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AGAINST THE CLOCK! GRAFT IMPLANTATION TIME MATTERS IN MARGINAL GRAFTS PREDICTING INFERIOR OUTCOMES

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Background: Marginal livers are increasingly utilized in the era of organ shortage. Our objective was to determine whether prolonged warm ischemic time during liver transplantation (LT) affects outcome of marginal organs.

Methods/Materials: 714 consecutive cadaveric primary LT between 2009 and 2014 at our institution were stratified according to low risk (DRI<1.8) [LR] and high risk (DRI>1.8) [HR] grafts as well as liver implantation time (IT) <45 and >45 minutes. Allograft and remote organ outcome was retrospectively analyzed.

Results: LR livers were significantly more often allocated to sicker patients (UKELD 56 vs 55, $p = 0.004$; MELD 17 vs 15, $p < 0.0001$) while HCC patients were likely to receive HR grafts (22% vs 16%, $p = 0.0681$). Both LR and HR grafts had comparable cold ischemic time, donor hepatectomy time and steatosis. Short- and long-term allograft and kidney function as well as overall non-malignant survival (patient 3y 91% vs 87%, graft 3y 87% vs 81%; $p = 0.1382$ and $p = 0.1236$) were similar for recipients of LR and HR grafts. IT>45 min subgroups had prolongation of each and every step in implantation (IVC anastomosis, PV anastomosis, arterialization time). Short-term but not long-term allograft and renal functions were significantly worse in recipients with long anastomotic (>45 min) time irrespective of organ risk stratification. Best overall patient (3y 90%) and graft (3y 86%) survival was achieved for fastest implantation of LR grafts (LR + IT<45 min). LR + IT>45 min and HR + IT<45 min achieved comparable survival outcome though inferior to the former. Most importantly, the worst transplant outcome occurred in prolonged implantation of high risk organs (HR + IT>45 min, patient 3y 73% and graft 3y 67%) ($p = 0.0026$ and 0.0073). This significance remained true when de novo/recurrent malignancy was excluded as cause of death.

Conclusion: Implantation time is critical for outcomes after LT and should be considered in graft-recipient matching as well as surgeons training.

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RESULTS FROM DONATION AFTER CIRCULATORY DEATH LIVER TRANSPLANT IN RECIPIENTS OLDER THAN 60 YEARS

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Background: Due to organ scarcity, donation after circulatory death (DCD) has become an acceptable alternative to donation after brain death (DBD). The decreased recovery capability associated with aging might compromise the ability of older patients to tolerate an aggression such as a liver transplant (LT), especially when combined with the deleterious effects of a suboptimal graft (DCD).

Methods/Materials: 713 LT have been performed between January 2006 and December 2015. 73 (10.2%) were from DCD (Maastricht II). We compare results in patients younger and older than 60 years (<60 vs. >60) after DCD LT.

Results: Average MELD scores were 15.3 + 4.6 (<60) and 13.7 + 4.9 (>60) ($p = 0.16$). Hepatocellular carcinoma was more frequent in the >60 group (63.9% vs.; 37.8%; $p = 0.26$). There were no significant differences found in ischemic times, pump flow rates or HCV infection rate (56.8% <60; 58.3% >60; NS). Patient survival for younger patients following DCD LT at 1, 3 and 5 years (91.9%; 85.7% and 85.7%) was significantly higher than that of the >60 group (72.2%; 57.9%; 54.9%; $p = 0.004$). Graft survival rates at 1, 3 and 5 years were 89.5%; 84.5% and 81.2% (<60) vs. 75%; 65.2% and 58.6% for the >60 group ($p = 0.00$). The most frequent cause of death among >60 was HCV recurrence (21.4%), while the <60 group showed a similar incidence of HCV recurrence, intraabdominal infection, primary non-function (PNF) and cerebrovascular accident (25%). There were no differences in graft PNF rates. 21% of patients in the <60 group underwent retransplantation, a significantly higher number than those in the >60 group (5.6%; $p = 0.04$). Ischemic cholangiopathy showed a similar incidence in both groups (33.3%).

Conclusion: Although liver transplantation for older patients has been shown to have acceptable if somewhat poorer results; when studying DCD LT both patient and graft survival decrease significantly in recipients over 60 years. These results might discourage the use of DCD grafts in this particular group.

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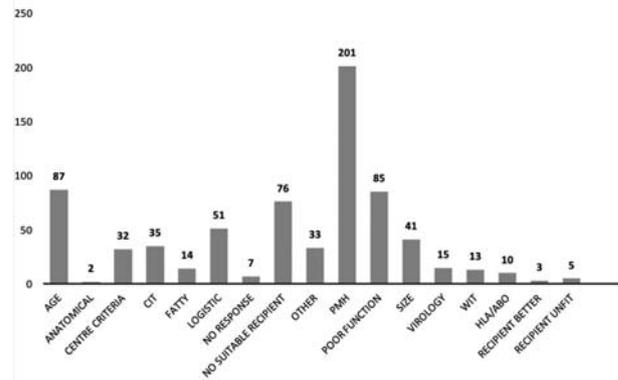
LIVER TRANSPLANT OUTCOMES FROM DECLINED LIVER ALLOGRAFTS: IS IT WORTH THE RISK?

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Background: Marginal liver grafts supplement the organ pool but there lacks a clear definition on marginality. In an era where nearly 200grafts/year are non-utilised upon offering, we aimed to analyse whether previous refusal by other transplant centres had any impact on transplant outcomes.

Methods: Organ offer of all adult liver transplants (LT) performed in December 2010–2015 were analysed. Data on previous refusal was captured from NHSBT EOS database. The reasons for refusal by other centres were categorised in to 03 groups; *quality, logistics and other reasons not specified*. Transplant outcomes were then analysed.

Results: Total of 206/909 (22.6%) LT were performed from grafts refused by at least one other centre. Majority [141(68.4%)] were DBD grafts. Donor liver dysfunction existed in 79 (38%) meanwhile 80(39%) donors had out-of-hospital cardiac arrest. Reasons for refusal are illustrated in Fig 1. The average refusal rate was 3.5/organ (4.2 vs. 3.2; DCD vs. DBD respectively). 44% (DBD) and 65% (DCD) grafts were refused by >4 transplant centres ($p = 0.006$). When refused by >1 centre, there was no agreement on reason for refusal in 65% of cases. By category, reasons for refusal were *organ quality* ($n = 120$; 58%), *logistics* ($n = 67$; 33%) and *other reasons* ($n = 19$; 9%). Main indication for transplantation was ALD ($n = 55$ patients; 26.7%). Median UKELD was 53 (32–68). 90-day mortality due to graft failure was 8/206 (3.8%); 6 were from quality refusal group, but none were DCD's. There was no difference in the 3 refusal groups in terms of post-operative complications ($p = 0.6$), rejection ($p = 0.9$) and in graft survival ($p = 0.9$).



Conclusion: The mortality rate due to graft failure is within acceptable rates, and these data highlight diverse opinions on graft assessment and acceptability amongst transplant surgeons. Most of the centres refused grafts claiming quality issues, this was proven to be correct only in minority of cases.

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SURGICAL FACTORS AND NOT DONOR TYPE PER SE ARE RISK FACTORS FOR ACUTE KIDNEY INJURY AFTER LIVER TRANSPLANTATION

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Background: Because Liver Transplantation (LT) using DCD has been shown to be risk factor for Acute Kidney Injury (AKI), we reviewed results at our center.

Patients and Methods: AKI was defined as decrease >50% eGFR (CKD-EPI) within 48 h postreperfusion (RIFLE). 106 first LT-only [63 DBD (59%) & 43 DCD (41%)] without pre-existing renal dysfunction (eGFR>60 ml/min/1.73 m², no renal replacement therapy) were performed from 2012 to 2016. Incidence/risk factors for AKI were assessed. Data: mean (IQR).

Results: Incidence of AKI was 33% (35/106). AKI-patients were more hospitalized before LT [9/16 (56%) vs 26/89 (29%), $p < 0.01$], with higher labMELD [16 (10–23) vs 12 (8–16), $p = 0.01$]. Donor type [11/43 DCD (25%) vs 24/63 DBD (39%), $p = 0.16$], donor hepatectomy time [38 min (26–50) vs 35 (25–42), $p = 0.37$], cold ischemic time [6 h (4.1–7.6) vs 5.1 (3.4–6.4), $p = 0.21$], time for anastomosis [44 min (35–49) vs 42 (38–48), $p = 0.53$], postreperfusion

syndrome [19/46 (42%) vs 27/46 (58%), $p = 0.07$] were similar between AKI & non-AKI groups. AKI was more frequent if lungs were procured first in the donor [23/48 (48%) vs 11/56 (19%), $p < 0.01$]. Recipient surgery was longer in the AKI group [5.2 h (3.9–6.3) vs 4.3 (3.4–4.8), $p < 0.01$]. AKI was more frequent if platelets were transfused during LT [19/42 (56%) vs 15/59 (44%), $p = 0.03$]. Blood volume administrated from the cell saver was larger in the AKI-patients [834 ml (300–750) vs 408 (0–550), $p = 0.03$]. AKI-patients have a higher peak AST [1235 U/L (310–1858) vs 812 (429–978), $p = 0.04$]. Haemoglobin [8.8 g/dl (7.4–9.9) vs 10 (8.5–11.7)] & platelets [69x103 (50 x 103–87 x 103) vs 89 x 103 (50 x 103–118 x 103)] at day 1 postreperfusion were significantly lower if AKI occurred. After multivariable analysis, thoracic procurement before liver [OR 5.75 (1.76–18.77), $p = 0.004$] & recipient surgery duration [OR 1.64 (1.15–2.32), $p = 0.006$] were only risk factors for AKI.

Conclusion: Rapid donor/recipient surgery and not donor type are key factors to prevent AKI-post-LT.

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THE USE OF OCTOGENARIAN LIVER GRAFTS: THE LESSONS LEARNED AFTER MORE THAN 200 TRANSPLANTS

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Background: Elderly grafts may provide favorable long-term results after liver transplantation (LT). However, they are associated with an increased risk for ischemic-type biliary lesions (ITBL) and hepatitis C virus (HCV) recurrence after LT compared to standard donor grafts.

Materials/methods: This was a retrospective, case-control analysis on use of elderly liver grafts (≥ 80 years) for LT at a single institution. From 01/2001 thru 09/2016, 1753 LT were performed at our Institution. After removing UNOS 1A, ABO-incompatible LT and donors and/or recipients < 18 years ($n = 125$), 217 LT with deceased donors ≥ 80 years vs. 299 LT with donors 18–49 years were selected. A Propensity Score Match (caliper 0.2) was done for the risk of post-LT death using as covariates: model for end-stage liver disease (MELD), HCC, HCV, cold (CIT) and warm ischemia time (WIT). Finally, a total of 217 recipients of grafts ≥ 80 years (Group A) were compared with 182 recipients of standard donor grafts (18–49 years, Group B). The primary end-point was graft and patient survival rate. The secondary end-point was assessment of ITBL and HCV-related graft loss.

Results: Graft survival was 86.7%, 80.3%, and 72.9% at 1, 3 and 5 years in Group A vs. 95.2%, 88.1%, and 85.8% in Group B ($p = 0.002$, log rank). In Group A vs. Group B, HCV-related graft loss was 11/217 (5.1%) vs. 5/182 (2.7%) ($p = 0.3$); incidence of ITBL was 25/217 (11.5%) vs. 3/182 (1.6%) ($p < 0.0001$), and incidence of ITBL-related graft loss was 6/217 (2.8%) vs. 0 (0%) ($p = 0.03$).

Conclusions: Although associated with a 5-year graft survival rate of 73%, liver donor grafts ≥ 80 years have a 2-fold increased odds for HCV-related graft failure and a 3-fold increased odds for ITBL, respectively. Novel antiviral treatments and continued management of ITBL will likely contribute to further

improvements of these results, reducing the gap between elderly and standard donor grafts.

Clinical Liver Allocation

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THE UK-DCD-RISK-SCORE - A NEW PROPOSAL TO DEFINE FUTILITY IN DCD LIVER TRANSPLANTATION

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Background: Primary-non-function (PNF) and ischemic cholangiopathy (IC) are the most feared complications leading to graft loss in DCD liver transplantation. With this analysis we aimed to design a new score on risk assessment in liver transplantation donated after circulatory death (DCD) based on donor, graft and recipient parameters.

Methods: Using the United Kingdom (UK) national DCD database, a risk analysis was performed in adult recipients of DCD liver grafts in UK between 2000 and 2015 ($n = 1153$). A new risk score was calculated (UK-DCD-Risk-Score) on the basis of regression analysis, and validated using the UNOS (United Network for Organ Sharing) database ($n = 1617$) and our own DCD liver transplant database ($n = 315$). Finally, the new score was compared with two other available prediction systems, the DCD risk scores from UCLA and Kings-College-Hospital, London.

Results: Seven strongest predictors of DCD graft survival were identified: functional donor warm ischemia, cold ischemia, recipient MELD, recipient age, donor age, previous OLT, and donor body-mass-index (BMI). A combination of these risk factors (UK-DCD-Risk-Model) stratified best recipients in terms of graft survival in the entire UK-DCD-database (Figure 1) as well as in the UNOS and in our own DCD population. Importantly, the UK-DCD-Risk-score significantly predicted graft loss due to primary-non-function or ischemic cholangiopathy. The new prediction model was superior to other available systems, as demonstrated by a C statistic of 0.79 compared to 0.71 and 0.65, respectively.

Conclusions: The UK-DCD-Risk-Score is a reliable tool to detect high risk and futile combinations of donor and recipient factors in DCD liver transplantation. It is simple to use and offers a great potential to better decide which DCD graft should be rejected or may benefit from functional assessment and further optimization by machine perfusion.

Figure 1: The UK-DCD-Risk-Score

