

## 023 KIDNEY

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## ECHOGRAPHY AND CARDIOVASCULAR RISK: WHAT'S THE RELATIONSHIP IN THE RENAL TRANSPLANT RECIPIENT?

Miguel Goncalves<sup>1</sup>, Micaela Neto<sup>2</sup>, Pedro Vieira<sup>1</sup>, Luis Resende<sup>1</sup>, Susana Gomes<sup>2</sup>, Jose Duraes<sup>1</sup>, Nuno Rosa<sup>1</sup>, Jose Alves Teixeira<sup>1</sup>, Gil Silva<sup>1</sup>

<sup>1</sup>Nephrology, Hospital Central do Funchal; <sup>2</sup>Cardiology, Hospital Central do Funchal

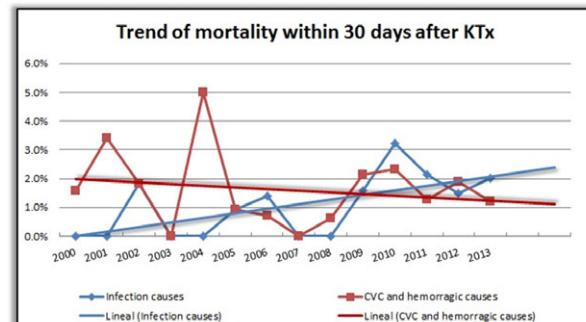
**Introduction:** Cardiovascular (CV) disease is the major cause of death among renal transplant recipients (RTR). Unlike end stage renal disease, it is unknown whether echocardiographic abnormalities are useful to identify RTR with high cardiovascular risk and risk of death.

**Objectives:** To characterize the metabolic profile, risk of major adverse cardiac events (MACE) and death in a population of RTR. Characterize cardiac function and morphology. Determine which echocardiographic abnormalities predict the risk of MACE and death.

**Methods:** Retrospective review of 107 RTR in follow-up at our institution, with a functioning and stable graft for longer than 12 months and an echocardiography performed in the last year. Risk of MACE and death using a CV risk calculator specific for RTR and echocardiographic parameters were analysed.

**Results:** Among 107 patients followed at our institution (57.9% males,  $50.4 \pm 13.9$  years old), 7-years risk for MACE was  $>10\%$  in 30.9% of patients and 7-years risk for death  $>10\%$  in 56.1%. Left ventricular hypertrophy (LVH) was present in 55.1%, diastolic dysfunction in 39.3%, dilated left atrium (LA) in 53.3%, high pulmonary artery systolic pressure (PASP) in 29.0%, valvular calcifications in 22.4% and moderate to severe mitral regurgitation (MR) in 3.7%. Mean Ejection fraction was  $68.36 \pm 6.87\%$ . Univariate analysis showed an increased risk of MACE in patients with LVH [6.9% vs. 14.5% ( $p = 0.032$ )] and valvular calcifications [OR 3.499 (1.115–10.982,  $p = 0.001$ )] and elevated PASP [OR 7.954 (2.412–26.238,  $p = 0.001$ )]. Risk for death  $>10\%$  in multivariate analysis had an independent association with diastolic dysfunction [OR 3.909 (1.261–12.115,  $p = 0.018$ )] and with elevated PASP [OR 4.319 (1.201–15.535,  $p = 0.025$ )].

**Conclusion:** Echocardiographic abnormalities identify RTR at increased risk of MACE and death. Valvular calcifications and elevated PASP are significant predictors of MACE whereas Diastolic dysfunction and elevated PASP are significant predictors of death.



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## TRANSPLANTING THOSE WAITING THE LONGEST

Aisling Courtney  
Belfast City Hospital

**Introduction:** Transplantation is the optimal form of renal replacement therapy for suitable patients with end stage renal disease. Long term outcomes improve when the time spent on dialysis is minimised, and individuals with prolonged waiting times can become unfit for transplantation. Those with pre-existing HLA antibodies often wait a disproportionately long time.

**Methods:** All patients in Northern Ireland (NI) active on the UK deceased donor renal transplant waiting list on 1 Jan 2013 were ranked according to waiting time. All waiting longer than 5 years were identified and those that were very highly sensitised reviewed. Antibodies that were currently not detectable or present at low titres were removed from the unacceptable antigens listed with NHS Blood and Transplant.

**Results:** There were 30 patients waiting longer than 5 years. The mean waiting time for transplantation was 8 years 5 months, (range 5 years, 1 month–21 years, 3 months) and mean panel reactive antibody sensitisation was 71%, (range 0–100%); 16 (53%) were very highly sensitised (>95% antibodies). The registered unacceptable antigens were altered in 10 (33%). Within 24 months, there were 30 transplants in 28 (93%) patients, one is now unfit for transplantation and one is currently suspended. 8 (27%) were from living donors. Alemtuzumab was given in 9 transplants and Rituximab in 2. The 12 month graft survival was 87%. Of the 4 grafts that failed: 2 had primary non-function due to donor characteristics, 1 failed due to non-recovery of recurrent episodes of AKI after 5 months, and 1 failed at 10 months due to recurrent anti-GBM disease. Two of these patients have been transplanted successfully. 12 month patient survival was 100%. In NI there are currently only 2 patients waiting longer than 5 years.

**Conclusion:** A proactive approach to highly sensitised patients can enhance the opportunities for transplant and should be considered for those with high HLA antibody levels before they have a prolonged duration on dialysis.

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## MORTALITY WITHIN THE FIRST MONTH AFTER KIDNEY TRANSPLANTATION – AN OBSERVATIONAL, COHORT STUDY

Izquierdo Valeria Andrade, Francine Bc Lemos, Ligia C. Pierotti, Maristela P. Freire, Neto Elias David, Flávio De Paula, William C. Nahas  
Hospital das Clínicas da Faculdade de Medicina da USP

Infection was the principal cause of death after the first year of kidney transplantation (KTx), but the cause of early mortality, was not well described in the actually.

We performed a retrospective, unicentric analysis of mortality in the first 30 days after KTx during January 2000 to May 2014. Older patients than 18 years who received single or combined organ transplantation (COT) from deceased or living donors were included. Data were obtained from medical records and necropsy evaluation. Variables analyzed were age, sex, race, ERSD etiologies, time in dialysis, BMI, living or deceased donor, induction therapy and COT. Statistical analysis was done by Mann-Whitney test, Chi-sq test and Step-wise logistic regression.

In this period, a total of 2390 patients were transplanted in our center. Mortality within the first 30 days after KTx occurred in 87 patients (3.5%), majority of them, were male (60%), white (59%), mean age was  $53 \pm 12$  years and a mean time of dialysis were 52 months. The principal ERSD etiologies were DM (29%), Hypertension (24%) and Glomerulonephritis (22%) and high percentage was transplanted with deceased donors (92%). The most frequent cause of death was infection with 31 cases (36%) followed by cardiovascular (23%), hemorrhagic (21%) and other causes (20%). We observed a raising trend increase of death by infection causes (DIC) during the period analyzed Chi-sq 9.09,  $p = 0.003$ , as opposed to cardiovascular and hemorrhagic causes, that's tended to reduce. Patients with DIC more frequently dead after the 7th day of hospitalization (73%  $p = 0.006$ ), were more often COT patients (58%  $p = 0.06$ ) and had less dialysis time before KTx ( $P = 0.07$ ), when compared with other causes of death. In multivariate analysis the differences between DIC and others death causes were COT  $p = 0.02$  OR 4.63 and death after 7th day of KTx  $p = 0.002$  OR 0.18.

Death by infectious diseases took a longer time to be set as a principal cause of mortality and were associated to more complexity surgery, as COT.

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## COMPARABLE TRANSPLANT OUTCOMES BETWEEN DBD AND DCD KIDNEY GRAFTS UP TO 5 YEARS POST-TRANSPLANT: SINGLE CENTRE EXPERIENCE

Hieu Le Dinh, Olivier Detry, Arnaud Deroover, Nicolas Meurisse, Jean Paul Squiflet, Michel Meurisse, Jean Marie Krzesinski, Catherine Bonvoisin, Josée Monard, Laurent Weekers  
University Hospital of Liege

**Introduction:** This study aimed to determine the most recent results of kidney transplantation (KT) from donation after brain death (DBD) and circulatory death (DCD). Primary endpoints were graft and patient survival, and graft function. Acute rejection and post-operative complications were assessed as secondary endpoints.

**Patient and Methods:** This retrospective mono-center review consisted of 226 DBD- and 104 DCD-KT between 2008 and 2014.

**Results:** Graft survival was comparable between two groups (95.1 vs. 91.1% at 1 year, 92.8 vs. 91.1% at 3 years and 89.2 vs. 91.1% at 5 years). 46% and 40% of graft loss were attributed to patient death with a functioning graft and rejection. Patient survival was comparable between 2 groups (97.8 vs. 95.1% at 1 year, 94.1 vs. 91.2% at 3 years, and 89.6 vs. 82.3% at 5 years). Etiology of patient death included cardiac arrest (16.7%), infection (16.7%), cancer (13.3%), and unknown cause (46.7%). Delayed graft function occurred in 14.6% of DBD- and 30.8% of DCD-KT ( $p = 0.001$ ). Primary non function was encountered in 2.6% DBD- and 4.8% DCD-KT ( $p = ns$ ). Graft function was worse in DCD than DBD up to 3 months post-transplant ( $p = 0.034$ ), however, no difference existed afterwards. Biopsy-proven acute rejection was found in 12.8% and 13.5% of DBD- and DCD-KT during an average 3 months post-transplant ( $p = ns$ ). This rate was 7.1% vs. 8.9% on surveillance biopsy performed between 3 and 6 months post-transplant ( $p = ns$ ). Post-operative

complication rate was comparable between 2 groups, concerning patient death, reoperation, transfusion, perirenal hematoma, macroscopic hematuria, urinary obstruction, wound problem, and infection. Nevertheless, contamination of preservation solution occurred more commonly in DCD than DBD (0.4% vs. 3.8%,  $p = 0.036$ ).

**Conclusions:** Despite worse early graft function, DCD-KT was not inferior to that originating from DBD up to 5 years post-transplant, therefore deserves to be used.

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#### EARLY PLASMA-CREATININE CHANGES PREDICT ONE-YEAR GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

Nicoline Valentina Krogstrup<sup>1</sup>, Bo Martin Bibby<sup>2</sup>, Camilla Aulbjaerg<sup>3</sup>, Bente Jespersen<sup>3</sup>, Henrik Birk<sup>4</sup>

<sup>1</sup>Institute of Clinical Medicine, Aarhus University; <sup>2</sup>Department of Biostatistics, Aarhus University; <sup>3</sup>Department of Renal Medicine, Aarhus University Hospital; <sup>4</sup>Department of Biomedicine, Aarhus University

**Background:** Validated surrogate endpoints for long term kidney graft function are needed in clinical kidney transplantation trials. This study evaluates the association between initial kidney graft recovery and graft function 1 year posttransplant.

**Methods:** A single centre, observational, cohort study including 100 kidney transplants followed 1 year at Aarhus University Hospital. All p-creatinine (p-cr) values at time of transplantation and 30 days posttransplant were registered along with relevant patient characteristics. In case of temporary dialysis posttransplant, p-cr was gathered until 30 days after the last dialysis. One-year p-cr and graft outcome were registered and in case of death or graft loss, patients were excluded from the analysis ( $n = 4$ ). The observed, time dependent changes in p-cr were modulated for each, individual patient by an exponential, logistic, or a linear model, and the time to a 50% decrease in p-cr was estimated. eGFR 1 year posttransplant was calculated using the simplified Modification of Diet in Renal Disease (MDRD) formula. A multiple linear regression model was used to analyse the association between the time to a 50% drop in p-cr and eGFR after 1 year.

**Results:** The time to a 50% drop in p-cr correlated negatively with eGFR at 1 year ( $n = 96$ ,  $r = -0.375$ , beta =  $-0.112$ ,  $p = 0.0002$ ). The correlation persisted when corrected for donor type, recipient age, gender, initial p-creatinine level, and cold ischemia time ( $n = 90$ ,  $p = 0.018$ ). A positive

correlation between the time to a 50% drop in p-cr and the total days of hospitalisation 30 and 365 days posttransplant, as well as the number of performed ultrasounds and kidney biopsies 90 days posttransplant, was also found.

**Conclusion:** Early graft function differences may be important for long-term outcome. Time to a 50% drop in p-cr might be used as a surrogate marker in renal transplant studies, and includes both patients with or without temporary posttransplant dialysis need.

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#### PATIENT-RELATED FACTORS AFFECTING THE INITIAL TACROLIMUS TROUGH LEVEL AFTER KIDNEY TRANSPLANTATION

Aureliusz Kolonko, Jerzy Chudek, Andrzej Wiecek  
Medical University of Silesia

**Background:** In general, the recommended tacrolimus (Tc) initial dose is calculated per kg of body weight and fixed at 0.1 mg/kg/dose BID. Some observations suggest that in selected groups of patients such dosing may result in Tc toxicity in the early posttransplant period. The aim of our study was to find the factors increasing an initial Tc trough level.

**Methods:** We performed the retrospective analysis (2000–2013) of 468 consecutive kidney transplant recipients initially treated with immunosuppressive regimen containing tacrolimus BID, mycophenolate, and steroids. The analysis included the first assessment of Tc trough levels and patient-related factors that might affect the pharmacokinetics of Tc.

**Results:** The mean initial Tc dose was  $0.095 \pm 0.002$  mg/kg BID. The analysis revealed that recipient's age, BMI, and pretransplant diabetes, but not gender or residual diuresis are explaining the variability of initial Tc trough level. Recipients  $>70$  years old had 46% greater Tc initial trough levels than those 30 years or less ( $16.5 \pm 7.1$  vs.  $11.3 \pm 6.3$  ng/ml,  $p < 0.001$ ). Higher concentrations were also observed in diabetics ( $16.6 \pm 8.0$  ng/ml) than nondiabetics ( $13.5 \pm 6.7$  ng/ml), and in overweight ( $15.3 \pm 7.0$  ng/ml) and obese ( $16.9 \pm 5.9$  ng/ml) than normal weight ( $13.0 \pm 6.7$  ng/ml) and underweight ( $10.9 \pm 7.2$  ng/ml) patients. The association between Tc trough level and BMI was independent from the influence of age. Additionally, there was no influence of early graft function on Tc trough level.

**Conclusion:** The reduction of recommended fixed Tc initial dose should be considered in the elderly, diabetics, and overweight/obese kidney transplant recipients.