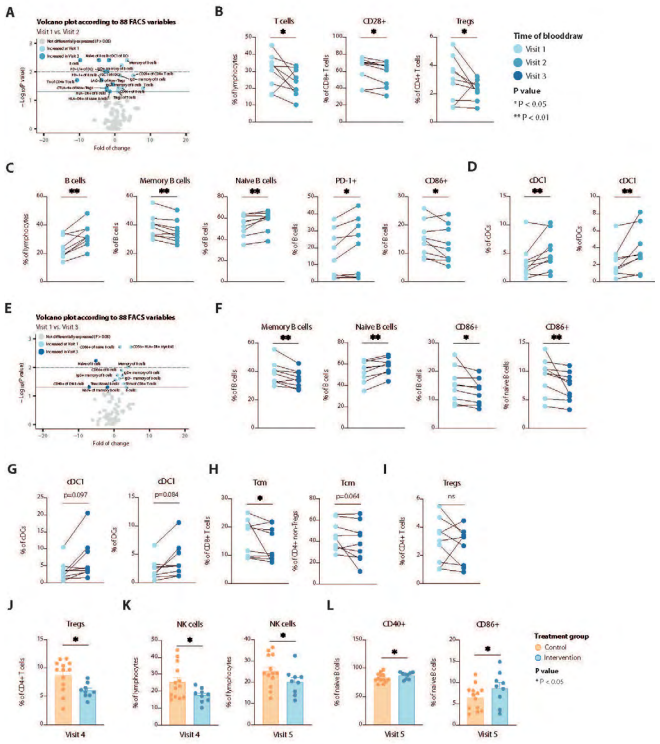

Figure 1: Alterations in immune cell populations

EP_631 URINARY MRNA BIOMARKERS FOR THE NON-INVASIVE DIAGNOSIS OF CALCINEURIN INHIBITOR TOXICITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Although immunosuppressive drugs have improved to reduce renal allograft rejection, renal allograft failure has not markedly diminished. Biochemical examination and invasive biopsy have low sensitivity for diagnosis of tacrolimus toxicity and kidney injury in kidney transplantation. Therefore, the development of non-invasive diagnosis for tacrolimus toxicity and acute and chronic kidney injury using expression level of urinary mRNA is required for long-term graft survival in the kidney transplant patients.

Methods: 110 urine specimens (35 stable, 30 acute rejection (AR), 15 acute calcineurin inhibitor nephrotoxicity (CNI), 10 chronic CNI and 20 acute tubular necrosis (ATN)) were collected after transplantation. RNA extracted from urine pellets was reverse-transcribed and 4 transcripts associated with calcinurin inhibitor toxicity in microarray results published by Maluf et al were investigated using real-time PCR.

Results: Four transcripts (LTF, NNMT, WFDC2, and HIF1A) were selected in published microarray data for diagnosing tacrolimus toxicity by real-time PCR analysis. The expression levels of LTF, NNMT, and HIF1A were significantly decreased in CNI group while 18S were increased. There was no difference of the expression of WFDC2 mRNA between groups. These transcripts discriminated patients with tacrolimus toxicity from patients with ATN and AR. A combination of mRNAs for 18S, LTF, NNMT, and HIF1A that distinguishes CNI from ATN and AR yielded the area under the curve of 0.94 and 0.87, respectively.

Conclusions: We investigated genetic biomarkers to develop a noninvasive diagnostic assay in urine of kidney transplant patients. These urinary mRNAs may be useful to non-invasively monitor allograft kidney in clinical decisions.

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EP_632 CAN THE PIRCHE ALGORITM BE USEFUL IN HEART TRANSPLANT?

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Background: Rejection in heart transplantation continues to be a challenge for clinicians. It is associated with morbidity and mortality. The use of algorithms can be a tool in the immunological risk assessment of heart transplant patients.

Methods: Retrospective observational study seeks to compare patients diagnosed with AMR or CMR to those without rejection, with the objective of identifying predictors of rejection during follow-up. The study population was divided into two groups: 100 patients without rejection episodes and 30 patients with rejection. Preoperative data were comparable in the study population. Patients were evaluated at a mean follow-up of 93 in which they underwent routine evaluations, including blood tests, TTE, viral load monitoring for CMV, EBV, and Toxoplasma. For patients diagnosed with CMR or AMR, the PIRCHE-II score was calculated.

Results: PIRCHE-II score was significantly higher in the rejection group, averaging 127.9 (±40.75), compared to 94.51 (±39.66) in the non-rejection group (p=<0.005).The logistic regression analysis conducted on several variables related to rejection risk after heart transplantation provides insightful findings. The first significant predictor identified was the use of **post-operative continuous venovenous hemofiltration (CVVH)**. This association is statistically significant, as indicated by the confidence interval (1.217 - 9.567), p-value of 0.02. **Post-operative mechanical ventilation (MV)** showed no significant relationship with graft rejection. The odds ratio of 1.001, (0.999 - 1.002). Another important finding was the role of **PIRCHE-II scores** as a predictor of rejection (p-value 0.001 (1.010 - 1.035).

Conclusions: This study underscores the significance of PIRCHE-II scores as a key predictor of rejection in heart transplant recipients. Our findings demonstrate a clear correlation between higher PIRCHE-II values and an increased likelihood of both antibody-mediated and cell-mediated rejection. Despite the valuable insights provided, the study's limitations, such as a small patient cohort and a relatively short follow-up period, suggest that further research with larger sample sizes and extended follow-up is needed.

EP_634 ASSESSMENT OF THE IMMUNE PROFILE OF B CELLS IN DIALYSIS PATIENTS UNDERGOING KIDNEY TRANSPLANTATION

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Background: Characterization of B cells in dialysis patients, candidates for kidney transplantation and the effect of haemodialysis duration and modality on B-cell subpopulations is limited.

Methods: Cluster analysis of the frequencies and absolute numbers of B cell subpopulations from 78 dialysis patients identified two distinct clusters when frequencies applied. One cluster included individuals with shorter dialysis duration, and the other with longer duration. Similarly, two clusters identified based on absolute numbers.

Results: When the identified clusters were compared, the resulting immune profiles differed whether frequencies or absolute numbers were considered. Frequency analysis revealed increase in total memoryCD19+IgD$^-$/IgD$^+$CD27$^+$, class-switchedCD19+CD27+IgD-, non-switchedCD19+CD27+IgD+, doublen-egativeCD19+CD27-IgD- and marginal zone BcellsCD19+CD27+IgM+IgD+ in the long-term dialysis patients, while naiveCD19+CD27-IgD+ and the regulatory B cells: mBregsCD19+CD24 ++CD27+,tBregsCD19+CD24++CD38++ and plasmablasts CD19+CD38++CD27++IgD+/- decreased. The pattern was reversed in the short-term dialysis group. The absolute numbers in the total B cell populations of the clusters decreased significantly in the long-term group, while significantly increased in the short-term dialysis patients. Frequency or absolute number differences in cluster populations were independent of dialysis modality. Age did not contribute to B-cell subpopulations absolute number changes, but it did to their frequency changes.

Conclusions: Kidney transplant candidates can be classified by means of cluster analysis into discrete B-cell immunophenotypic profiles, the architecture of which varies depending on whether cluster analysis is based upon cell frequency or absolute cell number. The distribution of B-cell subpopulations is subject to variation in accordance with the commencement of dialysis and the age of patients.

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EP_635 OPTIMAL FEASIBILITY TRIAL: OPTIMISING IMUNOSUPPRESSION FOR OLDER ADULT KIDNEY TRANSPLANT RECIPIENTS

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Background: Immune system ageing (immunosenescence) may mean that older adults have a lower risk of transplant rejection than younger adults, but higher risks of infection and malignancy. Age-related changes also alter the metabolism of medications, meaning older adults may be more likely to experience side effects with standard immunosuppressive regimens. Mycophenolate mofetil (MMF) is particularly poorly tolerated. Less immunosuppression can reduce the likelihood of infection, malignancy and medication side-effects, but increase the likelihood of rejection. Older adults may find the side-effects of treatment for rejection more severe than younger adults, and therefore may prefer to live with the risks and side-effects of standard immunosuppressant doses to avoid rejection and the accompanying escalation in immunosuppression. Older adults have largely been excluded from immunosuppression trials; therefore, the optimal kidney transplant immunosuppressant regimen in older adults is unknown. There are no national guidelines and there is centre variation in treatment. Randomised controlled trials (RCTs) in older transplant recipients are needed.

Methods: The NIHR-funded OPTIMAL trial is a pragmatic, multi-centre, feasibility RCT comparing MMF 1.5g/day with MMF 1g/day in individuals aged ≥65 years at the time of kidney transplantation. The primary aim is to determine the feasibility of undertaking a later effectiveness RCT. Participants will be randomised 1:1 to either MMF dose alongside tacrolimus and prednisolone for the first 3 months following transplantation. The study will be based at four NHS Trusts. Recruitment will run from 01/03/25-01/04/26. The target sample size is 40. Trial follow-up at 3 and 6 months will assess clinical, laboratory (immune function measures), patient-reported data, and protocol adherence.

Results/outcomes: The primary outcomes for this feasibility study are: • Size of eligible population. • Recruitment, protocol adherence, and retention. •Acceptability of trial methods/intervention. • Barriers to trial delivery

Conclusions: The study will report in 2026. A quantitative dashboard will guide decision-making regarding progression to a definitive RCT.

EP_636 RECURRENT FSGS IN KIDNEY TRANSPLANT RECIPIENTS: KUWAIT EXPERIENCE

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Background and aim of the study: Post-transplant FSGS is a major risk factor for graft loss. We therefore aimed to assess patients with FSGS in our cohort of kidney transplant recipients.

Patients and methods: In this retrospective study that aimed to investigate glomerular disease recurrence post-transplantation. Kidney transplant recipients (KTR) were screened for the diagnosis of FSGS between 1996 and 2023 and details were recorded about the transplant, clinical outcomes, treatments, and other risk factors.

Results: Among 3670 KTR screened for FSGS, 106 were identified to have FSGS as original kidney disease. Of them, 52 had a diagnosis of idiopathic FSGS. Most of the patients were Kuwaiti males who received their grafts from living donors (84.9%). Prophylactic plasma exchange (PE) was performed in 19 (38%). All patients were maintained on CNI based triple immunosuppression. FSGS recurrence was confirmed in 10 patients (17.5%). PE and rituximab were the most frequent treatment options (7 out of 10 patients received PE and rituximab) and 4 patients had recurrence despite prophylactic PE and rituximab. The remaining patients were managed by anti-proteinuric agents. At one year follow-up, complete remission was observed in 5 patients while the remaining showed partial remission. Two patients lost their grafts within 2 years while the remaining 8 are enjoying stable graft function. Patient or graft outcomes were comparable between primary and secondary FSGS cases(P>0.05).

Conclusions: Lower rate of recurrence of idiopathic FSGS in our cohort (15.3 %) and the comparable patient and graft outcomes might be due to the optimized immunosuppressive regimen.

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Transplant immunology & immunosuppression

EP_637 THE PROGNOSTIC IMPACT OF BLOOD TRANSFUSIONS PERFORMED WITHIN EARLY PERIOD AFTER TRANSPLANTATION

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Background: Blood transfusion is performed in 40-60% of kidney transplant recipients, but there is disagreement as to whether transfusion-induced de novo DSA production has an effect on transplanted kidney prognosis. In this study, we compared the prognostic impact of red blood cell transfusions performed within 1 week after kidney transplantation, when recipients were in the state of strong immunosuppression, with transfusions performed after 1 week of kidney transplantation.

Methods: We investigated the number of red blood cell transfusions during the first year after kidney transplantation in 176 kidney transplantation performed at our hospital between May 2007 and May 2024, and examined the relationship between timing of transfusion and prognosis of transplanted kidney.

Results: Transfusion were performed after kidney transplantation in 110 recipients, and the median transfusion volume was 4 units. The number of recipients did not receive transfusion had 61, recipients received within 1 week had 66, and recipients received after 1 week had 44. Recipients received transfusion within 1 week had no changes in prognosis, but recipients received transfusion after 1 week had a significantly worse prognosis compared to the recipients did not receive transfusions after kidney transplantation.

Conclusions: Transfusion within the first postoperative week did not significantly change the prognosis of rejection or the outcome of the transplanted kidney compared to the non-transfused group.

EP_638 SINGLE-CELL TRANSCRIPTOMIC ANALYSIS OF EARLY T CELL MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Allograft inflammation, primarily caused by rejection and infection, is a significant contributor to graft damage and loss in kidney transplantation (KT). This study aimed to characterize the molecular signatures in KT recipients with T cell-mediated rejection (TCMR) using single-cell transcriptomics.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from three KT recipients: one with stable kidney function and two with TCMR at three months post-transplantation. Single-cell libraries were generated using the BD Rhapsody Enhanced Cartridge Reagent Kit platform. Multiplexing data analysis was performed using the Cell-Ranger Pipeline, R and "Seurat" packages.

Results: A total of 9,849 cells were analyzed (3251 cells from a stable patient, 4036 and 2562 cells from TCMR patients). Fourteen distinct cell clusters were identified, each showing differentially expressed transcripts across samples. TCMR samples showed increased in memory T cells, naïve CD8+ T cells, and monocytes, with significant decrease in cytotoxic CD8+ T cells and CD4+ Th1 cells. Differential gene expression analysis revealed significant several gene alterations between TCMR and stable patient. Downregulated genes in TCMR included XIST (log2FC = -2.1), DUSP2 (log2FC = -1.8), and GRIP1 (log2FC = -1.7), while Y chromosome-linked genes including UTY, PRKY, and USP9Y were significantly upregulated (log2FC > 1.5). In TCMR patients, immune-related genes such as PIK3R1, CXCR4, and IL2RG were decreased in NK and T cells. Specifically, CCL4L2 was increased in NK cell, IL7R was increased in memory CD4+ T cells and TNFSF8 was decreased.

Conclusions: Single-cell transcriptomics provides a high-resolution view of cellular heterogeneity in TCMR, offering a comprehensive understanding of the immune response in graft rejection.

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EP_639 MABTHERA VERSUS THE BIOSIMILAR TRUXIMA AS DESENSITIZATION IN PATIENTS UNDERGOING KIDNEY TRANSPLANT

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Background: Truxima® (rituximab biosimilar) has been studied in various populations, but to our knowledge, no existing study has evaluated its effect on kidney transplant recipients. The aim of the study is to assess the efficacy and safety of biosimilar rituximab Truxima® compared with Mabthera® in desensitization therapy in patients undergoing kidney transplantation.

Methods: A single-center, retrospective, non-inferiority study comparing Mabthera® to its biosimilar Truxima®. Study was approved by Research Affairs (#2241146). All patients meeting inclusion criteria between January 2018 and December 2023 were included. The primary endpoint was biopsy-proven rejection within the first three months post-transplantation. Categorical variables were presented as percentages, while continuous variables were reported as median and interquartile range (IQR). Fisher's Exact Test was used for inferential analysis ($p < 0.01$). For the primary endpoint, a two-sided 95% confidence interval for the difference in rates was calculated assuming a binomial distribution (margin of 7%). Stata 14.1 was used for analyses.

Results: As a preliminary results, 112 samples were collected (56 in each group). Demographic data were balanced between the two groups. For rituximab indications, ABO incompatibility was more common in the Truxima® group (67.9%) than in the Mabthera® group (55.4%). Similarly, positive crossmatch was more frequent in the Mabthera® group (66.1%) compared to the Truxima® group (41.1%). For the primary endpoint, the percentage of overall rejection episodes was 17.90% for Mabthera and 30.40% for Truxima, indicating a risk difference of approximately 13% with a 95% confidence interval of -28.17% to 3.17% (p-value > 0.01). Factors associated with rejection were HLA-B and HLA Class II mismatches for ABO-incompatible transplants and previous transplants and donor age for positive crossmatch ($p < 0.01$).

Conclusions: Because of point estimate is even smaller than -7%, we can not confirm that Truxima is non-inferior to Mabthera in rejection rates. More prospective head-to-head studies with larger sample size are needed to determine how well these treatments compare to each other.

EP_640 COMPARISON OF TACROLIMUS FORMULATIONS IN DE NOVO KIDNEY TRANSPLANTATION RECIPIENTS-5 YEAR FOLLOW-UP

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Background: Complications after kidney transplants show a close relationship with immunosuppressive drugs in the short and long term. The most commonly used tacrolimus-containing drugs are key in preventing rejection, but their side effects are also well known. Pharmaceutical manufacturers are developing various techniques to achieve the lowest possible dose to maintain target blood concentrations, and clinicians are trying to establish risk assessment algorithms (e.g. concentration/dose (C/D) ratio).

Methods: In our study, we followed 100 de novo kidney transplant recipients for 60 months after surgery, of whom 50 received ER-tacrolimus and 50 received LCP-tacrolimus therapy. Serum creatinine, urea, sodium, potassium, triglyceride, cholesterol, CRP and blood count values were collected at a total of 10 time points, and tacrolimus blood concentration, C/D ratio and biopsy-proven acute rejections, morbidity and mortality data were summarized. Statistical methods were used to analyze the above characteristics of the two groups.

Results: At most time points, significantly ($p \leq 0.05$) higher C/D ratios can be measured in the LCP tacrolimus group, and here at time points later than 6 months, the C/D ratios continuously decrease. At most of the measurement points, the tacrolimus concentration was higher in the target range expected by our center in the LCPT group than in the ER group. No significant difference could be detected between the rejections, mortality and morbidity data in the two groups during the 60-month follow-up.

Conclusions: It can be stated that the newly developed LCP tacrolimus can be used similarly safely as the previously known ER formula, however, better results in preserving the quality of transplanted kidneys are expected from the LCPT formula, as they will be exposed to less tacrolimus. Individualization of immunosuppression and timely recognition of patients belonging to risk groups are essential in improving long-term results.

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EP_641 INFLAMMATORY CYTOKINES AND HYPERCOAGULABILITY IN KIDNEY TRANSPLANT PATIENTS WITH ANTI-HLA ANTIBODIES

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Background: The development of *de novo* anti-HLA donor specific antibodies (DSAs) leads to poor outcomes in kidney transplant recipients. In our previous work, we have shown that the presence of DSAs is associated with hypercoagulability as measured by the thrombin generation assay (TGA), and may contribute to the pathomechanism of antibody-mediated rejection (ABMR). Our aims were to investigate the relationship between de novo anti-HLA donor-specific antibodies, inflammatory cytokine profiles, and hypercoagulability in kidney transplant recipients.

Methods: In this observational cohort study, 27 kidney transplant recipients with DSAs (DSA+ group) and 16 without DSAs (DSA– group) were enrolled. Venous blood samples were obtained, and TGA and inflammatory cytokine profiling was carried out from platelet-free plasma. Cytokine profiling was performed using a bead-based multiplex immunoassay allowing the simultaneous quantification of 13 human inflammatory cytokines (IL1-β, IFN-α2, IFN-γ, TNF- α, MCP-1, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33).

Results: TNF-α and IL-6 were significantly increased in the DSA+ group as compared to DSA– patients (median TNF-α: 32.7; IQR:17.4-82.3 vs. 8.5; IQR:4.8-28.3 pg/mL, p=0.042 and median IL-6: 34.1; IQR:22.9-58.4 vs. 21.5; IQR:19.5-33.0 pg/mL, p=0.005, respectively). The extent of thrombin generation was significantly higher in the DSA+ group as compared to DSA– patients (endogenous thrombin potential median:1701; IQR:1382-1940 vs. 1458; IQR:1221-1660 nM*min, p=0.038). IL-10 levels demonstrated a significant negative correlation with TGA parameters.

Conclusions: Our findings reveal insights into the pathomechanism of ABMR, demonstrating that de novo DSAs in kidney transplant recipients are associated with elevated inflammatory cytokines (TNF-α and IL-6) and increased thrombin generation. The inverse correlation between IL-10 and TGA parameters highlights a potential regulatory role in hypercoagulability.

EP_642 IMPACT OF BOWEL SURGERY ON MYCOPHENOLATE MOFETIL PHARMACOKINETICS: A PROSPECTIVE COHORT STUDY

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Background: Mycophenolate mofetil(MMF) is a current immunosuppressive drug for preventing renal allograft rejection in transplant recipients. This study arises from a case of a 38-year-old male with advanced non-compacted cardiomyopathy who underwent orthotopic heart transplantation. On the 4th day post-surgery, he developed a paralytic ileum complicated with cecum perforation and faecaloid peritonitis that required emergent right hemicolectomy and terminal ileostomy. During follow-up pre-dose MMF levels were undetectable despite ensuring good adherence and increased MMF dose, meanwhile, tacrolimus levels were on target. After an ileostomy, the absorption process is affected leading to differences in drug concentrations. Therefore, this study aimed to evaluate the changes in MPA exposure before and after an intestinal resection in a cohort of solid-organ transplant recipients.

Methods: This is a prospective pharmacokinetic study of MMF or enteric/coated mycophenolate sodium(MPS) evaluating changes on drug exposure after bowel resection and bowel reconstruction. Complete hematological and biochemical profiles, surgical variables, anthropometrical measures, and concomitant medication were collected. Two pharmacokinetic profiles, under the ileostomy and after the bowel reconstruction were performed. Blood patient samples were collected at Pre-dose and different time points after immunosuppressor intake.

Results: Results on area under the curve (AUC) 0-12h were lower than the target recommended (30-50µg.h/mL). Curiously, despite patients showing an optimal peak of absorption measured by Cmax, no patients had any MMF/MPS detectable level after 4.5hours of drug administration, leading to an undetectable pre-dose concentration.

Conclusions: These results confirm that after the resection, the pharmacokinetic profile of MMF is affected, and there is not a second peak of absorption concluding an interruption of the drug enterohepatic circulation(EHC). Patients with ileostomy and solid organ transplant may be at risk of rejection given the lack of EHC of MMF/MPS. More intensive therapeutic monitoring of MPA with AUC0-12h is recommended to avoid MPA under or no-exposure and conversion to other immunosuppressants such as everolimus or belatacept instead of a CNI should be considered.

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EP_643 THE ROLE OF PANCREAS GRAFT BIOPSIES IN THE MANAGEMENT OF PANCREAS TRANSPLANT RECIPIENTS

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Background: Follow-up of pancreas transplant recipients is commonly based on exocrine, endocrine, allo-immune and auto-immune markers. However, histology remains the gold standard to diagnose rejection or auto-immune recurrence. Our purpose was to evaluate the performance of pancreas biopsies in the management of pancreas transplant recipients.

Methods: We included all patients followed at the university hospital of Lyon who received a pancreas transplantation (with simultaneous kidney transplantation or alone) from January 2011 to December 2022 and who underwent at least one pancreas biopsy between transplantation and October 2023.

Results: We collected 121 biopsies (96 for cause, 25 protocol biopsies) in 85 recipients (81% SPK). 21 (17%) were non-contributive. There were 7 (5.8%) biopsy-related minor complications and 1 severe complication without graft loss. 83% of contributive biopsies performed for lipase increase showed rejection without any link between lipase value and presence or severity of rejection. 1 out of 6 biopsies performed for de novo DSA without any other abnormality showed cellular rejection. 2 out of 15 biopsies performed for abnormal OGTT showed rejection that is closed to subclinical rejection founded in 3 out of 21 (14%) contributive protocol biopsies. 36% of simultaneous pancreas and kidney biopsies (n=59) results were discordant. One-year pancreas graft survival after a normal or indeterminate for rejection biopsy is 100 % without any treatment. Overall one-year pancreas graft survival after rejection treated with steroids is 85 % (94% for grade I rejection and 78% for grade II rejection).

Conclusions: Pancreatic graft biopsy is a safe procedure, essential in cases of lipase increase to diagnose rejection, guide treatment according to severity, and for graft prognosis. Concordance with kidney graft biopsies is poor. Treatment is not necessary if the result is indeterminate for rejection. Systematic biopsies at 1 year show 14% of subclinical rejection.

EP_644 THE APPLICATION OF DONOR-DERIVED CELL-FREE DNA TESTING FOR EARLY MONITORING AFTER RENAL TRANSPLANTATION

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Background: Graft rejection remains a major cause of reduced graft survival and graft biopsy is the gold standard of diagnosis. The use of new biomarkers capable of monitoring subclinical graft damage beyond the limitations of traditional approaches and avoiding unnecessary biopsies is a major challenge in transplantation. The aim of this ongoing study is to investigate the potential of dd-cfDNA as a biomarker for monitoring patients after kidney transplantation and for early diagnosis of graft rejection.

Methods: 34 patients who underwent kidney transplantation (19 living and 15 deceased) between October 2023 and July 2024 were randomly selected for dd-cfDNA quantification using the AlloSeq dd-cfDNA (CareDx Inc). Measurements of dd-cfDNA from patients' plasma were performed at 1 month, 3 months and 6 months post-transplant and in some cases prior to a "for cause" graft biopsy. Preliminary results of dd-cfDNA measurements were combined with established laboratory markers used to diagnose rejection (serum creatinine, proteinuria, DSAs) and tacrolimus levels at the time of measurement.

Results: Elevated values (equal or above the threshold of 0,5%) were found in 17/34 samples at 1 month after transplantation and correlated with TCMR, ACMR, mixed rejection and graft injury of other causes. The rejection group was biopsy proven in 7/17 patients (41.2%), 2/17 patients (11.8%) had no rejection (biopsy proven), 8/17 (47.1%) had graft injury (mainly urinary infection or trauma at the time of measurement). The dd-cfDNA values were higher in rejection group of recipients compared to no-rejection (0.68 vs 0.47) and in ABMR compared to TCMR (1.28 vs 0.5). ABMR had the strongest association with dd-cfDNA compared to the other laboratory markers. 28 patients in the sample underwent a second measurement at 3 months and 12 of them had a third measurement at 6 months with no significant differences in dd-cfDNA values between the rejection and non-rejection groups. Also, in cases of "for cause" graft biopsy the results were associated with the dd-cfDNA value.

Conclusions: Donor-derived cfDNA seems to be a new promising biomarker that contributes in the early detection of rejection. Threshold values and surveillance strategies in kidney transplant patients need to be established by further studies.

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EP_645 TACROLIMUS VS. NEORAL BASED MAINTENANCE IMMUNOSUPPRESSIVE REGIMENS AMONG KIDNEY TRANSPLANT RECIPIENTS: KUWAIT EXPERIENCE

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Introduction: Both tacrolimus and cyclosporine function as immunosuppressants by inhibiting calcineurin, which downregulates IL-2 and other cytokine gene translations, and the two show similar graft survival rates. Some studies are still debating the use of either of them in low-risk kidney transplant patients especially in terms of infection rates and cardiovascular risk profile.

Aim: we aimed to assess the safety and efficacy of Tac. And CsA among low risk kidney transplant recipients with living donors.

Patient and methods: Out of 3000 living kidney transplant recipients who were followed up in Hamed Al-Essa organ transplant center in Kuwait, 660 patients received their grafts from living donors under low immunological risk during the period between 2010 and 2023. In this retrospective study, patients were divided into two groups according to the CNI used: (Tac. Based therapy comprised group 1, n=328 patients) and (CsA based therapy comprised group 2, n=332 patients). The two groups were compared regarding their demographics and their outcome.

Results: The mean age was 42.2±17.2 with no significant difference between the two groups. The majority of patients were Kuwaiti males, and most of them reached end stage kidney disease due to diabetic nephropathy or chronic GN ($p>0.05$). The two groups were comparable regarding their demographics (dialysis mode, virology profile, IHD, DM, and hyperlipidaemia) apart from significantly higher number of HCV and TB sensitized patients in group 2($p<0.05$). We found significantly higher prevalence of CMV viremia in group 2($p=0.046$). Despite the significantly better immediate graft function in group 2, comparable number of rejection episodes, BK viremia, PTDM, and malignancies; the graft function and outcome were significantly worse in the same group ($p<0.05$) but patient outcome was comparable in the two groups.

Conclusion: In low risk kidney transplant recipients with living donor, tacrolimus based immunosuppression is associated with better graft outcome without significant impact on patient outcome.

Keywords: CNI, Tacrolimus, neoral, kidney graft, outcome

EP_646 GENERATION OF ANTIGEN-SPECIFIC HUMAN REGULATORY B CELL THERAPY TO IMPROVE OUTCOMES IN TRANSPLANTATION

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Background: Novel immunological strategies are urgently required to improve clinical outcomes in transplantation and reduce immunosuppression-associated morbidity. Regulatory B cells (Bregs) can prevent allograft rejection in animal models of transplantation and human Breg signatures predict renal transplant function and survival at 5 years. Human Bregs are enriched in tolerogenic signatures of operationally tolerant kidney transplant recipients and can induce regulatory T cells (Tregs). Similar to Tregs, Bregs are antigen-specific and may exert antigen-specific immunoregulation with minimal off-target effects when compared to polyclonal cell therapy or non-specific immunosuppression. We have developed novel in vitro methods to expand polyclonal human Bregs with in vivo function as a precursor to cellular therapy. We harnessed gene-editing strategies to generate antigen-specific human Bregs and provide a new class of B cell-based therapy.

Methods: We assessed two gene knock-in techniques to modify human Bregs. Utilising electroporation, CRISPR-mediated Homology Directed Repair (HDR) was designed to integrate single oligonucleotide insertions and HDR donor blocks within the B cell receptor. Integration was assessed by Sanger sequencing. In an alternative strategy, non-replicative viral particles encoding GFP were introduced by lentiviral transduction into the Breg genome. Transduction and integration were determined by flow cytometry.

Results: HDR achieved targeted DNA insertion into the Breg genome demonstrating 8-20% insertion of single nucleotides (n=3 human donors). However, reduced efficiency observed with larger GFP-encoding HDR donor block inserts may limit application in cell therapy. Lentiviral transduction demonstrated successful transduction of larger GFP constructs, achieving 21.4-26.9% transduction efficiency (n=3 human donors). GFP^+ Bregs maintained suppressive function in vitro.

Conclusions: Lentiviral transduction is a viable strategy to genetically modify in vitro expanded human Bregs. Transduction and expression of novel DNA constructs into human Bregs is achievable whilst maintaining suppressive function. These findings should form the basis for development of antigen-specific receptor constructs to generate antigen-specific human Breg.

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EP_647 COMPARISON OF RABBIT ATG AND BASILIXIMAB AS INDUCTION THERAPY IN ABO-I KIDNEY TRANSPLANTS: AN ANALYSIS OF KOTRY DATA

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Background: In ABO incompatible kidney transplants (ABOi KT), which pose high immunologic risk, appropriate induction therapy is paramount. This study sought to compare the effectiveness and safety of rabbit anti-thymocyte globulin (rATG) and basiliximab as induction agents in ABOi KT.

Methods: Leveraging extensive data from the Korean Organ Transplantation Registry (KOTRY), we retrospectively analyzed outcomes of 818 patients who received either of the two induction agents. Key measures included death-censored graft survival, rejection-free survival (effectiveness indicators), patient overall survival, infection-free survival, and malignancy-free survival (safety indicators).

Results: No statistically significant differences were found between the rATG and basiliximab groups in terms of both effectiveness (death-censored graft survival: p=0.208, rejection-free survival: p=0.296) and safety (patient overall survival: p=0.597, infection-free survival: p=0.294, malignancy-free survival: p=0.634) outcomes. Risk factor analysis did not demonstrate rATG usage as a significant negative or positive predictor for any outcome.

Conclusions: In conclusion, our findings suggest that the use of rATG as induction therapy in ABOi KT is comparable to the use of basiliximab in terms of both effectiveness and safety. This study adds valuable insights to the ongoing discussion about the optimal choice of induction therapy for ABOi KT.

EP_648 SPERMIDINE ENHANCES EXPANSION OF HUMAN REGULATORY T CELLS

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Background: Regulatory T cells (Tregs) are a key component to maintain immune tolerance. The efficacy of *in vitro* expanded Tregs for cellular therapy is being tested in clinical trials to minimise the dose of immunosuppressive drugs after transplantation. However, Treg expansion *in vitro* may fail to reach optimal numbers for cell production, especially in situations where the original number of Tregs are low, such as in antigen specific Tregs. Spermidine, a natural polyamine, has recently been reported to enhance T cell autophagy and fatty acid oxidation. Since autophagy and fatty acid oxidation are important metabolic processes for Tregs, we hypothesised that supplementation of spermidine would increase the expansion fold of Tregs during *in vitro* expansion.

Methods: Human CD4$^+$ CD25$^+$ cells isolated from healthy blood donors were expanded for 3 weeks *in vitro* in the presence of anti-CD3/CD28 beads with IL-2 and rapamycin. Spermidine was added in the experimental condition. After expansion, expression of FOXP3 and HELIOS were examined using flow cytometry. Treg function was examined using an in vitro suppression assay of autologous responder peripheral blood mononuclear cells.

Results: Spermidine supplementation doubled Treg expansion compared to the control condition (Fig 1a). Moreover, treated Tregs maintained their expression of FOXP3 together with a significant increase in HELIOS expression (Fig 1b). In vitro suppressive capacity was maintained (Fig 1c).

Conclusions: Spermidine treatment promoted Treg expansion and maintained Treg suppressive function. Expanded cells were enriched for HELIOS expression, suggesting a more stable phenotype. These findings highlight spermidine as a promising metabolic modulator to enhance Treg expansion, potentially overcoming current limitations in Treg expansion. Further work will examine underlying mechanisms and resistance to inflammatory conversion.

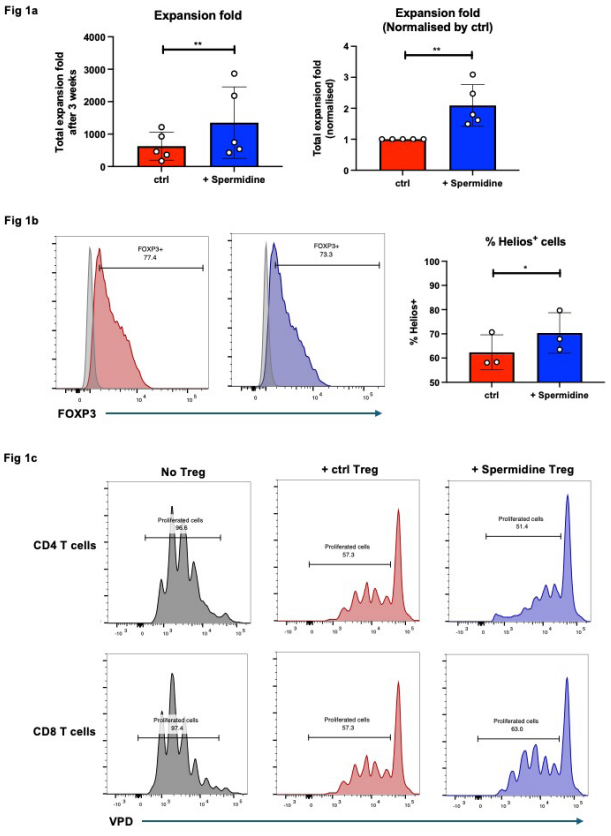

Figure 1a. Expansion fold of Treg after 3 weeks expansion b. Expression of FOXP3 and HELIOS and c. *in vitro* suppression assay. Each dot represents individual donors. *p<0.05, **p<0.01.

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EP_649 PHARMACOKINETIC VARIABILITY OF TACROLIMUS IN RENAL TRANSPLANT PATIENTS

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Background: Tacrolimus is a calcineurin inhibitor administered to prevent graft rejection in renal transplantation. This treatment has a high inter-individual pharmacokinetic variability, which can lead to side effects or graft rejection. 40% of this variability is explained by genetic polymorphisms in hepatic cytochrome P450 3A5. Other factors such as serum albumin, hematocrit level, age, sex, weight and P-gp expression level are also a source of variability in tacrolimus response. Plus, microbiota could also be an important factor in therapeutic variability of this molecule. Finally, endogenous urinary and plasma metabolites could contribute to the prediction of adequate tacrolimus doses.

Methods: An observational study was carried out in 30 renal transplant patients taking tacrolimus. Eligible patients were contacted by their physicians, and two sessions were held at 3-month intervals. At each visit, stool, urine and blood samples were collected for microbiological (stool), metabolomic (blood and urine) and genetic (blood) analyses. In addition, the Geneva phenotyping cocktail was administered to patients to measure CYP3A and P-gp phenotype by capillary blood sampling at 2h, 3h and 6h after cocktail ingestion.

Results: A significant positive Pearson correlation with a coefficient of 0.47 (p-value of 0.0066 at the 95% confidence level) was obtained between patients' necessary tacrolimus doses and their OH-midazolam/midazolam metabolic ratios relative to CYP3A. No correlation or significant difference in tacrolimus doses was found according to CYP3A5 genotypes as well as P-gp phenotypes and genotypes. Endogenous metabolites likely to correlate with tacrolimus pharmacokinetic parameters are cortisol, acetyl-arginine, phosphoethanolamine and 1-methylguanosine. Stool samples will likely reveal that the abundance of Faecalibacterium prausnitzii, a bacteria present in gastrointestinal tract, correlates positively and significantly with tacrolimus necessary doses, among other species of clostridiales order.

Conclusions: 47% of tacrolimus variability could be explained by CYP3A phenotype. Microbiological results and endogenous metabolites revealed by non-targeted metabolomics will be explored and complete the analysis of this variability.

EP_650 ASSOCIATION BETWEEN TACROLIMUS TROUGH LEVEL AND INCIDENCE OF NEW ONSET DIABETES AFTER KIDNEY TRANSPLANTATION

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Background: New onset Diabetes after Transplantation (NODAT) is a common but serious metabolic complication of kidney transplantation. Tacrolimus, a strong immunosuppressant, used for maintenance immunosuppression, reduces acute rejection rates but increases the risk of NODAT. Higher trough levels of tacrolimus during the first month after transplantation have been found to be a significant risk factor for the development of NODAT. The aim of this study was to identify the association between tacrolimus trough levels during the first year after kidney transplantation and NODAT.

Methods: A retrospective study was conducted in living-donor kidney transplant recipients of age >18 years who were free of diabetes before kidney transplantation and underwent kidney transplantation in between August 2022 and July 2023. The medical records were followed for 12 months after transplantation. Demographic and clinical data including tacrolimus trough level and corresponding tacrolimus daily doses were collected. NODAT was defined as at least 2 fasting blood glucose values >126 mg/dl after 3 months post transplantation according to World Health Organization criteria.

Results: A total of 77 patients were included in the study. The mean age was 34.08±9.86 years and 59 (76.6%) were males. The median time to NODAT diagnosis was 6 months (3-12 months). Patients with NODAT showed significantly higher first tacrolimus blood level.

Conclusions: Incidence of NODAT in the first year after kidney transplantation was 11.69%. Higher initial tacrolimus blood levels >10 ng/ml were associated with the higher risk of development of Diabetes after Transplantation.

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EP_651 AN OVERVIEW OF THE ROLE OF A PHARMACIST IN A MULTI-DISCIPLINARY PRE-ASSESSMENT CLINIC IN KIDNEY TRANSPLANTATION

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Background: The aim of this service review was to determine the impact and role of a pharmacist in the surgical pre-assessment clinic (PAC) in the renal transplant population. The current service provision is through a multi-disciplinary clinic. The role of the pharmacist includes undertaking an accurate medication history, management of immunosuppression dosing, providing advice to patients and healthcare professionals and counselling patients on medications in the peri-operative period.

Methods: Data was collected retrospectively between January 2022 – December 2022 using electronic health records. A data collection tool included the number of patients reviewed by a pharmacist, the number of patients counselled on their medications along with information on medications prescribed, prescriptions written by a non-medical prescribing (NMP) pharmacist and type of pharmaceutical intervention. All data was anonymised.

Results: There were 176 surgical pre-assessment patients who underwent surgery between January 2022-December 2022. N=166 (94%) patients were reviewed by a pharmacist in a surgical PAC. Of these, n=67 (40%) were live related kidney recipients and n=99 (60%) were kidney donors. N=166 (100%) of patients reviewed by a pharmacist were counselled on their medications. NMP pharmacists prescribed immunosuppression in n=29 (43%) of kidney recipients. The most frequent pharmaceutical intervention made was perioperative medicines management with advice given to patients about holding medication pre-operatively. In kidney recipients, the most frequent pharmaceutical intervention was advice on dosing immunosuppression and complex treatment plans. The estimated time required for a consultation per patient for kidney donors was approximately 10 minutes and for kidney recipients was 40 minutes.

Conclusions: This service review highlights the successful number of pharmaceutical interventions by pharmacists during a multi-disciplinary surgical PAC in potential kidney donors and recipients. Involvement in the PAC increases the pharmacist workload however with a projected increase in the number of live related donations and transplants the role of a pharmacist is integral to medicines optimisation in the peri-operative period.

EP_652 INTER- AND INTRA-INDIVIDUAL VARIABILITY OF DONOR-DERIVED CELL-FREE DNA IN STABLE KIDNEY AND LIVER TRANSPLANT RECIPIENTS

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Background: Donor-derived cell-free DNA (dd-cfDNA) is emerging as a non-invasive biomarker in kidney (KTx) and liver (OLT) transplant recipients for monitoring allograft health. Many studies have shown correlations between elevated dd-cfDNA fractions and graft rejections, potentially enabling earlier detection and treatment of graft dysfunctions. Our aim was to identify the inter- and intra-individual variability of dd-cfDNA in stable KTx and OLT within the first year after transplantation to determine baseline values and compare variability between absolute and relative dd-cfDNA quantification.

Methods: Blood and urine samples from KTx and OLT were collected longitudinally at regular visits. Mismatched HLA alleles between donor and recipient were used to determine absolute (cp/mL) and relative (%dd-cfDNA) quantities of dd-cfDNA using droplet digital PCR at three time points per recipient. Urinary dd-cfDNA was corrected for urine concentration using urinary creatinine (UCreat).

Results: The timepoints were not significantly different for any of the dd-cfDNA quantities of stable recipients (Tbl.A). Absolute and fractional dd-cfDNA quantities correlated significantly in plasma samples from KTx (r=0.47, p<0.001) and OLT (r=0.76, p<0.001) but not in urine samples of KTx (r=0.18, p=0.229). No significant correlation was found between plasma and urine samples of KTx (absolute: r=0.21, p=0.178; relative: r=0.22, p=0.144). Intra-individual variability was higher in plasma samples from KTx compared to urinary values or OLT (Fig.A). Adjusting absolute urinary dd-cfDNA quantities with the UCreat reduced the inter-individual variability (Fig.A).

Conclusions: We observed no significant dynamic of dd-cfDNA in the first year after transplantation of stable KTx or OLT. The contributions of inter- and intra-individual variability to dd-cfDNA quantities varied between OLT and KTx, and between urine and plasma, requiring further investigation including comparison to dd-cfDNA of non-stable KTx and OLT.

Table A: dd-cfDNA results of stable KTx and OLT.

KTx					
Fluid	**Sample timepoints (mean days post-transplantation)**	**Number of samples**	**Median dd-cfDNA cp/mL (IQR)**		**Median %dd-cfDNA (IQR)**
Plasma	T1 (54 ± 22)	16	5.80 (7.44)		0.086 (0.131)
	T2 (175 ± 34)	16	5.00 (6.15)		0.118 (0.218)
	T3 (351 ± 27)	16	4.19 (4.98)		0.119 (0.185)
Fluid	**Sample timepoints (mean days post-transplantation)**	**Number of samples**	**Median dd-cfDNA cp/mL (IQR)**	**Median dd-cfDNA cp/mL corr. UCreat (IQR)**	**Median %dd-cfDNA (IQR)**
Urine	T1 (54 ± 22)	14	246 (524)	47.5 (42.0)	17.5 (67.2)
	T2 (172 ± 33)	15	134 (522)	40.4 (80.1)	12.3 (41.6)
	T3 (351 ± 28)	15	70.3 (337)	19.8 (25.0)	11.6 (62.2)
OLT					
Fluid	**Sample timepoints (mean days post-transplantation)**	**Number of samples**	**Median dd-cfDNA cp/mL (IQR)**		**Median %dd-cfDNA (IQR)**
Plasma	T1 (64 ± 22)	11	95.5 (78.7)		1.98 (1.57)
	T2 (154 ± 29)	11	125 (155)		0.926 (3.98)
	T3 (386 ± 74)	11	112 (139)		3.78 (7.31)

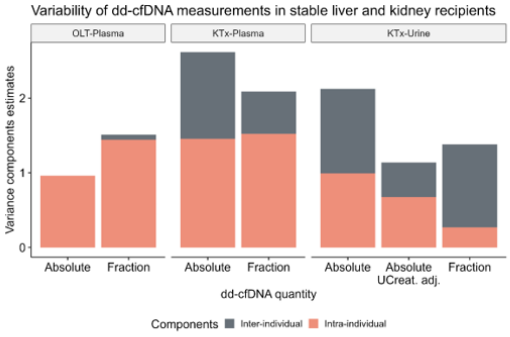

Figure A: The inter- and intra-individual variabilities calculated from the linear mixed-effects models for absolute and fractional dd-cfDNA in plasma (KTx n=16; OLT n=11) and urine (KTx n=15) samples with values normalized to the mean of each category.

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EP_653 HLA-ANTIGENS IN RESIDENTS OF REPUBLIC OF KAZAKHSTAN WITH DILATED CARDIOMYOPATHY

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Background: Dilated cardiomyopathy (DCM) is a disorder of myocardial function leading to cardiac insufficiency, in which ventricular dilatation and systolic dysfunction predominate. The association of DCM with human leukocyte antigens, particularly HLA-DR4, has been previously reported. In subgroup analysis by ethnicity, a significantly increased risk was found among Europeans HLA-DR4 was a low penetrance risk factor for the development of DCM in Europeans. The aim was to determine the association of HLA antigens with diagnosis in a cohort of patients screened for heart transplantation.

Methods: The frequency of HLA antigens was compared between patients diagnosed with DCM (n=354) and a control group (n=3694) for loci HLA-A, B, and DRB1. Differences were determined using Chi-square tests and odds ratios with a significance level of 0.05.

Results: The following HLA antigens were more frequent in the patient group than in the control group HLA-A34-0.28% vs. 0.05% (OR =5.23, χ 2=4.55), HLA-A66 -1. 55% vs. 0.39% (OR = 4, χ 2=17.72), HLA-A68-4.8% vs. 3.22% (OR = 1.52, χ 2=4.97), HLA-B52-4.66% vs. 3.06% (OR =1.55, χ 2 = 5. 35), HLA-B67- 0.42% vs.0.12% (OR = 3.49, χ 2 = 3.98), HLA-DRB1*13-13.42% vs.10.12% (OR = 1.38, χ 2 = 7.51). We also identified antigens that were most frequent in the healthy population HLA-B39-1.25% vs. 0.85% (OR = 1.81, χ 2 = 4.81), HLA-B51-9.42% vs. 6.64% (OR = 0.68, χ 2 = 6), HLA-DRB1*14-7.23% vs. 5.08% (OR = 0.69, χ 2 = 4.53). The occurrence of DRB1*04 antigen among patients (13.7%) and among controls (14.66%) did not differ (OR = 0.94, χ 2 = 0.32).

Conclusions: Frequently occurring HLA-A34, A66, A68, B52, B67, DRB1*13 antigens may be predisposing genes towards the development of DCM, whereas HLA-B39, B51, DRB1*14 antigens may be protective genes in this pathology. The association of HLA-DRB1*04 with DCM was not found in the Kazakhstan population, and perhaps the previously described DRB4 association is more characteristic of Europeans.

EP_654 ASSOCIATION OF HLA MISMATCHES ON OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS

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Background: One of the important barriers that impact the outcomes of kidney transplantation is HLA mismatch (MM). The aim of our study is to assess the impact of HLA-A, B, DR & DQ mismatch (0-8 MM) on the outcomes during the first year of living donor kidney transplantation.

Methods: All adult living donor kidney transplant recipients were included for analysis from January 2017 to December 2022 at King Faisal specialist Hospital & Research Centre, Riyadh. The data were analysed across each HLA mismatch category (0-8 HLA MM). The additional analyses were performed by grouping them into two: 0-4 HLA MM and 5-8 HLA MM group.

Results: 1229 recipients were included in this study. During the first year, the Acute Rejection (AR) rate increased with incremental increase in HLA MM (0 MM= 2.05%, 1 MM= 4.16%, 2 MM= 6.66%, 3 MM= 9.7%, 4 MM= 10.75%, 5 MM= 6.95%, 6 MM= 14.25%, 7 MM= 13.3%, 8 MM=0%). No rejection was noted in 8 HLA MM because of small numbers of recipients in this category. Among recipients with acute rejection, antibody mediated rejection (AMR) was observed 0%, 12%, 5.4%, 25%, and 37.5% in 0-2, 3, 4, 5, and 6 HLA MM categories despite no difference in a Flow cytometry X-Match before transplantation. DGF rate, serum creatinine (93.2 ± 35.14), graft and patients' survival (98.71% and 99.03%) at 1 year were not different across 0-8 HLA MM categories. Additional analysis of the 2 groups: 0-4 HLA MM and 5-8 HLA MM showed no significant difference in AR rates (p = 0.509). AMR rates were higher (18%) in 5-8 mm group vs 5% in the 0-4 HLA mm group (p = 0.058). DGF (p = 0.413), graft survival (p=0.164) and patient's survival (p=0.707) were not different in the 2 group.

Conclusions: HLA mismatches play an important role in the occurrence of acute rejection. With each increment in HLA MM, significantly increased number of AR and AMR was identified. However, 1 year serum creatinine, graft and patients' survival were the same across 0 to 8 HLA MM. AMR was also significantly greater in 5-8 vs 0-4 HLA MM group. In spite of the advancement of immunosuppression strategies, the role of HLA MM in causing acute rejection cannot be overlooked. A longer follow-up is recommended to determine the effect of those who developed AR and AMR on the development of donor specific antibodies (DSA's), proteinuria, graft and patients' survival.

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EP_655 IMMUNOLOGICAL HIGH-RISK TRANSPLANTATION: NOT ALL THE RISK IS IMMUNOLOGICAL

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Background: Transplantation of kidneys in highly sensitised patients is potentially considered to be associated with higher rates of postoperative surgical complications due to increased dialysis vintage, increased waiting times and immunosuppression burden. Hence, we decided to investigate the surgical complications in this group at our centre.

Methods: A retrospective notes review was conducted with data of kidneys transplanted from May 2013 to June 2024. All sensitized patients who received depleting induction agents (Thymoglobulin or Alemtuzumab) were included. Surgical complications were identified and classified based on Clavien Dindo grading. In addition to this, patient and graft survival were assessed by Kaplan Meier curve.

Results: 44 patients were included (22 female, 22 male) with a median follow up of 3.16 years (IQR 3.68), out of 744 patients transplanted during the study period. The mean age was 44 years (IQR 24) and dialysis vintage was 7.3 years (SD 5.2). Among the cohort, 12 patients (27%) had surgical complications post-transplantation. The total number of complications was 13 (29.5%), as one of the patients had 2 complications. The details of various complications are tabulated below. Four out of 12 patients had emergency readmissions within the first month. Patient survival was 100% at 3 years. Graft survival was 93% at 1 year and 84% at 3 years.

Conclusions: Highly sensitized patients can be transplanted with favorable outcomes. However, it is associated with a considerable burden of surgical complications. Patients should be counselled about these complications appropriately for them to make an informed decision.

Complication	Numbers (%)
Grade I • Wound infection & hematoma managed conservatively/ opened bedside (4) • Urine leak- managed with prolonged catheter (1) • Lymphocele- conservatively managed/ drain retained for prolonged time (2)	7 (15.9)
Grade II • Wound hematoma opened bedside requiring transfusion (1) • Wound infection opened bedside requiring antibiotics (1)	2 (4.55)
Grade IIIa • Ultrasound guided drainage of perinephric collection (2) • Surgical drainage of abdominal wall collection (1)	3 (6.82)
Grade IV • Graft nephrectomy with iliac thrombectomy for external iliac clot extending into graft renal artery (1)	1 (2.27)

EP_656 LUNG TRANSPLANTATION FOR PULMONARY EPITHELIOID HEMANGIOENDOTHELIOMA WITH PLEURAL INVOLVEMENT

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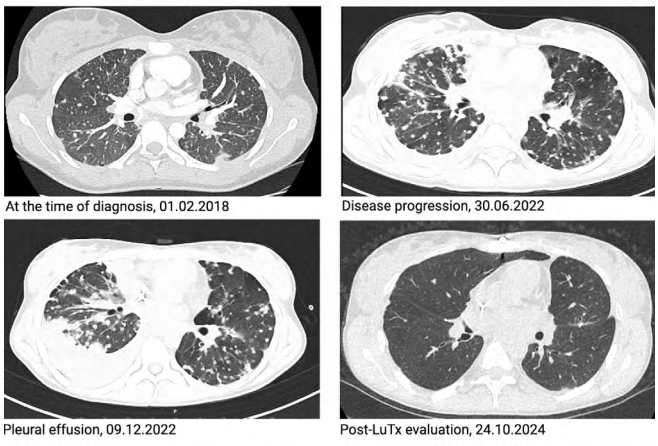
Introduction: Pulmonary epithelioid hemangioendothelioma (PEH) is a rare neoplasm of borderline malignancy with an unpredictable prognosis and heterogeneous clinical manifestation. Only a few cases have been reported where PEH was the primary indication for lung transplantation (LuTx).

Case study: A young female patient was diagnosed with PEH in 2018. Despite chemotherapy, the disease rapidly progressed, leading to respiratory insufficiency. With exhausted oncological therapeutic options, the patient was referred for LuTx, and after a thorough multidisciplinary evaluation, she was subsequently listed for the procedure. In August 2022, the patient developed right-sided pleural effusion, initially transudate but later hemorrhagic, raising suspicions of malignant pleural dissemination, which was confirmed by exploratory surgery. Given the absence of alternative treatment options and exclusively intrathoracic disease involvement, the decision to proceed with LuTx was made, using paclitaxel as bridging chemotherapy. In February 2023, at the age of 21, the patient underwent successful bilateral LuTx. The surgery was challenging due to extensive tumor-induced fibrous adhesions, resulting in significant blood loss. Given its antiproliferative effect, a mTOR inhibitor was incorporated into the standard maintenance immunosuppression 3 months post-transplant, administered in a 1:2 ratio with tacrolimus, with prednisone and a reduced dose of mycophenolate mofetil. Nearly two years post-LuTx, she is stable with satisfactory lung function and no evidence of disease recurrence. CT evolution is depicted in Figure 1.

Conclusions: Although metastatic malignancies are generally considered an absolute contraindication to LuTx, carefully selected cases of PEH with isolated pleural involvement may be an exception. This approach requires thorough evaluation and tailored immunosuppression. Further research and long-term follow-up are essential to assess outcomes and recurrence risk.

Figure: CT evolution of pulmonary epithelioid hemangioendothelioma and post-LuTx evaluation



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EP_657 MONOLAYER WHOLE ADHERENT ISLETS: A NOVEL TOOL TO STUDY DRUG INDUCED DIABETIC PHENOTYPE IN VITRO

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Background: To understand the mechanisms of diabetes and develop novel drugs, various animal and in vitro experimental systems have been established. Using isolated islets *in vitro* is associated with several problems: (1) discontinued blood microcirculation causing ischemia and central necrosis in isolated islets, (2) dissociation of islets into single cells reduces the total number of cells and impairs endocrine function. Here, we aim to establish a novel experimental method for characterizing cell physiology and drug effects using isolated islets.

Methods: We have developed a method to flatten islets into monolayers by culturing small, whole, non-disrupted mouse islets on laminin-521. In this culture, islet cells remain intact, and cell-cell junctions are not broken mechanically. Small mouse islets were cultured in a 96-well plate coated with laminin-521 for six days and then exposed to various concentrations of streptozotocin for 24 hours. Five days after the drug exposure, the islet function and endocrine cell types were examined.

Results: Monolayer islets exposed to 0.6 mM streptozotocin-induced a metabolic diabetes-like phenotype, i.e., islet cell death, predominantly of beta cells, causing a shift in the alpha-to-beta cell ratio. The stimulation index in a glucose-stimulated insulin secretion assay was reduced in streptozotocin-treated islets. However, insulin production per beta cell did not change significantly.

Conclusions: The monolayer whole islet assay format allows the collection of quantitative data regarding endocrine cell function, i.e., endocrine sensitivity (stimulation index) and endocrine power (amount of hormone secreted per cell). It is a versatile, user-friendly, semi-automated, and financially attractive experimental platform for evaluating drug effects on pancreatic islet cells.

EP_658 MIXED ACUTE REJECTION LINKED TO DE NOVO DONOR SPECIFIC HLA-DP ANTIBODIES AFTER KIDNEY TRANSPLANTATION: A CASE REPORT

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Background: The effects of HLA-DP mismatches and the pathogenicity of HLA-DP donor-specific antibodies (DSA) are not fully elucidated. Distinguishing the impact of anti-HLA-DP from other HLA antibodies is challenging in clinical practice. We report a case of mixed acute rejection associated with isolated de novo anti-HLA-DP DSA early after kidney transplantation.

Methods: High-resolution HLA typing by Next Generation Sequencing was performed for both recipient and donor. Anti-HLA antibodies specificities were determined by Single Antigen Bead (SAB) analysis (One Lambda). HLA Eplet Registry and HLA matchmaker were used for eplet analysis.

Results: A 23-year-old female with kidney failure in the setting of familial Mediterranean fever received a kidney graft from her father, who was mismatched (mm) at DRB1/3 (DRB1*11:04, DRB3*02:02, 5 mm-eplets) and DPA1/B1 (DPA1*02:01, DPB1*13:01, 17 mm-eplets). No mismatches were detected for HLA-A, -B, -C, and -DQA/B at the allele level. The patient had no history of sensitization or DSA pre-transplant. Immunosuppressive therapy included induction with basiliximab in addition to mycophenolate mofetil, tacrolimus and prednisolone. Serum creatinine was 1.13 mg/dl at discharge. Five months post-transplant, a kidney graft biopsy was performed due to increased creatinine (1.56 mg/dl) and low tacrolimus levels. Acute cellular and antibody-mediated rejection with features of thrombotic microangiopathy and diffuse C4d staining was revealed. Serum SAB analysis detected de novo DPA1*02:01, DPB1*13:01 DSA with a mean fluorescence intensity (MFI) of 9941 and other non-DSA anti-HLA-DP antibodies. Eplet analysis revealed 111R, a DPA1 eplet, and 84DEAV, a DPB1 eplet, both shared on mismatched DPA1/B1 donor alleles and non-donor DPA1/B1 reactive alleles. Non-HLA antibodies were not detected. The patient was treated with pulses of steroids, plasmapheresis and intravenous immunoglobulin. Six months later, HLA-DP reactivity was absent, and serum creatinine level decreased to 1.36 mg/dl.

Conclusions: De novo anti-HLA-DP DSA may induce adverse effects on the renal graft. HLA-DP typing and eplet antibody reactivity analysis could enhance immunological risk assessment in kidney transplantation.

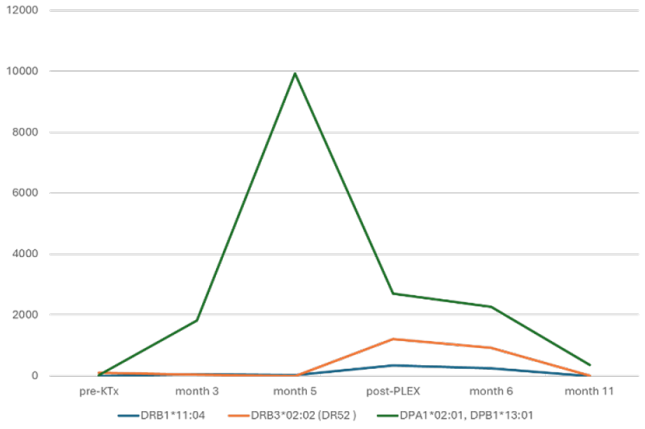

Figure. Donor-Specific Antibodies MFI levels

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Transplant immunology & immunosuppression

EP_660 IMPACT OF KIDNEY TRANSPLANTATION (KTX) ON ALBUMIN-BINDING CAPACITY (ABIC)

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Background: ABiC is a fluorescent dye-based biomarker reflecting transport capacity of plasma albumin for internal metabolites, hormones and various protein-bound drugs, including immunosuppressants. It is reduced in patients with chronic kidney disease. The impact of KTx on ABiC is currently unknown.

Methods: A prospective two-center study was carried out, including 51 patients who newly received a kidney transplant. These patients were observed over a period of 30 days and regular blood samples were collected. Using these we determined the eGFR and the Albumin-binding capacity. For statistical analysis t-Test for paired samples and Pearson´s correlation were used.

Results: Out of 51 patients (33 men) the mean age at KTx was 45,3 ± 14,3 years. The mean values of ABiC increased significantly from 68,74 ± 8,08% pre-KTx to 78,87 ± 12,29% day 14 post-KTx (p<0,001). The mean ABiC was at 86,28 ± 10,38% on day 30 post-KTx. The ABiC- increase was correlated with the increase of eGFR (r=0,491; p<0,001). In one patient (female, 55y) the ABiC initially increased to 100% but decreased subsequently to the lowest of 52% and the patient died during the hospital stay due to postoperative complications.

Conclusions: This is the first report on early post-KTx development of transport capacity of plasma albumin for drugs and internal metabolites. Essential drugs for KTx e.g. tacrolimus and mycophenolate primarily bind to albumin. ABiC might help clinicians to estimate pharmacokinetics for albumin-bound drugs in the early postoperative phase and improve the medication adjustment.

References: Klammt S, Wojak HJ, Mitzner A, Koball S, Rychly J, Reisinger EC, Mitzner S. Albumin-binding capacity (ABiC) is reduced in patients with chronic kidney disease along with an accumulation of protein-bound uraemic toxins. Nephrol Dial Transplant. 2012 Jun;27(6):2377-83.

EP_661 LONG-TERM SAFETY AND EFFICACY OF DT-DEC01 THERAPY IN DUCHENNE MUSCULAR DYSTROPHY PATIENTS POST-TRANSPLANTATION

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Background: Duchenne muscular dystrophy (DMD) is a lethal disease causing muscle degeneration due to a dystrophin gene mutation. This study presents the long-term safety and efficacy of DT-DEC01, a novel Dystrophin Expressing Chimeric (DEC) therapy, assessed after systemic-intraosseous transplantation.

Methods: A single dose of DT-DEC01 therapy (2x10^6 cells/kg) was administered intraosseously to three DMD boys aged 6-15, without immunosuppression. Safety was assessed by monitoring of Adverse Events (AE), Serious Adverse Events (SAE), DSA antibodies, and lymphocyte immunophenotyping. Efficacy was evaluated by: the 6MWT, NSAA, PUL test, grip strength, electromyography (EMG) - Motor Unit Potentials (MUP) duration, and daily activity (step/arm movements count).

Results: No study-related AE, SAE, or DSA antibodies were reported during the 24-month follow-up. Immunophenotyping confirmed normal distribution and activity of B-cells, T-cells, and NK-cells. Efficacy assessments at 12 months are as follows: Patient 1 (6-year-old, ambulatory, exon 3-12 deletion): Maintained 6MWD, improved standing from supine and 10-meter run; maintained PUL test, improved grip strength by 65%; EMG increased MUP in: deltoideus by 25%, rectus femoris by 11%, gastrocnemius by 53% and increased daily step count by 74%. Patient 2 (15-year-old, non-ambulatory, exon 48-50 deletion): Improved grip strength by 15% and PUL test by 13%; EMG increased MUP duration in: deltoideus by 34%, biceps by 149%, rectus femoris by 64%, gastrocnemius by 33% and increased daily activity by 184%. Patient 3 (6-year-old, ambulatory, nonsense mutation): Improved: 6MWD by 18%, standing from supine and PUL test; EMG increased MUP duration in: deltoideus by 60%, biceps by 32%, rectus femoris and gastrocnemius by 11% and increased daily step count by 54%.

Conclusions: This study confirmed the long-term safety of DT-DEC01 therapy as evidenced by the absence of AE, SAE, DSA and the lack of immune response up to 24 months after systemic-intraosseous transplantation. Efficacy was confirmed by improvements in standard functional tests, an increased MUP duration by EMG, and enhancements in daily step/arm activity. These findings introduce DT-DEC01 as a promising new therapeutic option for all DMD patients regardless of the gene mutation.

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Transplant immunology & immunosuppression

EP_662 RARE HISTOLOGICAL MANIFESTATIONS OF MYCOPHENOLATE MOFETIL (MMF) GASTROINTESTINAL TOXICITY: FOCUS ON CRYPT ATROPHY

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Background: Mycophenolate mofetil (MMF) is a widely used immunosuppressant in transplantation. While common gastrointestinal side effects are well-documented, histological changes, such as small intestine villous atrophy, are more commonly reported. Rare colonic lesions, including crypt atrophy, remain poorly recognized and require greater clinical awareness.

Methods: This study aims to describe rare gastrointestinal manifestations of MMF through two cases of colonic crypt atrophy.

Results: Case 1: A 38-year-old kidney transplant recipient (2022) treated with thymoglobulin, MMF, corticosteroids, and tacrolimus presented with severe diarrhea and graft dysfunction. Extensive testing, including CMV PCR, celiac serology, stool culture, thyroid function, and COVID PCR, was negative. Endoscopy revealed erosive gastritis, and colonoscopy appeared normal. Colonic biopsy showed rarefied and atrophic crypts. Case 2: A 26-year-old kidney transplant recipient (2023) on the same immunosuppressive regimen presented with diarrhea and rectal bleeding. Testing was similar and negative. Colonoscopy revealed recent bleeding and an ileocecal ulcer. Biopsy indicated edematous and atrophic colonic mucosa with mild nonspecific inflammation. MRI confirmed colonic atrophy. Management and Outcome: In the first case, switching MMF to azathioprine resulted in a favorable outcome, with cessation of diarrhea, correction of metabolic disturbances, and improvement in renal function, along with weight recovery. However, in n the second case, despite discontinuation of MMF after three weeks, the patient experienced persistent rectal bleeding. A second colonoscopy revealed the same ulcerated appearance of the ileocecal valve, with no possibility of performing an endoscopic intervention. The patient has been referred to surgeons for an ileocecal resection.

Conclusions: Rare colonic lesions, such as crypt atrophy, should be considered in transplant recipients treated with MMF who present with unexplained gastrointestinal symptoms. Early identification and adjustment of immunosuppressive therapy are crucial to prevent complications and improve patient outcomes.

EP_663 IMPLEMENTATION OF A CYTOMEGALOVIRUS IMMUNE ASSAY IN THE ROUTINE CLINICAL PRACTICE AFTER KIDNEY TRANSPLANTATION

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Background: Previous studies demonstrated that a cytomegalovirus (CMV) specific cell-mediated immune (CMV-CMI) assay can guide antiviral prophylaxis after kidney transplantation. In this multicentre cohort, we aimed to assess the feasibility, efficacy, and safety of the introduction of a CMV-CMI assay in the routine clinical practice in kidney transplant recipients.

Methods: Since September 2023, Swiss guidelines recommend the use of a CMV-CMI assay in CMV-seropositive (R+) kidney transplant recipients. Briefly, R+ patients receive antiviral prophylaxis and a CMV-CMI test (Elispot-CMV) is performed at 1-month post-transplant. If the result is positive, antivirals are stopped, and no further viral monitoring is done. If the result is negative, antivirals are continued for 2 additional months. Here are the preliminary results up to January 2025.

Results: Overall, 78 patients were analyzed. 76 (97.4%) received antiviral prophylaxis and 2 (2.6%) had a preemptive strategy. 39 patients (50%) received antithymocyte globulins (ATG). 71 CMV-CMI assays were performed at a median of 31 days post-transplant; 56 (79%) were positive, 11 (15.5%) negative, and 4 (5.6%) indeterminate. Prophylaxis was discontinued due to a positive CMV-CMI result (73%), end of the prophylaxis period (16%), toxicity (7.4%), or other reasons (2.9%). Duration of antiviral prophylaxis was significantly shorter in patients with a positive assay result (adjusted difference, -71.8 days, CI 95%, -101.9 to – 41.7 days; P<0.0001). 61 patients were followed at 4 months: 3 (4.9%) had a CMV syndrome at 44-, 87- and 98-days post-transplant, all in patients with a positive CMV-CMI. One patient had graft loss at 31 days. A comparison with a historical matched cohort is ongoing

Conclusions: Preliminary results suggest that routinely implementing a CMV-CMI assay is feasible and reduces the duration of antiviral therapy, without an unexpected high incidence of CMV events.

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EP_664 RISK FACTORS AND OUTCOMES FOR DEVELOPING RECURRENT IGA NEPHROPATHY AND GRAFT FAILURE AFTER KIDNEY TRANSPLANTATION

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Background: Up to 60% of kidney transplant recipients (KTR) with IgA nephropathy (IgAN) develop recurrent IgAN (rIgAN) after transplantation and 32% of these patients lose their transplant within 8 years. To understand potential risk factors for developing rIgAN we conducted a descriptive analysis of our KTR with end stage kidney disease (ESKD) due to IgAN.

Methods: A retrospective single centre cohort study in a tertiary renal centre of patients receiving a kidney transplant between 1994 and 2023 was undertaken. Demographic and clinical variables were analysed. Continuous variables were compared by independent-samples t tests, and categorical variables were compared using Chi-squared tests. P-value <0.05 was considered statistically significant.

Results: Our cohort included 89 patients, of which there were 96 renal transplants (7 patients had 2 transplants). 24% of this cohort developed rIgAN during the mean follow-up period of 9.5 years with a median time to diagnosis of 5.3 years. 27% presented with nephrotic range proteinuria (urine protein-creatinine ratio > 300 mg/mmol). MEST-C score for rIGAN patients was calculated with M1 and S1 being the most common lesions. Patients who received a transplant with fewer HLA mismatches, a living donor transplant, ciclosporin and prednisolone as part of their immunosuppression regimen were significantly more likely to develop rIgAN (Table 1). KTR with rIgAN had significantly increased risk of graft failure and reduced patient survival at 10 years (Table 1, Figure 1). Cox regression analysis showed developing rIgAN (HR= 5.6), being of black ethnicity (HR=16.9) receiving a kidney with increased HLA mismatches (HR=4.1) or experiencing rejection (HR=8.5), were associated with earlier onset of graft failure.

Conclusions: Our data highlights potential risk factors for developing rIgAN and graft failure. Small cohort studies are subject to bias so we plan to analyse these risk factors in a UK based cohort of patients with IgAN. Histological data analysis is ongoing.

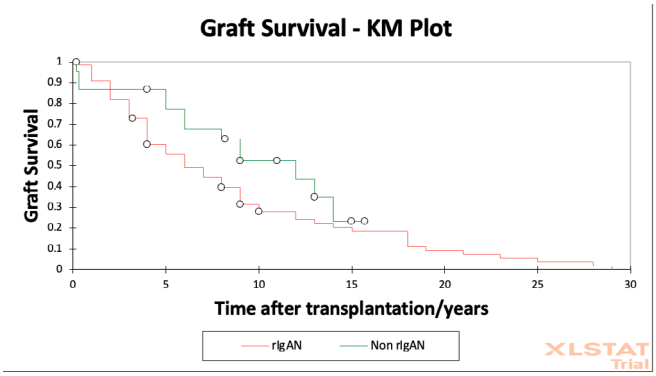

Figure 1: Transplant Survival Kaplan Meier Plot

Table 1: Clinical and demographic KTR variables with IgAN as the cause of ESKD

	No rIgA nephropathy n=73	rIgA nephropathy n=23	P value
Age at time of transplantation/ median/years (range)	42	42	0.07
Sex			
% Male	67%	83%	0.154
Ethnicity			
% White	59%	65%	
% Black	9%	0	0.30
% Asian	16%	26%	
% Other	16%	9%	
Type of Transplant			
%Living	62%	22%	<0.001
%Deceased	38%	78%	
HLA MM			0.101
% 000	4%	13%	
% 110,100,010	14%	13%	
% Other	74%	52%	
% Unknown	8%	22%	
Immunosuppression			
Tacrolimus			
%Yes	80	44	0.004
%No	15	39	
% Unknown	5	17	
Ciclosporin			
%Yes	14	35	0.008
%No	81	48	
% Unknown	5	17	
Prednisolone			
%Yes	95	83	0.090
%No	0	4	
% Unknown	5	13	
Acute rejection in first years after transplantation			
%Yes	32	39	0.024
%No	68	61	
MEST-C score			
M1		10	
E1		5	
S1		14	
T1		8	
T2		1	
C1		7	n/a
C2		0	
%Transplant failure at 10 years			
Yes	18	43	0.012
No	82	57	
Cause of graft failure			
Unknown	1	0	
Rejection	7	0	
IgA nephropathy	0	49	<0.001
CNI toxicity	1	0	
BK nephropathy	0	0	
Other	1	0	
RIP with functioning T	48	2	
%Patient death at 10 years			
Yes	8	4	0.533
No	92	96	

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EP_665 LOW-INTENSITY PULSED ULTRASOUND IN PREVENTING ACUTE REJECTION THROUGH ANTI-INFLAMMATORY AND ANTI-APOPTOTIC MECHANISMS

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Background: Acute renal allograft rejection is a critical complication in kidney transplantation, often resulting from ischemia/reperfusion injury (IRI). Low intensity pulsed ultrasound (LIPUS) has emerged as a promising non-invasive therapeutic modality that may mitigate renal injury through anti-inflammatory and anti-apoptotic mechanisms. This study investigates the efficacy of LIPUS in preventing acute renal allograft rejection in a rat renal transplant model.

Methods: A renal transplant model was established using male Sprague-Dawley rats, which underwent unilateral nephrectomy followed by transplantation of a donor kidney from a different strain. Post-transplantation, LIPUS was applied at 100 mW/cm² for 20 minutes daily for five consecutive days. Serum levels of blood urea nitrogen (BUN), creatinine, and cystatin C were measured to assess renal function, alongside histopathological evaluation of renal tissue.

Results: LIPUS treatment significantly improved renal function in the transplant model, resulting in a 55.2% reduction in BUN, a 52.4% reduction in serum creatinine, and a 30.1% reduction in cystatin C levels (all $p < 0.05$). Histopathological analysis revealed a 28.7% reduction in tubular injury scores in LIPUS-treated rats compared to controls. Additionally, LIPUS significantly decreased the expression of pro-inflammatory markers, including IL-6 (82.5% reduction in kidneys, 68.9% in spleens) and apoptosis-related proteins such as cleaved caspase-3 (39.8% reduction) and Bax (27.4% reduction), while increasing Bcl-2 levels by 45.6% (all $p < 0.05$).

Conclusions: LIPUS demonstrates significant potential as a non-invasive intervention to prevent acute renal allograft rejection by modulating oxidative stress and inflammatory responses. These findings advocate for further clinical exploration of LIPUS as a sustainable innovation in transplantation medicine, with the potential to enhance graft survival and improve patient outcomes.

EP_666 CONSTRUCTION AND IDENTIFICATION OF AN CHRONIC ANTIBODY-MEDIATED REJECTION MODEL OF RENAL ALLOGRAFT IN MICE

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Background: To construct and identify an chronic antibody-mediated rejection model of renal graft in mice.

Methods: Male BALB/c^{H2d} and C57BL/6^{H2b} mice were used as experimental mice and randomly divided into following groups: 1. The syngeneic control group (SYN14D); 2. T cellular-mediated rejection group (TCMR14D); 3. acute antibody-mediated rejection group (aABMR, BST5D+KT5D); 4. chronic antibody-mediated rejection group 1 (cABMR, TST2D+KT14D); 5. cABMR group 2 (TST3D+KT14D); 6. cABMR group 3 (TST4D+KT14D). Pathological staining and Banff score were performed to diagnose the transplanted kidneys, survival curves were plotted, the levels of complement fragment C3d deposition, peripheral blood IgG class DSA, serum Cr, and serum BUN were detected in the transplanted kidney tissues, and the expression of $CD3^+$T cells, $CD19^+$B cells, F4/80+ macrophages, Ly6G+ myeloid cells expression.

Results: The pathological injury of cABMR group 1 model met the diagnostic criteria of ABMR, the postoperative survival rate was 80%, and the expression of $CD3^+$T cells was not obvious, so cABMR group 1 was subsequently selected as the model of cABMR for experimental demonstration. Compared with SYN14D, the C3d expression of cABMR was significantly enhanced, the average fluorescence intensity of peripheral blood IgG class DSA was significantly higher, and peripheral blood serum Cr and BUN levels were significantly higher. Compared with aABMR, cABMR model of transplanted kidneys showed peritubular capillary haemorrhage and dilatation, single nucleus infiltration seen in the glomeruli, more typical tubular damage and brush border detachment in the tubules, significantly more positive areas of C3d expression, significantly higher mean fluorescence intensity of peripheral blood IgG class DSA, and significantly higher peripheral blood serum Cr and BUN levels. cABMR group renal interstitial and peritubular capillary $CD19^+$B cells and $CD3^+$T cells infiltration were not significant, renal interstitial F4/80 labelled macrophage and Ly6G labelled myeloid cell infiltration were more significant.

Conclusions: Our group constructed a cABMR model in which the survival cycle was prolonged, on the basis of which the effects of drug interventions on the prognosis of ABMR mice can be evaluated, which has high clinical application value.

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Transplant immunology & immunosuppression

EP_668 DE NOVO POST TRANSPLANT MICROANGIOPATHY (PT-TMA): CLINICAL EFFICACY OF RAVULIZUMAB, A SINGLE CENTRE EXPERIENCE

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Background: Post transplant thrombotic microangiopathy (PT TMA) is a rare but life- threatening disease that affects kidney transplant recipient (KTR), leading to loss of graft function, characterized by dysregulated complement activity resulting in thrombocytopenia, hemolytic anemia and multi organ failure, including acute kidney injury.

Methods: A 62-year-old woman suffering from Alport syndrome on peritoneal dialysis was transplanted from a deceased donor in March 2024. The induction was based on baliximab, prednisone, tacrolimus and mycophenolate mofetile with recovery of renal function. On May 2024 patient was admitted for acute kidney injury with creatinine level of 6.5 mg/dl and need of dialysis, anuria, abdominal pain, diarrhea with culture positive for Enterobacter MBL, so antibiotic therapy was started. Renal biopsy was performed with the diagnosis of TMA with associated acute tubular necrosis, without any systemic sign of disease and negative ADAMTS 13. Genetic testing revealed rare heterozygosity deletion of the CFHR3-CFHR1 region (unknown pathogenic significance). Immunosuppressive regimen was modified using low dose tacrolimus plus everolimus and prednisone. Treatment with Ravulizumab was soon started.

Results: At the start of the infusion on 24 May, the creatinine level was 6.5 mg/dl and there was an immediate increase in diuresis and dialysis withdrawal; after 6 months of follow-up, the creatinine level was 2.5 mg/dl.

Conclusions: PT TMA represents a major diagnostic and therapeutic challenge in KTR because clinical presentation is variable and insidious. Our case is emblematic because co existing different trigger factors, even if clinical status was no suggestive of TMA. Ravulizumab is a humanized monoclonal antibody engineered from eculizumab by the replacement of 4 amino-acids, with an extendend half life, allowing reducing dosing frequency. Even if Eculizumab is recommended for treatment and prevention of a HUS relapses after kidney transplant, and data on the use of Ravulizumab in KTR are limited, our experience demonstrated that KTR with de novo TMA can be initiated to therapy directly with Ravulizumab, without switching from Eculizumab, resulting in complete and sustained inhibition of alternative complement pathway.

EP_669 EXTRACORPOREAL PHOTOPHERESIS FOR BRONCHIOLITIS OBLITERANS SYNDROME

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Background: Bronchiolitis obliterans syndrome (BOS) is the most prevalent phenotype of chronic lung allograft dysfunction (CLAD). Moreover, BOS is a manifestation of chronic graft-versus-host disease (GVHD), a complication of allogeneic hematopoietic stem cell transplantation (HSCT). Extracorporeal photopheresis (ECP) has demonstrated promising outcomes in patients with BOS associated with either lung transplantation or HSCT. Here, we present our experience with five patients diagnosed with refractory BOS, additionally treated by ECP.

Methods: The study was conducted in Attikon University hospital of Athens, in the context of Greek Lung Transplant program, launched 5 years ago. We retrospectively recorded the characteristics of all patients with CLAD or GVHD after HSCT, treated with ECP, from September 2022 until January 2025. Therapy was performed with the THERAKOS® Cellex® photopheresis system. The treatment protocol included one cycle every 15 days for the first 3 months and then one cycle per month. Response to treatment was defined as clinical improvement and stabilization or slowing of lung function decline.

Results: During the study period, five patients underwent ECP sessions at our centre: three lung transplant recipients with CLAD and two patients with BOS secondary to GVHD following HSCT. All participants presented with severe symptomatic BOS, characterized by recent progressive decline in forced expiratory volume in one second (FEV1). No adverse events were observed during the study period. Following the initiation of ECP, FEV1 remained stable in all patients throughout the subsequent treatment cycles, in contrast to the progressive decline observed prior to therapy. Two patients demonstrated clinical improvement and continue to receive monthly ECP sessions. One patient underwent successful retransplantation. Unfortunately, two patients died during the study period: one patient was intubated, and the other was undergoing extracorporeal membrane oxygenation (ECMO) therapy. Due to their deteriorating clinical conditions, lung transplantation was not feasible.

Conclusions: ECP is an immunomodulatory therapy with an excellent safety profile, which may improve lung function decline and clinical outcomes in patients with BOS.

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EP_670 A COST-EFFECTIVENESS ANALYSIS OF ONCE-DAILY TACROLIMUS IN KIDNEY TRANSPLANT RECIPIENTS IN FRANCE: THE CHRONOS STUDY

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Background: Adherence to immunosuppressive treatments is critical for the long-term viability of transplanted kidneys and the health of kidney transplant recipients. Starting de novo once-daily tacrolimus (ODT) compared to twice-daily tacrolimus (TDT) formulation simplifies posology, potentially enhancing adherence and reducing clinical and economic burdens. The CHRONOS study aimed to assess the clinical and economic impacts of starting ODT in kidney transplant recipients in France.

Methods: A hybrid model combining a decision tree and a Markov framework was developed to project treatment adherence distribution, clinical outcomes, quality-adjusted life years (QALYs), and associated costs over a 15-year horizon. Inputs included data from the French REIN registry, published studies, real-world evidence showing that ODT much improves adherence and clinical outcomes compared to TDT formulation, and cost data from French National Health Insurance. Clinical outcomes assessed included kidney graft and patient survival, dialysis needs, and re-transplantation rates. Cost outcomes encompassed direct healthcare expenditures. Uncertainty was explored through deterministic, probabilistic sensitivity, and scenario analyses.

Results: For the annual incident cohort of 3,525 kidney transplant recipients in France, based on the average adherence gain, de novo ODT could prevent 80 kidney graft failures over 15 years. This would translate into 77 avoided dialysis treatment and 53 re-transplantations (Figure 1). While prolonged kidney graft survival increases follow-up costs by €3.0 million, avoided complications generate savings of €17.3 million, resulting in net savings of €14.3 million (Table 1). Moreover, avoided complications yielded an additional 74.4 QALYs, establishing ODT as a dominant strategy. In the sensitivity analysis, the number of estimated avoided graft failure primarily depended on the adherence gain with ODT.

Conclusions: Starting ODT is associated with significant clinical and economic advantages, enhancing adherence and reducing the burden of kidney transplantation management. These findings suggest supporting its adoption as a preferred strategy for kidney transplant recipients, with implications for clinical guidelines and healthcare policy optimization.

	Starting *de novo* once-daily tacrolimus	Twice-daily tacrolimus	Difference
Kidney graft failure	€ 1,098,480	€ 1,185,062	€ -85,582
Transplant monitoring	€ 490,752,921	€ 487,763,032	€ +2,989,889
Acquisitions costs (tacrolimus)	€ 35,451,794	€ 37,931,652	€ -2,479,858
Kidney transplantation	€ 37,806,350	€ 40,813,084	€ -3,006,734
Dialysis	€ 146,885,592	€ 158,565,129	€ -11,679,537
End-of-life care	€ 7,171,650	€ 7,204,708	€ -33,059
Total	**€ 719,166,786**	**€ 733,462,667**	**€ -14,295,881**

Table 1: Comparative Cost Analysis: Starting *de novo* once-daily Tacrolimus vs twice-Daily Tacrolimus Over 15 Years from a Healthcare System Perspective in France (3,525 Patients, costs updated to €2024).

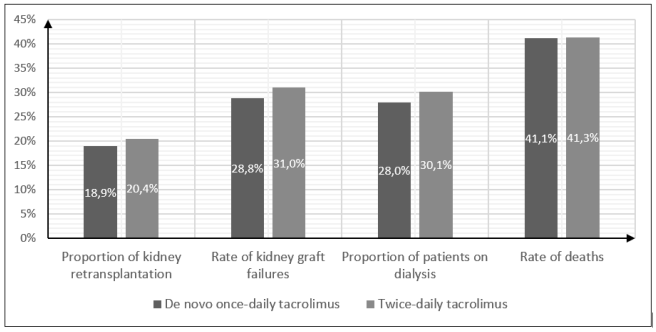

Figure 1: Long-term clinical outcomes of kidney transplant recipients under different tacrolimus formulations over a 15-year period.

EP_671 RESTRICTING DATASETS TO CLASSIFIABLE SAMPLES AUGMENTS BIOMARKER DISCOVERY IN SOLID ORGAN TRANSPLANTATION

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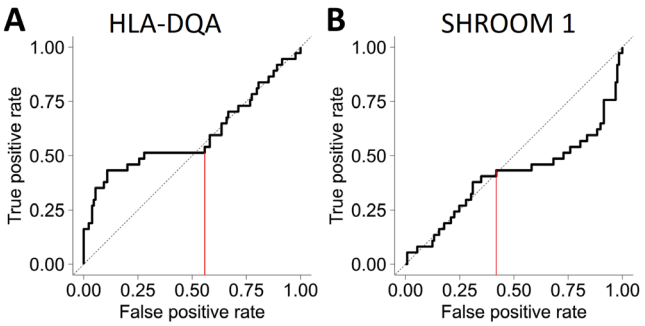
Background: Immunological diseases are typically heterogeneous in clinical presentation, severity and response to therapy. Biomarkers of immune diseases often reflect this variability, especially compared to their regulated behaviour in health. This leads to a common problem that frustrates biomarker discovery and interpretation – namely, unequal dispersion of immune disease biomarker expression between patient classes necessarily limits a biomarker's informative range. To solve this problem, we introduced *dataset restriction*, a computational procedure that splits datasets into classifiable and unclassifiable samples.

Methods: Synthetic flow cytometry data were generated with NBNode (https://github.com/ggrlab/NBNode). Restriction analysis was performed with restrictedROC (https://github.com/ggrlab/restrictedROC) on data from the INTERLIVER study (GSE193135). We applied restriction to normalized (RMA median-polish) gene expression data from 129 normal samples and 37 T cell-mediated rejection (TCMR) samples. Multivariate predictions were performed using random forests on highly variable genes within a cross-validation framework.

Results: Applied to synthetic flow cytometry data, restriction identifies biomarkers that are otherwise disregarded. In the INTERLIVER dataset, restriction finds 51 biomarkers with a multiple-testing corrected p-value < 0.005 for TCMR risk that were insignificant by conventional statistics; for instance, HLA-DQA (Figure 1A) or SHROOM1 (Figure 1B). By first applying restriction to all features in the INTERLIVER dataset, we created a multivariate model that accurately predicts TCMR with a cross-validated AUROC of 0.995 ± 0.012.

Conclusions: Dataset restriction augments discovery of TCMR-related biomarkers, increases predictive certainty for classifiable samples and improves multivariate models by incorporating biomarkers with a limited informative range. This principle can be directly extended to any classification task.



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EP_672 OUTCOMES OF RITUXIMAB MONOTHERAPY IN HIGHLY-SENSITIZED RECIPIENTS WITH LOW-MFI HLA-DSAS AT A SINGLE CENTER

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Background: Highly sensitized kidney transplant recipients with low mean fluorescence intensity (MFI) donor-specific antibodies (DSAs) face challenges related to antibody-mediated rejection (AMR). Rituximab, a monoclonal antibody targeting CD20+ B cells, has demonstrated efficacy in desensitization protocols. However, the outcomes of Rituximab monotherapy in low MFI patients remain underexplored. This study aims to determine the outcomes of Rituximab monotherapy in highly sensitized kidney transplant recipients with low MFI DSAs, focusing on graft survival, patient survival, and incidence of biopsy-proven acute rejection (BPAR).

Methods: A single-center retrospective cohort study was conducted on 22 highly sensitized adult kidney transplant recipients with low MFI DSAs (<5000). Patients were treated with Rituximab (200 mg or 500 mg) alongside standard induction and immunosuppression therapy. Clinical outcomes, including graft and patient survival, BPAR, and adverse effects, were assessed over a 1-year and 3-year follow-up period.

Results: The median MFI of DSAs was 899.5 (IQR: 437–1720). At 1 year, graft survival was 83.3%, with a 15.8% incidence of BPAR. Patient survival at 1 year was 85.0%. At 3 years, graft survival reached 100%, with no reported cases of BPAR. Patient survival was 80.0%, though renal function showed a gradual decline (e.g., serum creatinine increased from 1.10 to 1.35 mg/dL). Adverse events included urinary tract infections (31.8%) and cytopenias (13.6%), with no cases of infusion reactions.

Conclusions: Rituximab monotherapy effectively reduces rejection rates and maintains graft function in low MFI DSA recipients, offering a simpler and cost-effective alternative to combination therapies. Further research is needed to validate these findings in larger, multi-center cohorts and optimize treatment protocols for this population.

EP_673 MORE THAN HALF A CENTURY GRAFT SURVIVAL IN LIVING KIDNEY TRANSPLANTATION: A CASE SERIES REPORT

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Background: Kidney transplant is the therapy of choice for patients with end-stage renal disease, increasing their quality of life, survival and longevity. However, long-term graft survival is related to many factors including donor and organ procurement management, donor age, as ageing increases acute kidney damage and reduces tissue regenerative capacity. In addition, there are immunological and non-immunological factors related to kidney transplant deterioration and histological lesions that overlap with those observed in aged kidneys. We report the case of three living donor kidney transplant recipients with a graft survival of more than half a century.

Methods: three female patients with an unknown primary renal disease, received first kidney transplant from consanguineous living donors: In the first case, a 23-year-old patient received the left kidney from the 48-year-old mother at the time of transplantation. In the second case, a 20-year-old recipient of a right kidney from a 28-year-old brother. In the third case, a 27-year-old patient at transplantation, received a left kidney from a 56-year-old mother. All three procurement and kidney transplant operations were performed by the same surgeon, immunosuppressive regimen with azathioprine and steroid up to date.

Results: all three patients are still alive with functioning grafts. In case 1, current graft survival 52 years, total age of the kidney 100 years, current age of the recipient 75 years. Creatinine 1.4 mg/dL, eGFR 42 ml/min, proteinuria 0.3 g 24 h. In case 2, current graft survival 50 years, total age of the kidney 78 years, current age of the recipient 70 years. Creatinine 1.2 mg/dL, eGFR 62 ml/min, proteinuria 0.42 g 24 h. In case 3, current graft survival 53 years, total age of the kidney 109 years, current age of the recipient 80 years. Creatinine 1.7 mg/dL, eGFR 31 ml/min, proteinuria 0.23 gr 24 h.

Conclusions: Renal graft senescence is a complex process and its better understanding will be helpful in achieving longer graft survival. Even though kidney transplantation from living donor is known to have better results, it would be desirable to collect a database of more similar cases from many other Transplant center worldwide in order to understand and acquire genetics and molecular predisposing factors of such exceptional renal graft survival.

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Transplant immunology & immunosuppression

EP_674 EVALUATION OF ADHERENCE TO IMMUNOSUPPRESSIVE TREATMENT IN KIDNEY TRANSPLANT PATIENTS AT A FOUNDATION UNIVERSITY

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Background: Kidney transplantation is preferred because of its advantages such as decrease in mortality, increase in quality of life. The management of the process after kidney transplantation is very important. Organ rejection can occur at any time after the transplant. If the immunosuppressive drugs are not taken regularly, the body may reject the kidney even if many years have passed since the transplant. In this study, it is aimed to evaluate the adherence of kidney transplant patients with immunosuppressive therapy given after transplantation.

Methods: It is a descriptive study. A sociodemographic information questionnaire and "Immunosuppressant Therapy Adherence Scale" (ITAS) were administered to 36 kidney transplant patients at a BVU hospital in Istanbul.

Results: The mean age of the patients included in the study was 48,05±14,6 years , 58,3% male, 80,6% of those with hypertension, the mean time elapsed after kidney transplantation was 53,9±34.4 months, 58.3%of those who received a transplant from a living donor, 77,8%of them were on dialysis before the transplant (75% hemodialysis). 91,7% of the patients said that they received training on the postdischarge process (drug use etc.). 54.5%of the people who gave training to 33 patients who received post-transplant training were nurses. 38,9 %of the patients were hospitalized after transplantation. The minimum score of the patients on the ITAS was9 and the mean score was x=11.5±0.7. Age, gender, education level, marital status, occupation, income status, employment status, smoking and alcohol use, exercise, time since transplantation, donor type, pre-transplant dialysis, dialysis type, dialysis time, post-transplant education, post-transplant hospitalization characteristics were no statistically significant difference between ITAS scores (p>0.05).

Conclusions: After kidney transplant surgery, 91,7% of patients were trained on how to use immunosuppressive drugs. The mean ITAS score, which evaluates adherence to immunosuppressive therapy in kidney transplant patients, is remarkably high at 11.5 out of 12. The education given in our institution is sufficient and effective, and patients attach importance to treatment.

EP_675 ITALIAN SURVEY ON THE MANAGEMENT OF PREGNANCY IN RENAL TRANSPLANTATION

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Background: Pregnancy in a female renal transplant recipient is a high-risk condition for maternal-fetal complications that requires careful preconception counseling and multidisciplinary evaluation. The paucity of data in the scientific literature promoted us to conduct a questionnaire on the management of this pregnancies in italian transplant centers.

Methods: A questionnaire of 43 questions using the platform SurveyMonkey Software was sent to 40 Italian transplant centers, 26/40 responded.

Results: A total of 3078 patients in childbearing age undergoing renal transplantation were collected, 228 (7%) had achieved pregnancies after transplantation. In most centers (22/40, 55%) the time interval between renal transplantation and conception was ≥ 2 years. In relation to obstetric outcome 184 pregnancies resulted in live births (81%) while an abortive outcome occurred in 44 cases (19%). In the 184 evolving pregnancies we found a 53% rate of preterm delivery (< 37 gestational weeks). In 21 centers the most common method of delivery was cesarean section, while only 5 centers preferred the vaginal delivery option. The main obstetric complications recorded were gestational hypertension (24%) preeclampsia (15%), gestational diabetes (11%), fetal malformations (5%) and IUGR with fetal weight< 2500 gr (29%). In 24 centers, at the diagnosis of pregnancy, immunosuppressive therapy was changed with interruption of mycophenolate and switch to azathioprine. Seventy-six percent (76%) of the mothers did not breastfeed due to fear related to immunosuppressive therapy. Incidence of acute rejection was very low (3%), while deterioration of renal function occured in 24 cases (11%) of which 4 (17%) required dialysis.

Conclusions: Pregnancies in renal transplant recipients are burdened by a higher rate of complications compared to the general population in terms of gestational hypertension (24% vs 5%),preeclampsia (15% vs 1-2%), fetal IUGR (29% vs 7%) and preterm delivery (53% vs 7%). However, graft function and survival do not appear to be negatively affected. Further follow-up studies are warranted to definitely allow safe breastfeeding for patients on standard immunosuppression (tacrolimus , cyclosporine, azathioprine).

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EP_676 DESPITE HIGH DSA RATES, REJECTION EPISODES ARE LOW IN PATIENTS RECEIVING A ALEMTUZUMAB WITH STEROID SPARING PROTOCOL

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Background: The use of Alemtuzumab with steroid sparing maintenance immunosuppression has been associated with increased risk of de novo DSA. Early detection through screening enables an opportunity to enhance immunosuppression. This study reports on incidence and risk factors for dnDSA development in such patients, and describes outcomes following their detection.

Methods: 537 patients who were DSA negative at day 15 post-transplant were analysed. Patients with a CRF<85% receive tacrolimus monotherapy. All patients were HLA typed by high-resolution, and DSA screening was undertaken at 3 and 12 months and at the time of allograft dysfunction. Where DSA are detected, patients are offered a biopsy.

Results: DSA developed in 72 (13.4%) of patients; 3- and 12-month DSA free survival of 89.0% and 86.7% respectively. On adjusted analysis total ABDR (p<0.01), HLA Epitope mismatch (p<0.01) and younger age were associated with DSA (p=0.03) detection. Overall, 1-year rejection free survival was 91.8%; 97.7% and 52.9% in DSA- and DSA+ patients. 68 DSA+ patients underwent a biopsy; 33 (49.2%) showing no rejection, 34 (50.7%) features pf rejection and 1 C4d+WER (**Table 1**). DSA was detected later in patients with rejection, 66 (36-95) versus 93 (42-281) days (p=0.034). There was no difference in other antibody characteristics such as HLA class or MFI. Of the 465 DSA negative cohort, 20 patients had TCMR (11 BDL). With a median follow up post-biopsy of 2.05 (0.73-3.0) years, there was no difference in allograft survival by histological diagnosis (p=0.17), but all-cause graft survival was lower in the TCMR and mixed rejection groups (p=0.004).

Conclusion: BPAR is low in patients receiving Alemtuzumab and steroid sparing. DSA screening enables identification of patients at risk. Antibody characteristics do not inform risk of rejection, and other biomarkers of rejection may be beneficial in addition.

	No Rejection N=33 (%)	AMR^ N=15 (%)	TCMR^ N=12 (%)	Mixed N=7
Age	52 (41-62)	57 (53-67)	54 (40-73)	47 (36-59)
Female	11 (33)	5 (33)	4 (33)	2 (28.6)
DD Tx	23 (70)	14 (93)	11 (91.7)	7 (100)
cRF%	0 (0-52)	21 (0-45)	4 (0-36)	50 (8-56)
Primary Graft	30 (90.9)	15 (100)	11 (91.7)	7 (100)
MMF	5 (15.2)	1 (6.7)	1 (8.3)	1 (14.3)
Total ABDR	4 (3-5)	5 (3-6)	4 (3-4.5)	5 (4-6)
HLAEpMM	24 (19-27)	24 (16-31)	17 (14-24)	24 (18-30)
Time to DSA	66 (36-95)	41 (33-114)	100 (79-304)*	137 (102-305)*
Class I	13 (39.4)	7 (46.7)	3 (25.0)	2 (28.6)
Class II	16 (48.5)	4 (26.7)	8 (66.7)	3 (42.9)
Class I+II	4 (12.1)	3 (21.4)	1 (8.3)	2 (28.6)
CII Dominant	19 (57.6)	8 (53.3)	7 (58.3)	5 (71.4)
Peak ID MFI	4000 (2565-6950)	5900 (2900-8500)	4700 (2300-10250)	19750 (4950 – 19750)*
Time to Bx	33 (14-64)	18 (7-53)	34 (7.5-100)	21 (8-90)
DCGL	2 (6.06)	2 (13.3)	3 (25.0)	2 (28.6)
All-cause GL	2 (6.06)	2 (13.3)	4 (33.3%)*	4 (57.4%)*

^AMR (includes probable, AMR and CAMR), TCMR (includes Borderline, I and II)

Table 1. Clinical and antibody characteristics of DSA+ patients by histological diagnosis (no rejection group as comparator, * represents statistical significance)

EP_677 ESTABLISHING A GÖTTINGEN MINIPIG KIDNEY ALLOTRANSPLANTATION MODEL FOR LONG TERM EVALUATION OF TRANSPLANT OUTCOMES

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Background: Robust preclinical models are essential for kidney transplantation research. Göttingen minipigs are ideal due to their size, genetic consistency, and physiological similarity to humans. We aimed to establish a kidney allotransplantation model in Göttingen minipigs to enable long-term evaluation of kidney transplantation outcomes.

Methods: Göttingen minipigs (20–30 kg) were used. Donor (male) and recipient (female) pairs were selected based on mismatched swine leukocyte antigens. Donor kidneys were procured and preserved using static cold storage (SCS) or oxygenated hypothermic machine perfusion followed by sub normothermic machine perfusion at 34°C (sNMP), with the choice of sNMP informed by future research needs. Recipients underwent bilateral nephrectomy before receiving the donor's left kidney to the native site. Immunosuppressive therapy (Tacrolimus, Mycophenolate and Prednisolone/Solu-medrol) was initiated, and recipients were monitored via clinical observation and biochemical analysis. In cases of complications or signs of rejection, veterinarians and researchers evaluated the need for termination if interventions failed to improve the condition.

Results: A total of 13 minipigs underwent transplantation. Seven animals died from complications before discontinuation of immunosuppression (Table 1). Surgical complication rates were initially higher than expected, prompting procedural modifications, including switching from micro-cutting to taper-point vascular sutures, relocating the ureteropelvic anastomosis to a more distal position, and improving surgical conditions by replacing bedding material to reduce intestinal distension. Three animals in each group had immunosuppression discontinued as planned and were later terminated due to graft rejection. The time from immunosuppression cessation to graft rejection ranged from 6 to 102 days (Figure 1). One SCS animal (#1) developed tacrolimus toxicity due to a dosing error, resulting in elevated creatinine levels (Figure 1).

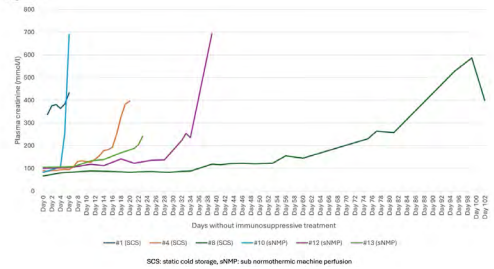
Conclusions: An effective protocol for allogeneic porcine kidney transplantation was developed and optimized towards extended graft survival rates. This model may facilitate testing new interventions supporting renal graft survival rates and improving patient's life quality.ç

Table 1

Animal	1	2	3	4	5	6	7	8	9	10	11	12	13
Weight at transplantation (kg)	24,6	25,2	27,1	25,9	30,1	23,9	23,0	24,9	27,2	22,6	24,3	27,6	31,1
Kidney storage	SCS	SCS	SCS	SCS	sNMP	SCS	SCS	SCS	sNMP	sNMP	sNMP	sNMP	sNMP
Day of termination	38	5	3	52	3	2	4	119	7	16	6	56	40
Cause of termination	Rejection	Ureter	Artery	Rejection	Thrive	Vein	Ureter	Rejection	Artery	Rejection	Thrive	Rejection	Rejection
Duration of immunosuppression (days)	32	-	-	32	-	-	-	17	-	10	-	17	17
Creatinine at discontinuation of immunosuppression (mmol/l)	338	-	-	90	-	-	-	67	-	82	-	100	105
Time to rejection after stopping immunosuppression (days)	6	-	-	20	-	-	-	102	-	6	-	39	23

SCS: Static cold storage, sNMP: sub normothermic machine perfusion (34 °C), Rejection: Expected graft rejection as described by humane endpoints, Ureter: Complication related to the ureteropelvic anastomosis or internal ureter catheter, Artery: Arterial thrombosis or complications related to the arterial anastomosis, Thrive: Lack of thrive due necessitation termination according to the experimental animal permission, kidney function was in this case normal Vein: Venous thrombosis or complications related to the venous anastomosis.

Figure 1



SCS: static cold storage, sNMP: sub normothermic machine perfusion

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EP_678 CLINICAL SIGNIFICANCE OF INTRA-PATIENT VARIABILITY AND TACROLIMUS EXPOSURE IN OLDER KIDNEY TRANSPLANT RECIPIENTS

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Background: Low tacrolimus (TAC) exposure and high intra-patient variability (IPV) are associated with increased risks of de novo donor-specific antibodies (DSA) and graft failure. However, the clinical significance of these factors in older kidney transplant recipients (≥60 years), who may exhibit reduced alloimmune responses, remains unclear

Methods: This retrospective cohort study included adult kidney transplant recipients (≥18 years) from 2006 to June 2023, stratified into four groups based on TAC trough levels and IPV: 1) low TAC/low IPV, 2) high TAC/low IPV, 3) low TAC/high IPV, and 4) high TAC/high IPV. Primary outcomes included death-censored graft survival (DCGF) and secondary endpoints such as patient survival, biopsy-proven rejection, renal function, and de novo DSA development. Median follow-up was 92 months

Results: Among 1,951 eligible recipients, the impact of TAC exposure and IPV on graft survival differed by age group (P=0.007). In recipients under 60 years, the low IPV/high TAC group showed the best graft survival, while the high IPV/high TAC group had the worst outcomes. Conversely, in recipients aged ≥60 years, the low IPV/low TAC group demonstrated the highest graft survival, whereas the high IPV/low TAC group exhibited the poorest outcomes. Cox regression confirmed high IPV as a significant risk factor for DCGF in older recipients, regardless of TAC levels. Differences in patient survival among TAC/IPV groups were not statistically significant (P=0.221).

Conclusions: This study highlights age-specific differences in the clinical significance of TAC exposure and IPV. For older kidney transplant recipients, reducing IPV and careful optimization of TAC exposure are critical to improving graft outcomes. These findings underscore the need for tailored immunosuppressive strategies in this population.

EP_679 LIVER TRANSPLANT PATIENT SURVEY- EXPERIENCES WITH IMMUNOSUPPRESSION MEDICATION SUPPLY

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Background: UK Liver transplant recipients receive their immunosuppression (IS) medication via 4 main routes. Since 2013 NHSE have required transplant centres to retain the prescribing of IS, reflected in the 2017 NHSE liver transplant specialist commissioning document. Work by the UK Liver Transplant Pharmacists Group indicates geographical variation, and barriers to repatriating IS supply. GP IS provision is no longer commissioned in England. Hepatology pharmacy workforce standards indicate geographical staffing variation, defining outpatient workload as enhanced services requiring resource. Patient group representatives (PGRs) highlight geographical variation in patient experience of IS supply. Optimising patient IS supply experience is an important factor in supporting adherence.

Methods: A short digital survey to obtain a snapshot of current patient experience among adult liver transplant recipients was developed and shared with PGRs who shared widely via social media.

Results: Of 324 responses, more than 70% were 3 years plus post-transplant, with 52% overall receiving medication from the transplant hospital and 30% via GP. Figure 1 indicates 87% of respondents reported a level of satisfaction (satisfied or very satisfied) with their method of supply route.

Conclusions: The high proportion still receiving IS via the GP (52% are 10 years plus), highlights a potential repatriation burden in England. This result may be skewed by England vs UK differences. The high level of patient reported satisfaction indicates positive work of services to achieve this. There are still many who are dissatisfied, with needs improvement, long wait and insufficient supply frequently mentioned as issues. This snapshot is a useful indicator to prompt further work to reduce inequalities and address sustainability challenges. The patient voice and perspective is important to co-design improvements in services.

Number of patients		Years post-transplant					
Route of supply	**Total (%)**	**<1**	**1-2**	**2-3**	**3-5**	**5-10**	**>10**
Transplant hospital delivered	102 (32)	14	12	11	14	29	22
Transplant hospital collected	65 (20)	6	16	11	8	12	12
GP	97 (30)	4	6	2	14	21	50
Homecare	39 (12)	4	6	2	6	13	8
Referral centre (delivered or collected)	16 (5)	2	1	1	4	5	3

Table 1: Route of medication supply

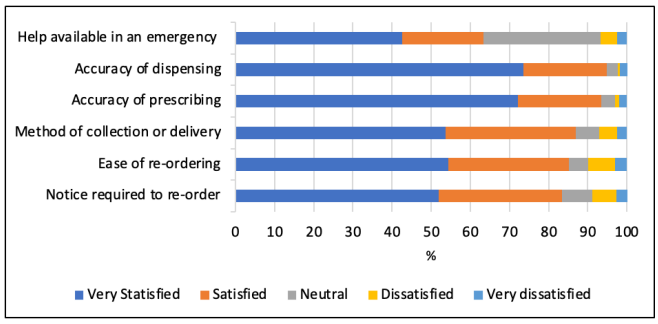

Figure 1: Level of satisfaction with medication supply via 5 point Likert scale

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Transplant immunology & immunosuppression

EP_680 FUNCTIONAL SCREENING IDENTIFIES NOVEL MECHANISMS OF HUMAN ITREG INDUCTION

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Background: Infiltrating regulatory macrophages (Mregs) are indispensable for allograft acceptance in immunosuppressed and tolerant recipients. Mregs restore immune homeostasis within transplanted tissues, in part through local induction of TIGIT+ Tregs. Targeting Mreg-T cell interactions could reduce chronic allograft injury by strengthening intragraft regulation. Here, we report a functional screen using primary human cells for unbiased discovery of mechanisms controlling human Mreg-induced Treg (miTreg) development, stability and function.

Methods: We optimized and scaled-up an established coculture assay to measure iTreg induction by allogeneic Mregs. Three libraries were screened and validated using our miTreg assay – 159 FDA-approved drugs, 120 clinical monoclonal antibodies (mAbs), and 400 mAb against tumor-associated macrophages (TAM).

Results: Screening small molecule drugs confirmed the stable performance of our assay and identified known inhibitors of miTreg generation. Encouragingly, it also returned new substances, including a prominent class-effect of statins, implying a role for mevalonate pathway-derived mediators. Screening clinical mAb identified known receptors (eg. IL-2R) and others involved in APC-T cell interactions. 25 of 120 mAbs showed significant activity, corresponding to 12 pathways. Excluding previously known targets, we confirmed 7 hits in repeatability studies. Of these, 5 targets (CD11a, EGFR, PDL1, GM-CSF, CD52) were reproduced using alternative drugs. Screening of 400 rh-mAb against human TAM returned one significant, repeatable hit.

Conclusions: These proof-of-concept experiments demonstrate reliability of our miTreg assay as a screening tool. We now aim to compile a comprehensive list of druggable targets involved in Mreg-T cell interactions. This will enable us to select targets and/or lead substances for post-screening investigation based upon effect size.

EP_681 A HARMONISED LABORATORY PROTOCOL FOR GENERATING PHOTOPHERESATES

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Background: Extracorporeal photopheresis (ECP) is a safe and effective therapy with long-established indications in treating T cell-mediated immune diseases, including steroid refractory graft-versus-host disease and chronic rejection after heart or lung transplantation. The ECP procedure involves collecting autologous peripheral blood leucocytes that are driven into apoptosis using 8-methoxypsoralen (8-MOP) and UVA irradiation before being reinfused intravenously. ECP acts primarily through in situ exposure of recipient dendritic cells and macrophages to apoptotic cells, which then suppress inflammation, promote specific regulatory T cell responses and retard fibrosis. To better study these reactions, participants in the EU-funded exTra consortium needed a reproducible, harmonized method to generate photopheresates for research.

Methods: A consensus meeting of project stake-holders decided the following experimental variables should be systematically optimized: 8-MOP concentration and incubation time; UVA dose; composition and density of peripheral blood mononuclear cells (PBMC) suspensions. Conditions were modified so research-grade photopheresates had comparable rates of apoptosis induction to clinical products from the CELLEX™ device.

Results: Freshly isolated human PBMC suspended in DBPS with 10% human AB serum were exposed to 8-MOP and UVA. The optimal cell density in 3 ml total volume was 107 cells/ml. The optimal 8-MOP concentration was 400 ng/mL with an incubation time of 30 min. A UVA dose of 2 J/cm² yielded the most consistent rates of apoptosis. Flow cytometry analysis of lymphocyte and monocyte apoptosis in research-grade photopheresates and clinical products showed similar kinetics over 48 h.

Conclusions: This work establishes a harmonised protocol for generating research-grade photopheresates, which will help to ensure comparability of results generated by groups participating in the exTra consortium.

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EP_682 TORQUE TENO VIRUS LOADS AND LEUKOCYTE POPULATIONS IN STABLE OUTPATIENT KIDNEY TRANSPLANT RECIPIENTS

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Background: Plasma concentrations of Torque teno virus (TTV) have been proposed as a biomarker of immune function, which could aid in personalized dosing of immunosuppressive medication after solid organ transplantation. It has been suggested that after replication, TTV enters the circulation through release from leukocytes, particularly granulocytes, or cells within the bone marrow. We hypothesize that leucocyte subpopulations are associated with circulating plasma TTV concentrations in kidney transplant recipients (KTR). We therefore aimed to explore the association of leucocyte subpopulations with plasma TTV concentrations in KTR.

Methods: A total of 350 KTR with both detectable TTV load and leukocyte population counts at 1 year post-transplantation were selected from the Transplant-Lines Biobank and Cohort Study. TTV load was measured by real-time PCR assay (TTV R-GENE®, bioMérieux) and leukocyte populations were counted by a Sysmex XN hematology analyzer. Linear regression analyses were performed to assess associations between leukocyte populations and TTV load.

Results: Mean age of the included KTR was 56.3 ± 14.5 years, and 133 (38.0%) were female. In multivariable regression analysis, after adjusting for age, sex, smoking behavior, alcohol intake, C-reactive protein, tacrolimus and mycophenolic acid trough levels, and other granulocyte subpopulations, we found that immature granulocyte count was positively associated with TTV load (st. β = 0.44, $p < 0.001$) and neutrophil count was negatively associated with TTV load (st. β = -0.39, $p < 0.001$).

Conclusions: These results support the theory that TTV replicates in immature granulocytes. The mechanism underlying the negative association between neutrophiles and TTV load remains to be determined. Potential explanations include the suppression of TTV load by antiviral properties of neutrophiles or the possibility that TTV affects the lifespan of neutrophiles. Understanding these relationships might improve the interpretation of TTV load as a marker of immune function in clinical practice.

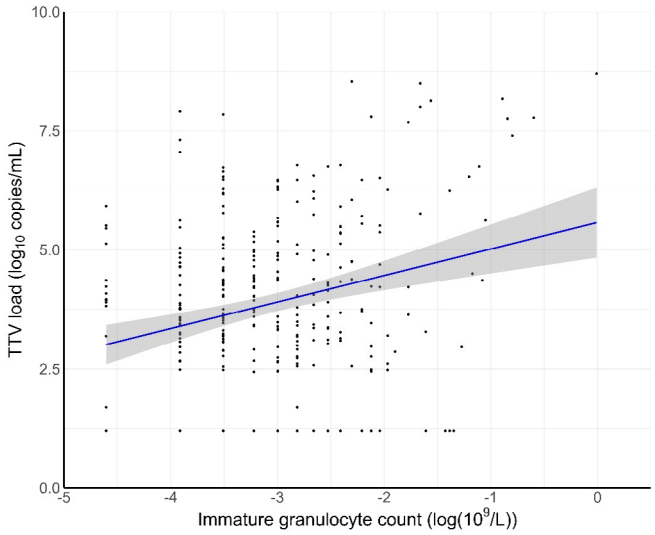

Figure: Association between immature granulocyte count and TTV load.

EP_683 COMPLETE REMISSION OF POST TRANSPLANT RECURRENT OR DE NOVO IGA NEPHROPATHY WITH ORAL BUDESONIDE TREATMENT

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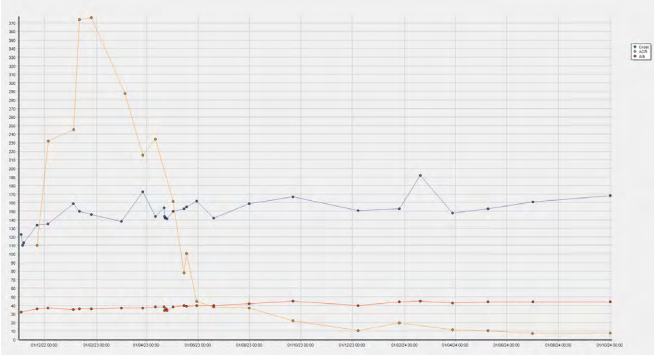
Background: IgA nephropathy (IgAN) is a leading cause of kidney disease characterized by the deposition of immunoglobulin A (IgA) in the glomeruli. In kidney transplant recipients, recurrence of IgAN or the development of de novo disease can occur. Budesonide, a corticosteroid with minimal systemic side effects, has been proposed as an effective treatment for IgAN due to its anti-inflammatory properties and reduced side effect profile compared to traditional corticosteroids.

Methods: A 52-year-old male with a history of end-stage renal disease secondary to unknown etiology underwent a second deceased donor kidney transplant in 2020. His first kidney transplantation, done in 2015, was lost due to early renal vein thrombosis. In January 2023, the patient presented with worsening proteinuria, and a renal biopsy revealed features consistent with recurrent or de novo IgA nephropathy. Electron microscopy showed para mesangial electron-dense deposits and granular IgA staining. Following the biopsy, the patient was started on Budesonide and response in ACR and creatinine was monitored for over 12 months.

Results: Once commenced on budesonide, over the following 12 months, proteinuria (ACR) gradually improved from 376.2 mg/mmol to 10.8 mg/mmol. By the end of the treatment period, complete remission was achieved. Budesonide was switched back to prednisolone after completion of treatment. Patients ACR hadn't worsened despite being on prednisolone for 6 months now.

Conclusions: This case demonstrates the successful use of oral budesonide in achieving complete remission of post-transplant recurrent or de novo IgA nephropathy, adding to the limited number of reports in this area. The patient experienced significant improvement in proteinuria, highlighting the potential of budesonide as an effective treatment for IgAN in post-transplant patients. Further research is needed to establish long-term outcomes and the role of budesonide in this patient population.



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EP_684 EVEROLIMUS VS MYCOPHENOLATE IN 196 LIVING DONOR KIDNEY TRANSPLANTS: A RETROSPECTIVE ANALYSIS

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Background: Strategies to reduce Calcineurin Inhibitors (CNI) exposure combining the mTOR inhibitor everolimus (EVR) with low-dose CNI have been studied in several controlled clinical trials, such as the TRANSFORM study, where a mixed population of deceased and living donor (LD) kidney transplant recipients were investigated. We assessed the effects of EVR + low dose CNI vs mycophenolate (MMF) + standard dose CNI in a subset of LD only kidney transplants.

Methods: We retrospectively evaluated outcome measures such as renal function, graft and patient survival, incidence of rejection and infections in 196 living donor kidney transplant recipients performed at our center from 2011 to 2023. Patients were allocated to two immunosuppressive regimens: EVR + low dose CNIs or (MMF) + standard dose CNI and followed-up at 1 and 3 years.

Results: The average age of recipients at the time of transplant was 42.7 years [18-77], male/female 66.8%/ 33.2%. There were 26 AB0-i transplants (13.3%), 12 retransplants (6.1%) 3 of which with IgG DSAs at transplant (1.5%). Univariate analysis did not show any statistically significant difference at 1 year between the two groups in terms of graft and patient survival, rejection, overall infection incidence, incidence of CMV infection, malignancy, surgical site complications (wound infections or lymphocele) and renal function. In addition, at 3 years, a protective role of EVR was confirmed by a reduction of the incidence of CMV infections (chi-square 4.9, p-value 0.03); no statistically significant differences were observed in the other outcomes.

Conclusions: This analysis confirms also in LD kidney transplant recipients the non-inferiority of EVR compared to MMF, confirming a protective role of EVR against CMV infections at 3-years follow-up.

EP_685 VALUE OF PLASMA CXCL9 AND CXCL10 FOR GUIDING ANTI-REJECTION THERAPY AFTER KIDNEY TRANSPLANTATION

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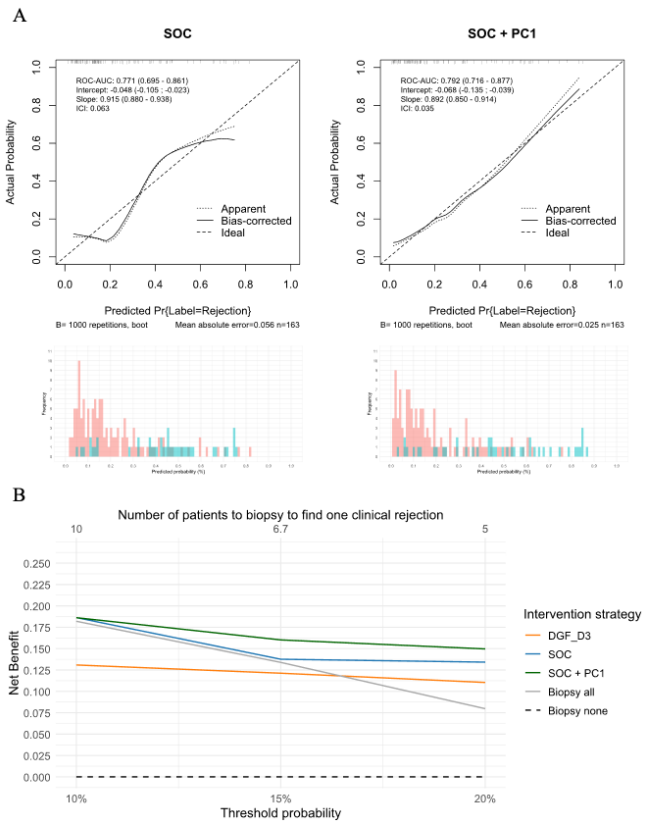
Background: There is an increasing interest in evaluating the clinical utility of minimally-invasive biomarkers for allograft rejection after kidney transplantation. Here, we studied whether adding early plasma CXCL9 and CXCL10 measurements to a standard-of-care (SOC) model predicting the need for anti-rejection therapy leads to improved model predictive ability.

Methods: A SOC model was developed using recipient and donor age, human leukocyte antigens (HLA) mismatches, and dialysis need in the first three days post-transplantation. A principal component analysis (PCA) was performed on day-three plasma CXCL9 and CXCL10 measurements to summarize the two into one predictor (PC1). We added either CXCL9, CXCL10, or PC1 to the SOC model and assessed the added value of the markers through likelihood ratio tests (LRT). Model discrimination was assessed through the area under the receiver operating characteristic curve (ROC-AUC), calibration through flexible calibration curves, and clinical utility through net benefit (NB) analysis. Model optimism was assessed through bootstrapping.

Results: Forty-three of 163 (26.4%) patients required anti-rejection therapy between days three and twenty-one after kidney transplantation. All biomarker-extended models outperformed the SOC model (LRT p-value<0.01), presenting higher optimism-corrected discriminative ability (delta ROC-AUC of 0.02) and better calibration. Only the SOC+PC1 model showed equal or higher NB than the SOC model and biopsy strategies based on protocol or graft dysfunction for all considered risk thresholds for decision, i.e. number of patients a clinician would be willing to biopsy to find one case of clinical rejection.

Conclusions: This study provides evidence that adding plasma CXCL9 and CXCL10 information could improve a SOC model for anti-rejection treatment. Moreover, adopting a clinical model or a model added by the summarization of the chemokines could improve patient care as they showed consistent NB over standard intervention strategies.



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EP_686 ALBUMIN CORRECTION REVEALS ADVERSE EFFECTS OF FK506 TROUGH LEVEL VARIABILITY IN PEDIATRIC RECIPIENTS

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Background: High intrapatient tacrolimus trough level variability (TC-IPV) has been associated with poor graft outcomes and donor-specific antibody formation in (pediatric) kidney transplant recipients due to its narrow therapeutic index. Interpretation of routine trough levels (measured in whole blood) is potentially confounded by changes of its major binding sites (erythrocytes and albumin). This has not yet been considered for the interpretation of TAC-IPV.

Methods: All pediatric kidney transplant recipients between 2010 and 2020 were included in this retrospective study at the Medical University of Vienna. Patients with insufficient follow-up data and other immunosuppression than tacrolimus were excluded. Hematocrit correction was conducted as previously published and modified and jointly corrected for serum albumin levels. TAC-IPV and corrected TAC-IPV was calculated in six month moving windows and associated with estimated glomerular filtration rate (eGFR) six months later using mixed-effects models.

Results: A total of 39 patients were included in this study and followed for a median of 552 days (IQR 517-561). Median age was 10 years (IQR 5-16), 72% were male. Donor-recipient HLA mismatch was at median 3 (IQR 2-3). Contrary to crude TAC-IPV and hematocrit-corrected TAC-IPV (estimate -0.31, p=0.23 and -0.09, p=0.71) combined higher hematocrit- and albumin-corrected TAC-IPV was significantly associated with lower eGFR six months later (estimate -2.84, p<0.001).

Conclusions: This study assesses the potential of combined albumin and hematocrit correction of whole blood tacrolimus trough level variability in pediatric kidney transplant recipients. For the first time, we showed eGFR-relevant underestimation of TAC-IPV without appropriate albumin- and hematocrit-correction in a pediatric single-center cohort.

EP_687 DIFFERENCES IN PROTECTION FROM COMPLEMENT AND COAGULATION IN GENETICALLY MODIFIED PORCINE ENDOTHELIAL CELLS

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Background: Multigene modifications in pigs can overcome interspecies innate immune barriers in xenotransplantation. As the first cells encountered by the recipient, endothelial cells (ECs) and their glycocalyx layer play a crucial role in determining the fate of xenografts. Therefore, it is essential to understand the effect of genetic modification (GM) of the pig ECs on the host's innate immune system.

Methods: Here, we compared the functional effect of two GM sets on porcine ECs: GGTKO/hCD46/hTBM (3GM) and GTKO/CMAHKO/hCD46/hCD55/hCD59/hHO1/hA20 (7GM). We perfused the ECs with normal human serum (NHS) and recombinant human (rh)TNF to simulate inflammatory and xenogeneic conditions and characterized the complement activation, cell activation, clot formation, and transcriptome changes. We also performed EC glycocalyx profiling using a capillary gel electrophoresis with laser-induced fluorescence detection.

Results: We showed that 7GM-ECs provided better protection from complement activation when perfused with NHS or rhTNF-? +NHS. Interestingly, 7GM-ECs also showed better prevention of clot formation after NHS perfusion. However, when perfused with rhTNF-?+NHS, 3GM-EC provided significantly higher protection against clot formation. We also observed different N-glycan and glycosphingolipid profiles in the two ECs. Distinct transcriptome changes in genes associated with coagulation and inflammatory responses were also observed during inflammatory and xenogeneic activation, possibly influencing the complement and coagulation states of each cell.

Conclusions: The GM sets used to overcome rejection in xenotransplantation provide differential protection against complement activation and coagulation dysregulation. A complete set of xenoantigen deletions, along with the expression of human complement, coagulation, and inflammation regulatory genes, may be necessary for the survival of xenografts, although we still lack an understanding of the respective effects on the glycocalyx.

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EP_688 TOCILIZUMAB REDUCES INJURY-REPAIR-ASSOCIATED TRANSCRIPTS IN THE TREATMENT OF CHRONIC-ACTIVE ANTIBODY-MEDIATED REJECTION

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Background: Chronic-active antibody-mediated rejection (caAMR) is a leading cause of late allograft failure in kidney transplant recipients (KTRs), with limited effective treatment options. Tocilizumab (TCZ), an interleukin-6 monoclonal antibody, has been proposed as a potential therapy improving long-term outcome. We examined gene expression changes in follow-up biopsies after TCZ treatment in comparison to optimized standard immunosuppression (sIS) alone.

Methods: KTRs with biopsy-proven caAMR >6 months post-transplantation and available follow-up biopsies were included. Biopsy-based transcriptomics were assessed using the Molecular Microscope Diagnostic System (MMDx). Six KTRs received monthly TCZ (8 mg/kg IV) plus optimized sIS (tacrolimus/mycophenolic acid/prednisone), and three KTRs received sIS only.

Results: In the TCZ group, there was a decrease in injury and repair-associated transcripts (IRAAT, median 0.24; 0.03) and a slight decrease in atrophy-fibrosis transcripts (IFTA, median 0.65; 0.51). Rejection classifier scores (median 0.66; 0.6) and AMR classifier scores (median 0.51; 0.58) remained stable, with a marginal decrease in all AMR score (median 0.92; 0.81). The rejection archetype cluster significantly evolved from early-stage AMR (R4 score, median 0.53; 0.23; p=0.004) to fully developed AMR (R5 score, median 0.27; 0.47; p=0.041). In contrast, in the sIS group, IRAATs (median -0.11; 0.40) and IFTA (median 0.22; 0.60) increased. Rejection classifier (median 0.81; 0.65) and AMR classifier scores (median 0.79; 0.45) decreased, with no change in AMR archetypes.

Conclusions: TCZ compared to sIS alone did not improve molecular AMR activity or halt progression from early to fully developed AMR. However, it reduced IRAAT scores, which are linked to graft failure, suggesting potential benefits. Further investigation in a larger cohort is needed to determine whether IRAAT scores could serve as early markers of treatment response.

EP_689 NOVEL UMBILICAL CORD-DERIVED MULTI-CHIMERIC CELL THERAPY FOR INDUCING TOLERANCE IN TRANSPLANTATION

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Background: Cellular therapies are regarded as the most promising approach for inducing transplant tolerance without life-long immunosuppression in solid organs and vascularized composite allotransplantation (VCA). Currently, no therapies are achieving this goal. This study introduces a novel Human Multi-Chimeric Cell (HMCC) line created by the fusion of umbilical cord blood (UCB) cells from three unrelated donors as an alternative therapeutic approach for tolerance induction in solid organ and VCA transplantation.

Methods: We performed eighteen ex vivo polyethylene glycol-mediated fusions of human UCB cells from three unrelated donors to create HMCC. Mononuclear cells labeled with PKH26, PKH67, and eFluor™ 670 fluorescent dyes were fused and sorted, creating a new population of triple-labeled (PKH26/PKH67/eFluor™ 670) HMCC. Flow cytometry and confocal microscopy confirmed the creation of HMCC from three unrelated human UCB donors.

Results: Genotyping analyses determined the tri-chimeric state of HMCC by the presence of parent alleles and selected loci specific for each UCB donor. Phenotype characterization confirmed hematopoietic markers distribution, comparable to UCB donors. HMCC maintained viability and displayed a low apoptosis level. The COMET assay revealed the absence of genotoxicity, confirming fusion safety. Colony forming units assay showed clonogenic properties of HMCC.

Conclusions: This study confirmed the feasibility of HMCC creation from three unrelated human UCB donors and characterized tri-chimeric state, hematopoietic phenotype, viability, safety, and clonogenic properties of HMCC. The created HMCC line, representing the genotype characteristics of three UCB donors, introduces a novel therapeutic approach for bone marrow, solid organ, and VCA transplantation.

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EP_690 A NOVEL APPROACH USING DARATUMUMAB DESENSITISATION IN A HIGHLY SENSITISED HEART TRANSPLANT CANDIDATE

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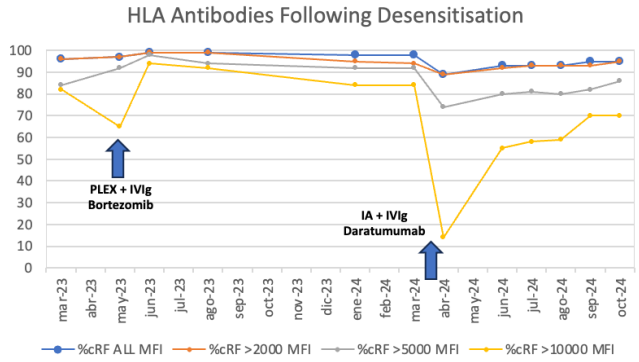
Background: Patients who are highly sensitised wait longer on the heart transplant list. We present our experience with a desensitisation regime to expand the number of suitable donors in a highly sensitised patient on the heart transplant waiting list.

Methods: We present a case report of a 61 year old female with heart failure due to coronary artery disease was listed for heart transplant with a total calculated reaction frequency (cRF) of 99%. Given the level of desensitisation, the decision was made to give plasma exchange (4 cycles), intravenous immunoglobulin (IVIg) (1g/kg) and bortezomib (4 x 1.3mg/m^2 doses). The patient experienced grade 1 peripheral neuropathy with bortezomib, however did not require a dose modification. Plasma exchange was poorly tolerated haemodynamically by the patient. Following these therapies, her %cRF >10000 mean fluorescence intensity (MFI) reduced from 83% to 65%, however her total %cRF remained high at 97% (Figure 1), decreasing this would enable us to consider transplanting across specificities with a combined MFI below this level. She subsequently received additional treatment with immunoadsorption (IA) with IVIg (1g/kg) and daratumumab, a human IgG1k monoclonal antibody directed against CD38 (4 x 1800mg doses). Following these therapies, her %cRF >10000 MFI reduced from 84% to 58% and her total %cRF reduced to 93%. No adverse drug events were reported during therapy. Daratumumab binds to CD38 expressed on lymphocytes affecting the flow cytometry crossmatch test and at low levels on red blood cells which may result in a positive indirect Coombs test. The patient is currently still active on the urgent heart transplant waiting list.

Results: Figure 1 shows a graph of the %cRF over the time period of the desensitisation protocol:

Conclusions: The desensitisation strategy of IA, IVIg and daratumumab showed a reduction in the %cRF. It appears to be well tolerated and may offer an effective strategy in highly sensitised heart transplant candidates on the heart transplant list, creating a window of opportunity in an otherwise extremely difficult antibody profile. However, several questions remain including, the duration of effect for a sustainable response and long-term outcomes post-transplant.



EP_691 ECP AS A POTENTIAL TREATMENT FOR LIVER REJECTION AFTER TRANSPLANTATION - INFLUENCE OF CELL DEATH ON T CELL ACTIVATION

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Background: Transplantation of marginal livers is increasingly common, so too are attendant complications that reflect previous disease and worse ischemia-reperfusion injury (IRI). Novel strategies to reduce early transplant injury and inflammation are a priority. Extracorporeal photopheresis (ECP) is a safe and effective therapy with long-established indications in T cell-mediated diseases, notably in the management of heart and lung transplant rejection. ECP leverages the potent suppressive effects of apoptotic cells to control T cells and dampen acute inflammation. Here, we investigated whether ECP suppresses γδ T cells, which are a major driver of IRI.

Methods: Samples of clinical and research-grade ECP products were obtained before and after apoptosis induction with 8-methoxypsoralen (8-MOP) and UVA irradiation. These photopheresates were indirectly cocultured with CD3/28/2-stimulated human T cells across a 0.4 µm transwell. The activation status of T cells was subsequently assessed by flow cytometry after 24h and 48h.

Results: Coculture with clinical products reduced CD69 expression in αβ (7.25±11.99 %, p=0.0244) and γδ (9.26±19.62 %, p=0.0302) T cells in ECP-treated compared to untreated samples (n=14). Likewise, coculture with research-grade products reduced CD69 expression in αβ (7.23±3.29, p=0.0312) and γδ (8.80±4.48, p=0.0312) T cells in ECP-treated compared to untreated samples (n=6). Research-grade ECP products also significantly suppressed CD25 expression in αβ (4.04±2.28, p=0.0312) and γδ (2.9±2.01, p=0.0312) T cells.

Conclusions: Our results show that mediators from photopheresates pass through transwells to suppress polyclonal αβ and γδ T cell activation. These mediators, which presumably derive from apoptotic leucocytes, may include soluble factors (eg. cytokines, metabolites or miRNAs) or small particulates, including extracellular vesicles.

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EP_692 USE OF BASILIXIMAB IN LIVING DONOR LIVER TRANSPLANT RECIPIENTS WITH RENAL DYSFUNCTION

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Background: Renal dysfunction before and following liver transplantation is a known complication that affects recipient and graft survival. Calcineurin inhibitors are the primary immunosuppression in transplants but are associated with an increased incidence of renal dysfunction. Short-term antibody induction with delayed introduction of calcineurin inhibitors has been one strategy for protecting renal function.

Methods: This was a retrospective observational study comparing the postoperative outcome of the use of basiliximab in recipients with perioperative renal dysfunction between July 2019 and December 2022.

Results: 427 living donor liver transplants were performed during the study period from 25th July 2019 to 29th December 2022. The incidence of hepatorenal syndrome and postoperative acute kidney injury was 17.1% and 5.8% respectively. Preoperative peak serum creatinine level was 1.27±0.45mg/dl in the basiliximab group and 1.46 ± 0.62 mg/dl in the non-basiliximab group (p=0.08). The lowest preoperative mean eGFR in the basiliximab group was 69.6±37.77 ml/min/1.73m2 and 57.2±27.85 ml/min/1.73m2 in the non-basiliximab group (p=0.06). The Basiliximab group had more renal dysfunction immediately before transplant (day minus one) (mean creatinine 1.15±0.21 vs 0.93±0.27, p<0.0001 and eGFR 68.56±15.31 vs 89±38.19, p=0.0016). There was a significant difference in the tacrolimus initiation and first 3 mean tacrolimus trough concentrations (p=0.002, 0.04, 0.02, and 0.07 respectively) and overall tacrolimus trough concentration was less in the basiliximab group. Recipients without preoperative acute kidney injury who developed acute kidney injury in the postoperative period and received basiliximab, had significantly better serum creatinine (p=0.04) and eGFR (p=0.047) at 6 months. The incidence of infections was significantly higher in the non-basiliximab group (28.5% vs 9.5% p value=0.02).

Conclusions: Basiliximab with delayed introduction of tacrolimus is a safer and effective regimen in liver transplant recipients with post-operative renal dysfunction without increasing risk of infections. Its renal sparing effect is significantly higher in recipients who had developed acute kidney injury only in the postoperative period.

EP_693 OUTCOME OF HLA INCOMPATIBLE RENAL TRANSPLANTS UNDER STANDARD DESENSITIZATION TREATMENT

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Background: HLA incompatible transplantation should be considered in highly sensitized recipients and desensitization therapies based on the combination of apheresis, intravenous immunoglobulins (IVIG) and rituximab has been considered the standard of care. We reviewed the experience at our department and classified transplants according to donor recipient flow cytometry crossmatch (FC-XM).

Methods: We reviewed HLA incompatible renal transplants performed between 2011 and 2022 who had a FC-XM done before transplant and underwent standard desensitization. All patients had a negative CDC crossmatch. Desensitization was based on the combination of apheresis, IVIG (2 g/kbw) and Rituximab (375 mg/m2). Induction treatment with thymoglobulin and maintenance therapy with tacrolimus, MMF and steroids was administered. Patients were monitored with 3- and 12-month surveillance biopsies.

Results: During the study, 41 patients were included (28 with a negative FC-XM and 13 with a positive FC-XM; 9 for B cells, 2 for T cells and 2 for T and B cells). Main baseline demographic, clinical and immunological characteristics of donors, recipients and transplant-related variables are depicted in the table. Early (11% vs. 46%) and subclinical rejection at 3 and 12 months (table) was significantly more frequent in the FC-XM positive group. Renal function during the first year, patient and death-censored graft survival at 5 years were not different between groups (table). Graft loss was related to chronic ABMR in 3 patients with positive FC-XM and in 1 patient with a negative FC-XM. Patient death was mainly related to COVID-19 pneumonia (n=3) in patients with a negative FC-XM.

Conclusions: Standard desensitization in negative CDC/positive FC-XM HLA incompatible transplants is associated with a high incidence of clinical and subclinical antibody-mediated rejection but offers acceptable clinical results in the mid-term to high-immunological risk recipients.

Variable	FC-XM negative (N=28)	FC-XM positive (N=13)	p-value
Baseline demographic, clinical and immunological characteristics			
Patient age (years)	50±15	41±16	0.044
Patient sex (male/female)	11/17	7/6	0.503
First Transplant / Re-transplantation	10/18	1/12	0.201
cPRA (%)	77±30	97±5	0.050
Donor type (deceased / living)	19/9	10/3	0.719
Donor age (years)	54±15	49±15	0.144
Donor sex (m/f)	20/8	10/3	1.000
Number of repeated HLA MM	0.1±0.4	0.3±0.7	0.385
DSA type (class I / class II / class I+II)	4/19/5	4/7/2	0.503
Number of DSA	1.6±0.8	2.0±0.8	0.165
MFI immunodominant DSA at transplant	4689±4055	9787±6659	0.004
Cumulative dose of thymoglobulin (mg/kg)	4.6±0.6	4.7±0.5	0.902
Pre-Tx apheresis (no/yes)	20/8	8/5	0.074
Post-Tx apheresis (no/yes)	14/14	3/10	0.173
RTX (no / yes)	8/20	0/13	0.040
Main clinical outcomes			
Mean follow up (months)	49±34	73±37	0.047
Early BPAR prior to 3 months (n/y) (%)	25/3 (10.7%)	7/6 (46.1%)	0.018
Time of early BPAR (days)	36±21	41±23	0.769
eGFR 3 months (mL/min/1.73 m2)	58±20	60±21	0.717
Proteinuria 3 months (mg/g)	965±2938	553±780	0.624
MFI immunodominant DSA at 3 months	2132±2780	5696±6683	0.003
Subclinical rejection at 3 months (no/yes) (%)	14/3 (21.4%)	1/5 (83.3%)	0.009
Late BPAR 3 to 12 months (n/y) (%)	25/3 (10.7%)	12/1 (7.6%)	1.000
eGFR 12 months (mL/min/1.73 m2)	55±20	56±22	0.941
Proteinuria 12 months (mg/g)	846±378	444±88	0.455
MFI immunodominant DSA at 12 months	1025±1858	5740±6821	0.003
Subclinical rejection at 12 months (no/yes) (%)	12/4 (25%)	1/8 (88.8%)	0.004
Overall BPAR (clinical & subclinical) at 12 months (n/y) (%)	22/6 (21%)	3/10 (77%)	0.002
Type of BPAR			
• TCMR	1	1	
• ABMR	4	8	
• Mixed	1	1	
CMV disease (n/y)	28/0	13/0	1.000
BK nephropathy (n/y)	27/1	12/1	0.539
Graft loss at last follow up (no/yes)	25/3	9/4	0.181
Death-censored graft survival 5 years	92%	83%	0.423
Patient death at last follow up (no/yes)	24/4	12/1	1.000
Patient survival 5 years	82%	92%	0.411
eGFR at last follow up (ml/min/1.73 m2)	50±17 (n=25)	53±22 (n=9)	0.360
Proteinuria at last follow up (mg/g)	867 ±1342 (n=25)	1031±973 (n=9)	0.451

Abbreviations. cPRA: calculated PRA, DSA: HLA donor-specific antibodies, BPAR: biopsy-prove acute rejection.

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EP_694 DE NOVO DONOR SPECIFIC ANTIBODIES AFTER KIDNEY TRANSPLANTATIONS: LONG-TERM OUTCOMES

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Background: Current literature describes 15 to 30% risk of rejection after kidney transplant, therefore immunosuppressive therapy is still fundamental to avoid it. De novo Donor Specific Antibodies (dnDSA) are one of the principal predictors for the development of an antibody-mediated rejection. The study aims to understand the incidence of dnDSA in kidney transplant patients and correlate it to 5-10 years graft survival, patient's survival, hematic levels of immunosuppressant and donor-recipient HLA mis-match.

Methods: A single center retrospective study which includes 436 patients subjected to kidney transplant from January 2010 to March 2023 by the Transplant Unit of Policlinico ''Tor Vergata'', with a medium follow up of 5 years. DnDSA levels were dosed for each patient using either *FlowPRA* Screening Tests or Class I and II-IgG Luminex Single Antigen Beads (positivity cut-off=MFI >1000). Pre and post-transplant data were collected and compared for each patient, including the presence of HLA mismatches, PRA levels, blood level of immunosuppressive therapy and the development of complications.

Results: dnDSA occurred in 81 patients (18.58%). Rejection was more frequent in patient with dnDSA compared to who did not developed dnDSA (25.93% vs 6.48%, p=0.0001). There was a correlation between the development of dnDSA and graft lost at 5 years (p=0.0109) and at 10 years (p=0.0020). There was no correlation between dnDSA and Tacrolimus blood levels. Patients who received induction therapy were more likely to develop dnDSA (p=0.0001). Moreover patients with dnDSA had higher PRA levels (p=0.0119) and they were more likely to have eplet DR4 (p=0.0095), DR11 (p=0.0310) and DQ5 (p=0.0175).

Conclusions: Patients with dnDSA are particularly exposed to the risk of rejection and of graft failure. Immunological characteristics are one of the principal risk factors for the development of dnDSA, while we did not find any correlation with Tacrolimus blood levels.

EP_695 MEAN FLUORESCE VALIDATION BETWEEN LUMINEX 200 AND 3D. IMPACT IN CUT-OFF VALUES AND DELISTING STRATEGIES

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Background: The Single antigen bead (SAB) is the assay widely used for both screening and identification anti-HLA in the histocompatibility laboratories. The technical differences between the instruments have been previously described. The Luminex 3D allow to expand the number of beads acquired, increasing the ability to better characterize anti-HLA reactions with expanded panel beads. From the quantitative point of view, the MFI levels between 1,000-1,500 is accepted as cut-off value or positive reactions. The aim of the study was to validate and verify the MFI levels obtained in the readouts of anti-HLA antibody test within the cut-off value range accepted

Methods: A total of 30 sera (3 independent runs) LABScreen and 27 sera (in 4 independent runs) for both SAB class-I and calss-II panels (Thermofisher, One Lambda, CA), were acquired in parallel in a Luminex 200 and 3D. To assess the potential skew of MFI values obtained in both instrument Bland-Altman analysis and Spearman correlation test were used.

Results: For screening and SAB, three levels of MFI: <1,000 (low, with 2077 values); 1,000-1,500 (medium, with 313 values) and >1,500 (high, with 184 values) were settled. A linear correlation in low and medium MFI levels was observed (p<0.001). The mean difference Lx200 vs 3D in low values were -3.66 MFI with limits (-127 – 120 MFI), in the medium values group was: 190 MFI with limits (-328 – 707MFI) whereas in high group: 1498 (-1,700 – 4,708 MFI) for SAB class-I panel. The mean difference Lx200 vs 3D in low groups were +2.54 MFI with limits (-57 – 62 MFI), in the medium MFI values group was: 204 MFI with limits (-184 – 592MFI) whereas in high group: 3123 (-4,202 – 10,449 MFI) for SAB class-II panel. Despite the differences found, the concordance of result interpretation for both screening and SAB was 100%.

Conclusions: The SAB assay by Luminex is validated for qualitative measurement of anti-HLA antibodies. Despite the differences found between Luminex instruments in terms of MFI values, a full concordance in of results was found. However, in other procedures where MFI levels is important, as in delisting strategies, the cut off MFI value used should be reassessed when different instruments are used.

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EP_696 DONOR SPECIFIC ANTIBODIES EVOLUTION AFTER CONVERSION FROM TACROLIMUS TO BELATACEPT: REAL-LIFE DATA

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Background: In the field of kidney transplantation immunosuppression, belatacept has been increasingly used over the last decade, due to increased availability and encouraging results. Conversion from tacrolimus to belatacept might be an interesting option to limit humoral alloreactivity. In this study, we investigated the evolution of Human Leukocyte Antigen (HLA) Donor Specific Antibodies (DSA) in patients converted from tacrolimus to belatacept.

Methods: We retrospectively investigated kidney transplant recipients followed at Grenoble University Hospital and converted from tacrolimus to belatacept (Tac-to-Bela), for decreased graft function and calcineurin toxicity, independently of their de novo DSA status. Tac-to-Bela conversion was performed over a 3-months window, together with mycophenolate (500 mg bid) and no steroid. DSA monitoring was performed using a Luminex platform single antigen assay.

Results: Between 2016 and 2023, a total of 278 patients underwent Tac-to-Bela conversion and had available Luminex data. Conversion was performed at a median time of 4.06 years (IQR 2-7.6) post-transplantation. There were 38 graft losses over a median follow-up of 2.72 years, occurring at a median time of 2.41 years (IQR 1.29-4.63). Pre-conversion, the numbers of patients with class 1, class 2 or both classes DSA were 7, 34 and 8, respectively. Post-conversion, these patients' numbers were 7, 35 and 3. Focusing on Mean Fluorescence Intensity (MFI), class I DSAs decreased from a median of 983 (IQR 751-1490) to 874 (IQR 695-1042) (Wilcoxon test p=0.019), and class II DSAs decreased from a median of 2600 (IQR 964-5671) to 1361 (IQR 896-3405) (Wilcoxon test p<0.001). Using a mixed effect model accounting for intra-patient variability, Tac-to-Bela conversion significantly reduced DSAs MFIs (mean reduction -1548.4, p<0.001). There were 5 (1.8%) biopsy proven acute rejection (BPAR) episodes over the first-year post-conversion.

Conclusions: Late Tac-to-Bela conversion allowed to significantly reduce DSAs MFI and was associated with a low incidence of BPAR. The number of DSA targets was however not modified by the Tac-to-Bela conversion.

EP_697 CLINICAL AUDIT OF ACUTE REJECTION OUTCOME AT A SINGLE CENTRE FOLLOWING THE IMPLEMENTATION OF A COLLABORATIVE APPROACH

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Background: Malaysia, with a population of 34 million, has seen an increase in kidney transplantations over the last five years, rising from 3-4 to 8 per million population. The Ministry of Health (MOH) has two laboratories performing transplant workups, including the National Blood Centre (NBC), which started providing transplant lab services in late 2020. However, NBC faces limitations, such as performing only T-cell crossmatches and lacking donor typing during out-of-hours pre-cadaveric transplants, due to budget and expertise constraints. In 2023, NBC collaborated with the Nephrology Department of Hospital Kuala Lumpur (HKL) to monitor transplant outcomes and improve immunology services despite these challenges. In 2024, NBC adopted a more proactive approach to managing laboratory results, offering immunological input to nephrologists based on observed immunological risks and shifts in crossmatch results.

Methods: A retrospective analysis was conducted on 211 kidney transplant patients at HKL between January 2023 and December 2024, including both living and cadaveric donors, to compare graft rejection outcomes in 2023 and 2024.

Results: Biopsy-proven rejection rates decreased from 17.3% in 2023 to 9.9% in 2024. In 2023, rejections were mostly caused by antibody-mediated rejection (ABMR) (42%) and mixed T-cell-mediated rejection (TCMR) and ABMR (26.3%). In 2024, ABMR and TCMR were similar at 30%, and mixed rejections accounted for 20%. Cadaveric transplants represented about one-third of cases, with rejections in 2023 at 22.9%, decreasing to 8.1% in 2024. The use of Basiliximab induction agents decreased from 60% in 2023 to 48.5% in 2024, while thymoglobulin use increased from 48.6% to 70.3% among cadaveric recipients.

Conclusions: The reduction in rejection rates from 2023 to 2024 may be attributed to the collaborative effort by proactive approach in managing laboratory results and changes in immunosuppressive therapy. Further large-scale studies are needed to confirm these findings.

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EP_698 IMPACT OF DONOR/RECIPIENT CYP3A5 POLYMORPHISM MISMATCH ON RENAL GRAFT SURVIVAL

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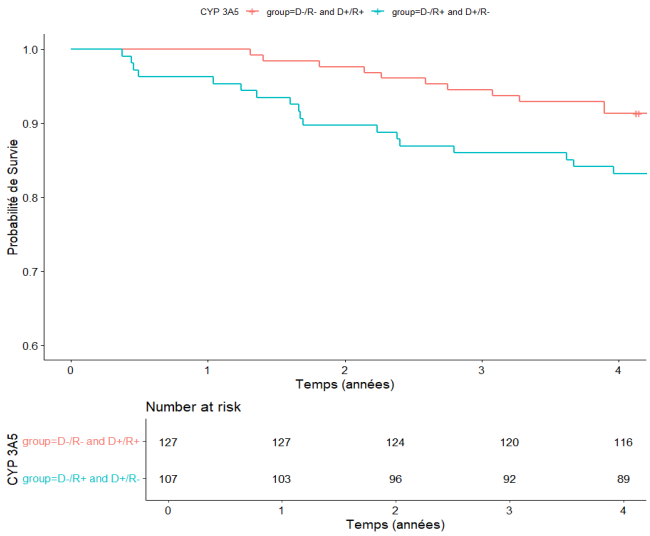
Background: Tacrolimus is the primary immunosuppressant in renal transplantation, with its therapeutic efficacy and infection risk linked to systemic exposure, measured by residual C0 levels. Rapid metabolizers carrying the *1 allele of CYP3A5 (R+) require higher doses of tacrolimus to achieve the same C0 as slow metabolizers (R-), increasing the risk of nephrotoxicity and infections. The impact of donor kidney CYP3A5 status (D+ or D-) on tacrolimus metabolism and the effect of donor-recipient genotype mismatches are not well understood. In Réunion, genetic diversity and grafts from mainland France contribute to frequent mismatches. We hypothesized that mismatched donor-recipient genotypes influence tacrolimus metabolism and graft survival.

Methods: This retrospective study included renal transplant recipients in Réunion (2015-2020). CYP3A5 genotyping was performed on both recipients and donors. The impact of donor CYP3A5 status on tacrolimus exposure (C0, C0/dose) and nephrotoxicity was assessed, along with graft survival in mismatched donor-recipient pairs (D-/R+ and D+/R-).

Results: Among 234 donor-recipient pairs, 151 (64.5%) were R+ (71 D+ and 80 D-) and 83 (35%) were R- (56 D- and 27 D+). A mismatch was found in 127 pairs (55%). No difference in C0 was observed between the groups. Among R+ patients, the C0/dose was significantly lower compared to R- patients. R- patients with D+ donors had a higher C0/dose than those with D- donors at 3 months, with no difference observed at 12 months. At 12 months, interstitial fibrosis and tubular atrophy (IFTA) lesions ≥2 were more frequent in R+ patients (26.6% vs. 11.8%, p = 0.028). At 4 years, 212 patients (90.6%) had a functioning graft. Graft survival was lower in mismatched pairs (83.2% vs. 91.3%, p = 0.048), particularly in D-/R+ recipients (graft loss 5% at 1 year, p = 0.09; 11% at 2 years, p = 0.05).

Conclusions: Donor-recipient mismatches are common in Réunion and increase early graft loss risk. Considering both donor and recipient genotypes is crucial for optimizing tacrolimus therapy in renal transplantation.



EP_699 KIDNEY TRANSPLANTATION IN SENSITIZED PATIENTS: RISK STRATIFICATION AND IMPACT OF DONOR SPECIFIC ANTIBODIES

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Background: The presence of donor-specific antibodies (DSA) represents a significant barrier to kidney transplantation due to the risk of acute rejection. In Algeria, 35 % of dialysis patients have DSA, prolonging their dialysis time. Crossmatch tests using three techniques—complement-dependent cytotoxicity (CDC), flow cytometry(FCM), and single antigen(SA)—are employed to stratify immunological risk.

Methods: We have analyzed sensitized patients from the university hospitals of Bab El Oued and Batna since 2021, assessing their sensitizing levels through crossmatch techniques to facilitate their access to transplantation. After transplantation, DSA monitoring and protocol biopsies were performed.

Results: Ninety sensitized patients were studied; 50% underwent complete immunological stratification using all three techniques. Among them, only 2% had positive crossmatches across all methods, 14 % had positif cross match in CMF and SA, 60 % had positif cross match only in SA and 24% had a positif historic test in SA. Kidney transplantation was performed without desensitization for patients with negative crossmatches in LCT and CMF but positive in SA. Most of patients showed DSA disappearance after transplantation with no observed rejections. Patients with a positive crossmatch in SA and CMF, but negative in LCT, are candidates for desensitization prior to transplant. This approach aims to achieve a negative crossmatch in CMF, thereby reducing the risk of rejection and improving transplant compatibility.

Conclusions: Preformed DSA alone does not preclude transplantation. Combining the three crossmatch techniques is crucial for identifying eligible patients for desensitization and minimizing rejection risks while avoiding potential infections. This stratification also has significant financial implications.

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EP_700 DRUG INDUCED THROMBOTIC MICROANGIOPATHY POST COMBINED HEART AND LUNG TRANSPLANTATION IN A YOUNG FEMALE

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Background: This case report details the occurrence of Drug-Induced Thrombotic Microangiopathy (DITMA) in a young female patient following a combined heart and lung transplant. Studies have shown that TMA can occur in up to 30% of patients receiving solid organ transplants who are on CNI therapy.

Case Report: A 19-year-old female with a history of untreated VSD in childhood leading to Eisenmenger syndrome presented with symptoms of severe pulmonary hypertension and cyanosis. Due to the progressive nature of her condition, she was evaluated for a combined heart and lung transplant and subsequently, she underwent successfully CHLTx in March 2022. 28 months postTx on 3rd July her tac levels were 11 and on 11th July her Hemoglobin dropped to 5.21 gm/dl, leading to evaluation for cause of severe anaemia, including reticulocyte 12.06%Thrombocytopenia 81000 Elevated lactate dehydrogenase 1036 Presence of schistocytes in peripheral blood smear - 5%, Hypertension, Proteinuria, AKI serum creatinine 4.22 mg/dl. She also developed symptoms consistent with TMA. Other causes of TMA like complement-mediated, toxin-mediated and TTP were ruled out. A renal biopsy was done which showed atrophic tubules with fibrin thrombin in the glomerulus. The TMA-eliciting drug was identified as tacrolimus (a calcineurin inhibitor, CNI) and removed from the patient's immunosuppression regimen and replaced with belatacept. Additionally, the patient underwent multiple sessions of plasmapheresis and was administered IVIG along with steroids. These treatments aimed to reduce the severity of TMA and manage the underlying causes.

Results:

Conclusions: This case highlights the importance of vigilant monitoring for TMA in patients undergoing thoracic organ transplantation requiring higher doses of CNI. In its most severe form, DITMA can have a high mortality rate, ranging from 60% to 90%. Identifying and removing the TMA-eliciting drug, along with plasmapheresis and IVIG, can be effective in managing, leading to favorable outcomes.

EP_701 KINETICS OF PCT, CRP, IL-6 AND PRESEPSIN IN CARDIAC TRANSPLANT PATIENTS UNDERGOING THYMOGLOBULIN INDUCTION THERAPY

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Background: This study aimed to evaluate the effectiveness of inflammatory biomarkers, specifically C-reactive protein (CRP), procalcitonin (PCT), presepsin, and interleukin-6 (IL-6), in detecting early postoperative infections in heart transplant patients. Given the challenge of differentiating infection from systemic inflammatory responses (SIRS) in immunosuppressed individuals, this research focused on finding more reliable markers for timely clinical interventions.

Methods: The study was a retrospective analysis conducted at the Cardiac Surgery of Policlinico of Bari. 135 heart transplant patients, treated between January 2022 and September 2024, were divided into two groups: 35 patients with postoperative infections and 100 without. Inflammatory markers were measured preoperatively and during specific postoperative intervals.

Results: A proportion of infected patients were in Intermacs class 1-2 (92.3% vs. 46.0%, $p = 0.004$), indicating a more severe preoperative condition. Additionally, patients with acute onset heart failure were more likely to develop infections (38.5% vs. 4.0%, $p = 0.003$). Preoperative CRP levels were significantly higher in infected patients (133 mg/L vs. 4 mg/L, $p < 0.001$), suggesting that elevated CRP might be predictive of postoperative complications. No significant differences were observed between the groups in terms of intraoperative variables. CRP levels were significantly higher in infected patients only on day 10 postoperatively ($p < 0.001$), with no significant differences observed on earlier days. Presepsin levels were significantly higher in infected patients as early as day 1 postoperatively and remained elevated through day 10 ($p < 0.001$ for all time points).IL-6 levels showed significant differences between the groups starting from day 3 postoperatively and continuing through day 10 ($p < 0.001$). PCT levels did not show significant differences between infected and non-infected patients until day 10 postoperatively ($p = 0.001$).

Conclusions: Presepsin and IL-6 are more reliable than CRP and PCT for the early detection of infections in heart transplant patients. Their early elevation post-surgery suggests these markers could improve timely diagnosis and intervention, potentially enhancing patient outcomes in the critical postoperative period.

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EP_702 TOPICAL TACROLIMUS IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION - A SYSTEMATIC REVIEW

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Background: Topical tacrolimus (TT) is a potential immunosuppression agent though clinical data is only in pre-clinical studies for skin containing vascularized composite allotransplants (VCA). We performed a systematic review aimed to evaluate the use of TT in VCA to better understand current clinical use for managing acute rejection and reducing reliance on systemic immunosuppression (SI).

Methods: PRISMA guidelines using PubMed, Scopus, and Web of Science review was performed using the following search terms: “local” or “topical” + “administration” or “delivery” + “tacrolimus” or “Protopic” + “VCA”. Studies included patients who underwent VCA and received TT. Study details, demographics, VCA type, HLA and blood type matching, induction and SI, complications, rejection (AR) episodes, and treatment plans were collected.

Results: 11 articles (15 unique patients) met inclusion criteria in 4 face (26.7%), 6 single hand (40.0%), and 5 bilateral hand (33.3%) recipients. Mean age was 39.9 ± 16.5 years. Overall, 32 AR episodes were reported, 22 (68.8%) were treated with TT. The only strength of TT reported was 0.1%. AR Banff grades ranged from I to III, with no significant associations between Banff grade and use of TT. Duration of TT use was 16.8 ± 20.9 days. There was no significant difference in resolution of rejection when using TT (p = 0.883). 2 AR episodes (6.25%) resolved with TT therapy alone and no adjustment to SI. A higher percentage of AR episodes required increased systemic tac when not using TT (25% vs 18.8%; p = 0.210). A higher percentage of AR episodes also required increased mycophenolate dosages without using TT (28.1% vs 12.5%; p = 0.036). Oral steroids were administered more frequently in cases where TT was used (p = 0.044).

Conclusion: Current clinical use of TT during acute rejection includes the 0.1% TT formulation most commonly for 16 days. 2 cases of AR were treated with TT alone. TT may permit less intense escalation in SI for treatment of acute rejection. As clinical data continues to grow, further research is essential to establish benefits TT in VCA.

EP_703 RELIABILITY AND CLINICAL VALUE OF DONOR-DERIVED CELL-FREE DNA FOR THE DETECTION OF HEART ALLOGRAFT REJECTION

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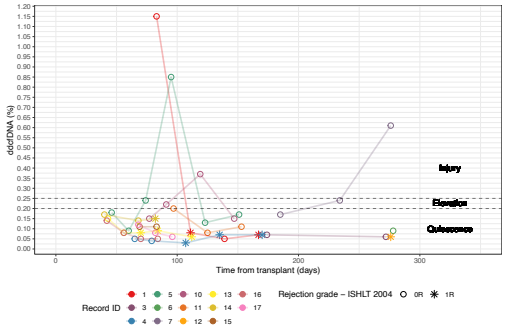
Background: Heart transplantation (HT) is the definitive treatment for end-stage heart failure. Despite its overall success, acute allograft rejection remains a major cause of long-term allograft failure and mortality. Endomyocardial biopsy (EMB) remains the gold standard for monitoring acute rejection in heart transplant recipients. However, EMB is limited by invasiveness, costs, high interobserver variability in the anatomopathological interpretation, and low sensitivity to detect early rejection. A reliable non-invasive early marker of donor organ injury could enhance outcomes for patients experiencing allograft rejection. Donor-derived cell-free DNA (dd-cfDNA), collected non-invasively from recipients’ blood, may serve as an early marker of rejection, enabling earlier and potentially more effective treatment.

Methods: 14 patients were followed during the post-transplant period: 46 blood samples were collected prior to perform routinary EMB and dd-cfDNA levels were measured. EMB samples were graded according to the 2004 ISHLT classification. Acute cellular rejection (ACR) was defined as a histologic grading ≥ 2. For the dd-cfDNA analysis, the threshold value for discriminating positive tests from negative ones was set at 0.25%. The dd-cfDNA test output were compared with results of the EMB histology, and sensibility and specifity were calculated.

Results: the mean dd-cfDNA value was 0,10 % [IQR range: 0,07 – 0,16]. No ACR was found in the 46 of the endomyocardial biopsies performed. Sensitivity was undefined, while specifity was equal to 91%.

Conclusions: In our study population there were no true positive cases. As a result, the sensitivity of the biomarker could not be adequately assessed, limiting our ability to draw definitive conclusions about its performance. Given these limitations, additional data is needed to better understand the dd-cfDNA’s reliability and diagnostic value. Further studies with larger and more diverse samples are essential to comprehensively evaluate the test’s effectiveness and ensure accurate interpretation of results.



		Overall, n=14
Sex (%)	Female	4 (28.6)
	Male	10 (71.4)
Weight (mean (SD))		71.36 (15.73)
Height (mean (SD))		174.21 (7.00)
Ethnicity (%)	White	14 (100.0)
Age (mean (SD))		49.29 (7.94)
BSA (mean (SD))		1.85 (0.22)
BMI (mean (SD))		23.33 (3.84)
HF diagnosis (%)	Nonischemic cardiomyopathy	0 (0.0)
	Ischemic cardiomyopathy	2 (14.3)
	Hypertrophic cardiomyopathy	2 (14.3)
	Restrictive cardiomyopathy	0 (0.0)
	Myocarditis	0 (0.0)
	Other	10 (71.4)
Retransplant(%)	Yes	0 (0.0)
	No	14 (100.0)
MCS (%)	None	7 (63.6)
	Left ventricular assist device	1 (9.1)
	Temporary circulatory support	3 (27.3)
	Total artificial heart	0 (0.0)
Donor age (mean (SD))		39.64 (13.98)
Donor sex (%)	Male	11 (78.6)
	Female	3 (21.4)
Donor Weight (mean (SD))		78.00 (9.47)
Donor Height (mean (SD))		177.11 (6.33)
Donor BMI (mean (SD))		24.86 (2.78)
Donor cause of death (%)	Anoxia	1 (7.7)
	Cerebrovascular accident	4 (30.8)
	Head trauma	5 (38.5)
	Other	3 (23.1)
Chest trauma (%)	Yes	0 (0.0)
	No	13 (100.0)
Donor ethnicity (%)	White	13 (92.9)
	Hispanic	1 (7.1)
CMV (%)	D−/R−,	1 (7.7)
	D−/R+,	1 (7.7)
	D+/R−,	6 (46.2)
	D+/R+	5 (38.5)

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EP_704 IMPACT OF SWITCHING AMONG BRANDED AND GENERIC POSACONAZOLE ON TACROLIMUS LEVELS IN CARDIOTHORACIC TRANSPLANT

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Background: Generic drug preparations offer significant cost benefits. For many medicines, switching between preparations can be done with little or no monitoring. However, Posaconazole (POSA) in cardiothoracic transplant recipients presents an interesting challenge due to drug-drug interactions with concomitant immunosuppressants such as Tacrolimus (TAC), which has a narrow therapeutic window requiring careful supervision and therapeutic monitoring.

Methods: Between December 2021 - September 2022 cardiothoracic transplant patients stable on longterm POSA and TAC were contacted and consented to undergo formulation switch from Noxafil® to Cipla generic. Each patient was thoroughly counselled, and a coordinated plan was agreed for repeat bloods and levels. POSA and TAC levels were measured bi-weekly post-switch for 2-3 weeks; levels were reviewed by transplant pharmacists and doses optimised where appropriate. POSA and TAC levels pre-switch were collated and compared. In 2024, the same method was utilised for the formulation switch, Cipla to ABDI Farma Non-Cipla.

Results: A total of 15 patients were successfully switched from Noxafil® to Cipla in 2021-2022 (Figure 1a), and 13 patients switched from Cipla to ABDI Farma Non-Cipla in 2024 (Figure 1b). Mean TAC and POSA levels were calculated to present data. Therapeutic POSA levels (>1mg/L) were maintained in both switches. Supratherapeutic TAC levels were measured in 20% (n=3) and 15% (n=2) in respective switches; subtherapeutic TAC levels were measured in 7% (n=1) patients switched from Noxafil® to Cipla; 69% (n=9) of patients switched from Cipla to ABDI Farma Non-Cipla required TAC dose changes to maintain levels within target range.

Conclusions: The use of generic POSA formulations provide cost-effective alternatives in the management of fungal infection in cardiothoracic transplant recipients. Whilst switching may affect POSA levels, therapeutic levels were preserved, however, the subsequent impact on TAC levels often required dose adjustments. Hence, consideration on maintaining patients on single generic POSA formulations is advisable, with switches requiring supervision and close TAC therapeutic drug monitoring.

Table 1: Demographics for patients included in Noxafil to Cipla switch and Cipla to Abdi Farma Non-Cipla switch

Demographics	Noxafil to Cipla	Cipla to ABDI Farma
Type of Transplant (Heart:Lung)	2:13	1:12
Gender, Male (n [%])	8 [53]	11[85]
Weight kg, Median [IQR]	58 [13.5]	72 [18]
Time post Transpant months, Median [IQR]	72 [94]	96 [89]

Figure 1a: Posaconazole and Tacrolimus (Prograf) levels for patients switched from Noxafil to Cipla generic

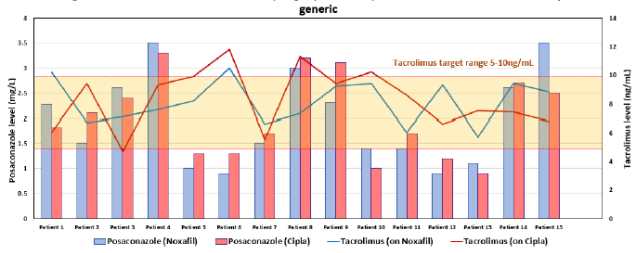
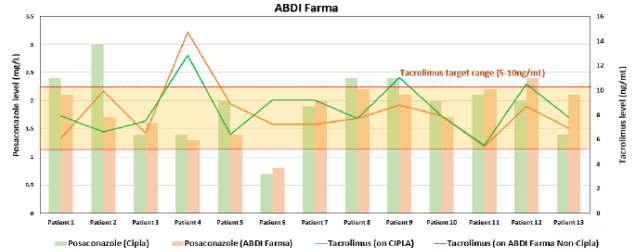


Figure 1b: Posaconazole and Tacrolimus (Prograf) levels for patients switched from Cipla to ABDI Farma



EP_705 BASILIXIMAB INDUCTION VS. A DUAL ATG-BASILIXIMAB APPROACH IN FIRST LIVING NON SENSITIZED RTRS WITH REDUCED HLA MATCHING

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Background: Individualizing induction therapy based on immunological risk is crucial for optimizing outcomes in kidney transplantation.

Methods: A retrospective analysis included 157 first living non-sensitized renal transplant recipients (RTRs). Within this cohort, 96 individuals exhibited low HLA matching (5-6 HLA mismatches). The low HLA match subgroup was categorized into 52 RTRs receiving basiliximab alone and 44 recipients treated with a combined single ATG dose of 1.5 mg/kg and basiliximab. The primary endpoint was early acute cellular rejection (ACR) within 6 months post-transplant while secondary outcomes encompassed infection rates, renal allograft function, length of stay (LOS), and overall admissions.

Results: Transitioning from basiliximab to combined ATG-basiliximab reduced early ACR (from 23.1% to 9.1%, p=0.067). Age was a predictor for rejection, and subgroup analysis showed consistent rejection reduction across age groups. No significant differences were observed in admission for transplant LOS or in peri-operative complications, nor in infections rate including BK and CMV viremia, allograft function and number of admissions up to 6 months post-transplant.

Conclusions: In non-sensitized first living RTRs with reduced HLA matching, a dual single ATG-basiliximab induction approach significantly reduced early ACR without compromising safety.

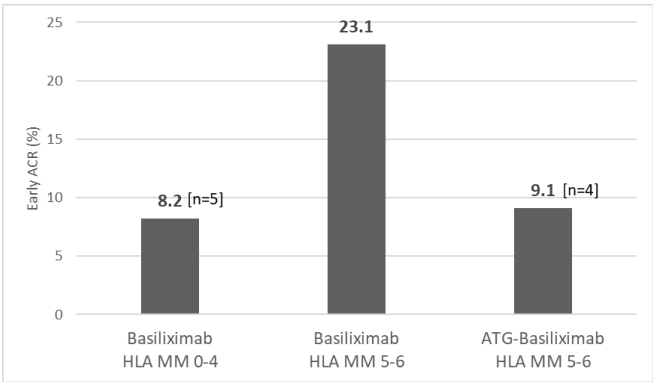

Figure: Early ACR rates in non-sensitized RTRs with first kidney transplants, contrasting high HLA match RTRs with Basiliximab and low HLA matches RTRs with Basiliximab and ATG-Basiliximab induction.

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Transplant immunology & immunosuppression

EP_706 ATOPIC STATUS IS ASSOCIATED WITH KIDNEY TRANSPLANTED RECIPIENTS' OUTCOMES

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Background: Atopy is a complex genetic and environmental predisposition associated with an increased risk of type 2 inflammatory diseases such as allergic asthma, allergic rhinoconjunctivitis, atopic dermatitis and food allergy. It has recently been shown that type 2 inflammation has a detrimental effect on autoimmune disease (lupus, chronic urticaria) and solid organ transplantation. Our team has also demonstrated a link between blood eosinophilia and the increased risk of kidney transplant rejection. The aim id the study was to assess the impact of atopy on the occurrence of an immune event and/or the loss of a kidney transplant over time

Methods: We took advantage of a single-centre prospective cohort of kidney transplant patients with follow-up censoring in October 2022, combined with a bio-collection with serum samples at transplantation (M0), at 12 months (M12) and at the time of an immune event (Mi). Atopy was defined by the presence of a positive Phadiatop® at each follow-up point in the patients' sera. We used time-dependent survival models adjusted for confounding factors to assess the association between atopy and the occurrence of an immune event and/or transplant loss.

Results: 516 transplants were included in the study with a median follow-up of 6 years, with 74 rejections, 61 de novo anti-HLA immunisations and 40 deaths with functional transplants. The prevalence of atopy in the kidney transplant population was 28%, with no significant difference in pre-transplant demographics between atopic and non-atopic patients, apart from a male sex ratio. Atopy emerged as a risk factor for the occurrence of rejection (HR = 1.7; CI95 1.08-2.67), de novo anti-HLA IgG immunisation (HR = 1.33; CI95 1.03-2.13) and graft loss (HR = 1.63; CI95 1.02-2.82).

Conclusions: In a cohort of over 500 patients, atopy, and more specifically IgE sensitisation to pneumallergens, is associated with an increased risk of rejection, de novo anti-HLA immunisation and transplant loss. The immunological mechanisms at work remain to be studied.

EP_707 ANTIBODY MEDIATED REJECTION IN THE MAIN FACTOR FOR THE GRAFT LOST

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Background: Protocol kidney biopsy is an usual practice in many transplant centers in the world. They are performed in a specific time after the surgery, from 2 weeks until 12 months. Despite the possibility of complications, protocol biopsies are performed to detect pathohistological changes in renal graft tissue before clinical symptoms appear.

Methods: Protocol biopsies were performed in 50 patients (42 from living and 8 from deceased donors), 12 months after the surgey. The all patients had an induction with ATG and triple drug treatment with CNI, mycophenolat mofetil and steroids. The renal function was stable with no any clinical sign of acute and chronic rejection and mean creatinin was 114.25 μmol/L. Renal tissue lesions were reviewed for evidence of chronic and acute changes, as well borderline rejection (BL), interstitial fibrosis and/or tubular atrophy (IF/TA) and vasculopathy by the same pathologist. The histological findings were classified using the Banff 2013 system.

Results: Ten years graft and patients survival were 70 %, and 86%, respectively. Seven deaths (14%) were noticed, three due to the complication from COVID 19 with functional grafts, one due to the malignancy of pancreas and two from cardio-vascular event. Eight pts returned on HD (16%). The distribution of findings according to the Banff classification was: fifteen biopsies (30%) were normal, 4 (8%) are a pure form of anibody mediated rejection (ABMR) and T-cell mediated rejection (TCMR), 4 (8%) in BL + TCMR , 5 (10%) IF/TA , and 5 (10%) in the category "others". But 17(34%) histological findings were "mixed" in which predominantly has participated ABMR: 7(14%) ABMR + IF/TA, 2 (4%) ABMR + BL, 5 (10%) ABMR+BL+ IF/TA and 3 (6%) BL+ IF/TA (6%). Analyzing the results it has been noted that 9 patients with ABMR (pure or part of the "mixed") have lost their grafts in comparison with two grafts lost with other histological features (16% vs 4%, p<0.001). Therefore, ABMR alone or in "mixed" form is responsible for the graft loss in the 10 year of follow up.

Conclusions: ABMR is a most serious finding in the kidney histology. Every features of ABMR, not only as a pure form but also in the mixed forms of rejections must have a full attention. Protocol biopsies, in experienced hands are safe and valuable means of detecting subclinical disease and can modify the therapy.

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Transplant immunology & immunosuppression

EP_708 IMPACT OF INNATE REJECTION ON HEART TRANSPLANTATION: INITIAL FINDINGS ON MISSING SELF INDUCED MICROVASCULAR REJECTION

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Background: Missing self (MS), the inability of donor endothelial cells to deliver HLA I-mediated signals to inhibitory killer cell Ig-like receptors (KIRs) on recipient natural killer (NK) cells, can lead to microvascular inflammation (MVI) in kidney transplantation, independently of donor-specific anti-HLA antibodies (DSA). The clinical significance of MS in heart transplantation is unknown. We aimed to evaluate the role of innate rejection mediated by NK cells in heart transplanted (HT) patients.

Methods: All adult (>18y) HT recipients in our Centre between 2014-2022 with available DNA samples from donor and recipient were included. High-resolution HLA typing was conducted for HLA-A, -B, and -DR in our Immunology Lab; HLA-C and recipient KIR genotype was assessed at an external institution. We analyzed the prevalence of MS in the overall cohort and in pts with histological AMR, and the impact of MS on major adverse cardiovascular events (MACE) in patients with AMR, expressed as 5 years survival rate.

Results: We included 113 recipients (age at HT 51±11 y, 27% female, 26.5% with preformed DSA); 44 pts (38.9%) had MS. Mean follow up was 4±2 years with an incidence of MACE of 83.1±3.9%. 27 pts (23.9%) developed pAMR, at a median distance of 2 months (1 week-3 years) from HT and only 4 of them developed de-novo DSA. MS was detected in 44 (38.9%) recipients, with no difference between pts with or without pAMR (22.7% vs. 24.6%; P=0.8). The 10 recipients with MS and pAMR showed a higher estimated incidence of MACE as compared with those with pAMR and no MS. (50.0±15.8% vs. 88.2±7.8%, p=0.06).

Conclusions: The preliminary results of our pilot study suggest the role of the missing self pathway of NK activation also in HT recipients, in line with what observed in kidney transplantation. By suggesting the potential prognostic value of this pathway in patients with pAMR, our results highlight the role ofNK cells in DSA negative-AMR, thus suggesting a potential new therapeutic target.

EP_709 COMPLEMENT SYSTEM EVALUATION IN BLOOD GROUP INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION

Diana Rodríguez Espinosa[1], Julia Martínez[2], Anna Manonelles[3], Elena Guillén[4], Carlos Couceiro[5], Josep Maria Cruzado[6], Miquel Lozano[7], Nuria Esforzado[8], Ignacio Revuelta[9], Fritz Diekmann[10], Ana Belan Larque[11], Marta Palomo[12], Maribel Díaz-Ricart[13], Miquel Blasco Pelicano[12]

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Background: Blood group incompatible living donor kidney transplantation (ABO-iLKT) may allow expanding the living donor pool up to 10-30%, although a high-risk rejection exists due to anti-blood group antibodies (isoagglutinins) presence and infection rates. Complement dysregulation and endothelial damage are key factors in regulating the immune-mediated injury. We aimed to study complement system and endothelium involvement as potential main elements and to explore *in vitro* the effect of a complement inhibitory drug (eculizumab) and an endothelial protective agent (defibrotide) as potential therapeutic strategies in ABOi_LKT.

Methods: Terminal complement dysregulation was studied through the analysis of C5b-9 deposition on endothelial cells culture in ABO-iLKT patients (n=10) classified by isoagglutinin levels (high (escriure dilució que hem agafat en cada interval), intermediate and low). Plasma samples were collected at pre-transplantation (T1) and 48h post-transplantation (T2). T2 condition was also incubated *in vitro* with eculizumab or defibrotide. Area percentage of C5b-9 deposition was expressed in fold increase with respect to T1 of each group of patients.

Results: The group with high isoagglutinin levels showed a significant increase of C5b-9 deposition at T2 and it was significantly reduced in presence of eculizumab and defibrotide (fold increase: 1.6, 0.2 and 0.7, $p<0.05$, respectively). In the group of intermediate isoagglutinin levels, a slight increment in T2 was observed (fold increase: 1.1), and T2 incubated with both drugs showed a significant reduction (fold increase: 0.4 and 0.4, $p<0.05$, respectively). The group of low isoagglutinin levels exhibited less C5b-9 deposition in T2 and in presence of eculizumab and defibrotide (fold increase: 0.6, 0.2 $p<0.05$, and 0.6, respectively).

Conclusions: An increment of C5b-9 deposition after transplantation in ABO-iLKT patients with elevated isogglutinin levels indicates an overactivation of terminal complement system. This overactivation could be related with higher risk of rejection when isoagglutinin levels are increased. The role of terminal complement blockersand defibrotide can be considered as therapeutic targets in ABO-iLKT context.

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EP_710 EFFECTIVE MANAGEMENT OF RECURRENT IGA NEPHROPATHY WITH BUDESONIDE THERAPY

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Background: IgA nephropathy (IgAN) is one of the most prevalent glomerulonephritides, characterized by mesangial deposition of galactose-deficient IgA1 (Gd-IgA1), hematuria, proteinuria, and progression to end-stage kidney disease (ESRD). Kidney transplantation is the definitive treatment for ESRD secondary to IgAN, but recurrence rates range from 9% to 61%, posing a significant challenge. Advances in immunosuppressive therapies have shown potential in reducing recurrence risk and preserving allograft function, but long-term outcomes remain uncertain.

Case Presentation: A 29-year-old female with CKD stage 4 (eGFR 17 mL/min/1.73 m²) due to IgAN underwent pre-emptive living donor kidney transplantation in 2016. Post-transplant, she was started on tacrolimus, methylprednisolone, and mycophenolate mofetil (MMF). In 2020, MMF was replaced with azathioprine due to pregnancy, and renal function remained stable. Postpartum, MMF was resumed but was later discontinued by the patient without consultation. Approximately one year later, proteinuria and kidney function decline occurred. A biopsy confirmed recurrent IgAN (Oxford: M3 E0 S1 T1 C1) (Fig1-10). Treatment with Budesonide (3 mg three times daily), reintroduction of MMF, and continuation of tacrolimus and an angiotensin receptor blocker (ARB) led to marked improvement in kidney function and complete resolution of proteinuria. A follow-up biopsy after 9 months showed significant histological improvement (Oxford: M1 E0 S1 T0 C0) with no crescents or tubulitis(Fig. 1-10).

Results: Adherence to immunosuppressive therapy is crucial in preventing IgAN recurrence. MMF not only suppresses T and B lymphocytes but also reduces mesangial proliferation, a key driver of IgAN pathology. Budesonide effectively reducing proteinuria with fewer systemic side effects compared to traditional corticosteroids. The combination of MMF and Budesonide resulted in significant clinical and histological improvements in this case, emphasizing their synergistic effects.

Conclusions: This case highlights the importance of adherence to immunosuppressive therapy in preventing IgAN recurrence. MMF and Budesonide therapy offer effective options for managing recurrent IgAN, warranting further studies to optimize treatment strategies.

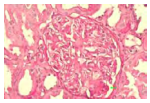


Fig. 1. Mesangial Hypercellularity

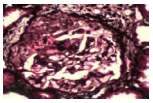


Fig. 2. Segmental fibrocellular crescents

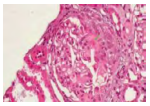


Fig. 3. Fibrinoid necrosis and crescent

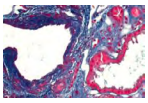


Fig. 5. Arterial fibrosis

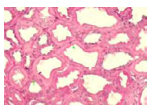


Fig. 5. Tabulates

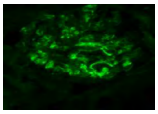


Fig. 6. IgA staining 4+

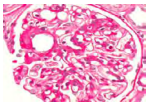


Fig. 7. Mesangial hypercellularity

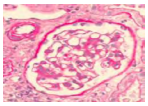
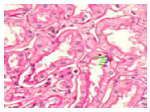


Fig.8. Mesangial hypercellularity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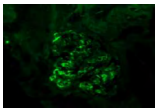
Fig.10. IgA staining 3+

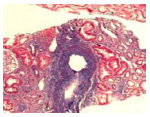
Fig.11. Arterial Fibrosis

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