

Congress Abstracts 2018

14th to 16th March, Brighton Centre, Brighton

Medawar medal presentations 10:45 Thursday 15th March – The Auditorium

M01

Chronic renal histological changes at implantation and subsequent deceased donor kidney transplant outcomes: a single-centre analysis

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Introduction: Chronic histological changes within kidneys at transplantation may predict graft outcomes, suggesting that preimplantation biopsies can inform organ utilisation decisions. Analyses from Cambridge have shown an inconsistent association between the Remuzzi score on wedge biopsy and graft survival. We sought to determine whether histological changes at transplantation were predictive of graft outcomes.

Methods: We performed a retrospective analysis of adult single deceased donor kidney-only transplants between 2005-2015. Core biopsies (16G) taken after re-perfusion were examined by consultant renal histopathologists, and a Karpinski (K) score was assigned (0-12). Donor and recipient variables were collected; 1-, 3-, and 5-year graft function (eGFR – 4 variable MDRD) and death-censored graft survival (DCGS) were recorded. Recipients were grouped by K-score threshold (group A <4; group B 4+; group C <5; group D 5+). Multivariate and linear regression analyses were performed to determine independent risk factors for DCGS and 1-year eGFR, respectively.

Results: 587 recipients had biopsies performed. 401 (68%) were adequate for K-scoring (DBD/DCD 267/134; median (IQR) donor age 51 (41-59) years; K-score 4 (2-5)). There were no differences in DCGS between groups A and B (p=0.17) or C and D (p=0.14), but 1-year eGFR trended downwards with increasing K-score (A 52.7 (40.0-67.0); B 42.0 (30.8-54.9) – p<0.01) (C 51.7 (37.8-65.0); D 40.5 (29.9-51.5) – p<0.01). Cold ischaemia time (CIT) was the only independent predictor of reduced DCGS (p=0.01). K-score, CIT and UKKDRI were independently associated with lower 1-year eGFR (p<0.01; p=0.03; p<0.01, respectively).

Conclusion: This large risk-adjusted analysis does not demonstrate a clear association between K score thresholds and deceased donor kidney transplant DCGS, though increasing K score was associated with lower 1-year eGFR. Variations between single-centre studies might be explained by differences in biopsy and scoring techniques, or histological interpretation.

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Accurate viability assessment and cryopreservation of pancreatic islets requires prolonged incubation with viability dyes and cryoprotectants for more than 12 hours

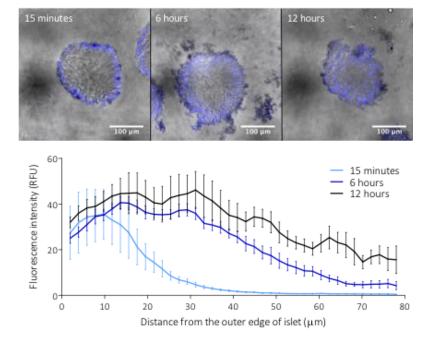
<u>Nikola Dolezalova</u>^{1,2}, Till Moreth³, Kevin O'Holleran⁴, Martin Lenz⁴, Krishnaa Mahbubani¹, John Casey⁵, Francesco Pampaloni³, Nigel Slater², Kourosh Saeb-Parsy¹

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Introduction: Determining diffusion kinetics of dyes and cryoprotectants into the core of pancreatic islets is essential for accurate viability assessment and improved cryopreservation. We examined the impact of incubation time on solute diffusion into islets as a prelude to improving islet viability assessment and cryopreservation.

Methods: Mouse pancreatic islets were incubated with Hoechst 33342 nuclear dye for 15min, 6h or 12h and cryosectioned for confocal microscopy. Live islets were stained with Hoechst 33342, fluorescein diacetate and propidium iodide for up to 24h and imaged using confocal, two-photon and light-sheet microscopy. To examine the impact of cryoprotectant incubation time on post-thaw viability, human islets were cryopreserved after 2h or 24h incubation with cryoprotectant trehalose.

Results: Viability staining and imaging of islets by confocal microscopy revealed that short incubation periods used in current viability staining protocols only assess surface cells, with minimal staining of the core seen by two-photon and light-sheet microscopy. Dye gradient towards the core was present even after 24h of incubation. Sectioning confirmed that fluorescence intensity equilibrated only to a depth of ~10 μ m by 15min and continued to increase at the core beyond 12h:fluorescence intensity was 1.35±0.20, 21.40±3.00 and 34.38±4.21 RFUs at depth of ~45 μ m after 15min, 6h and 12h of incubation respectively, demonstrating ongoing dye diffusion into the core (p<0.0001). Incubation of human islets with trehalose for 24h vs. 2h significantly enhanced post-thaw viability (22.2±9.3% vs. 3.4±3.2%, p=0.036).



Discussion: Results suggest that solute diffusion into islet tissue can take up to 24h. Current viability assessment and cryopreservation protocols, fail to target the core of pancreatic islets and do not accurately assess whole-islet viability. Incubation times with viability dyes and cryoprotectants should be prolonged to ensure exposure of cells in the core of islets to the minimal effective concentration.

The likelihood of re-transplantation in patients undergoing allograft nephrectomy

<u>Gaetano Lucisano</u>¹, Paul Brookes², Eva Santos-Nunez², Nicola Firmin², Nicola Gunby², Sevda Hassan¹, Alexander Gueret-Wardle¹, Michelle Willicombe¹, David Taube¹

Introduction: Transplant nephrectomy (NX) is a known cause of allosensitisation after graft failure. As yet, there is no consensus for the management of the patient with a failed graft returning to dialysis with respect to NX and the potential impact of NX on the likelihood of re-transplantation has not been hitherto investigated.

Methods: Patients were divided into two groups according to whether they underwent NX after transplant failure (NX+, n=61) or not (NX-, n=48). Sera were assessed for HLA-A/B/Cw/DR/DQ at the time of NX/transplant failure and after 3, 6, 12 and 24 months using the single antigen Luminex assay. Matchability analysis estimates the relative ease (high score) or difficulty (low score) a patient may have in finding a good HLA matched donor taking into account blood group, HLA type and unacceptable class I and II HLA antigens. Transplant matchability was calculated using the tool provided by the Organ Donation and Transplantation UK.

Results: Matchability analysis did not differ at the time of NX/failure and 3 months, although we found a significant difference in the matchability score starting from the 6-month time point (Figure 1), which resulted in a significantly higher prevalence of patients with "difficult" match in the NX+ group compared to NX-, persisting up to 24 months later.

Discussion: NX leads to significant long-term allosensitization and this negatively impacts on the likelihood of receiving a second transplant. NX after allograft failure should only be undertaken if clinically indicated.

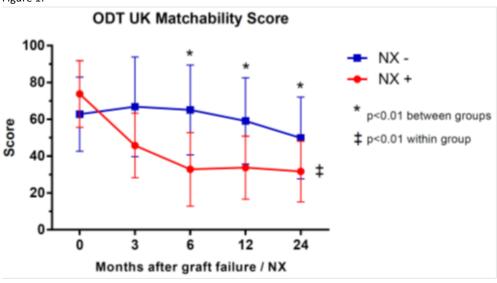


Figure 1:

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Shared HLA specificities between the blood and transplant donor increases the risk of de novo DSA development following transfusion in transplant recipients

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Introduction: Blood transfusions post-transplant have been shown to be associated with the development of de novo DSA and inferior allograft outcomes. The mechanisms behind this phenomenon are not understood.

Methods: We performed HLA typing on 244 blood donors of transfusions received by 86 renal transplant recipients. Sequential screening of a de novo alloimmune response against the blood (transfusion specific antibody, TSA) and transplant donor (DSA) was performed and analysed.

Results: TSAs developed against 150/244 (61.5%) blood donors. 80/150 (53.3%) were TSAs alone, whilst 70/150 (46.7%) were TSAs in conjunction with DSA. 86/150 (57.3%) TSAs were HLA class I, 35/150 (23.3%) class II and 29/150 (19.3%) class II-II. TSA+DSA- patients were more likely to have class I HLA Abs compared with TSA+DSA+ patients, HR:4.66 (2.0-10.9), p<0.01. There was no difference in the overall ABDR mismatch between the blood donor and recipient in the TSA+ and TSA-groups. However, mismatching between the blood donor and recipient at HLA-B and HLA-DQ was higher in TSA+ compared with TSA- patients, p=0.02 and 0.014 respectively. Importantly, the ABDR HLA match between the blood and transplant donor was greater in the TSA+DSA+ compared with TSA+DSA- patients, p<0.0001. There was no difference in the baseline demographics between the TSA+ and TSA- recipients. However, allograft outcomes were inferior in the TSA+ compared with the TSA- group, with an increased risk of graft failure (p=0.007) and AMR (p<0.001).

Discussion: This study provides important novel evidence for the benefit of HLA selected blood in transplant patients requiring transfusion. An alloimmune response against the blood donor is common despite immunosuppression. Shared HLA specificities on the blood and transplant donor may provide a greater antigenic stimulus for antibody development and should be avoided.

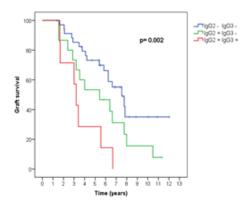
Class II anti-HLA IgG2 and IgG3 DSAs predict poorer outcomes in chronic antibody mediated rejection of renal allografts

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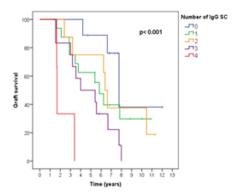
Introduction: Whilst the development of IgG3 and C1q binding de novo [dn] HLA DSAs are associated with a poor outcome in acute antibody mediated rejection, relatively little is known about the role of IgG HLA subclasses in chronic antibody mediated rejection [cAMR]. In this study we describe the significance of dn HLA IgG DSAs and their subclasses in cAMR.

Methods: 1667 CDC/FCXM negative renal transplant recipients receiving a steroid sparing, tacrolimus based regimen with monoclonal antibody induction were studied. Sera from patients were routinely screened for IgG DSA post-transplant at months 1, 3, 6, 12 and yearly or at times of allograft dysfunction. 90 patients with cAMR [diagnosed according to the Banff 2015 criteria] were studied. Patients with a positive IgG DSA went on to have IgG subclass testing.

Results: Graft survival was significantly worse [p=0.015] in the 57/90 patients with DSA+ cAMR compared with the 33/90 DSA-cAMR patients. Graft survival in patients with DSA+ cAMR was significantly worse in the presence of a class II DSA (p=0.021) and the presence of class II IgG subclass 2 and/or 3 was particularly associated with significantly inferior graft survival (p=0.002).



The cumulative total number of subclasses present worsened graft survival with a full house of IgG1-4 subclasses having the poorest graft survival (p<0.001).



Discussion: This study shows that the presence of class II IgG DSAs in cAMR is particularly detrimental to graft survival and also highlights the significance of IgG2, IgG3 and cumulative subclasses in predicting poor outcomes. Characterisation of IgG DSAs in cAMR may help to predict outcome and target patients for particular therapeutic strategies.

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Highly specific RIPK1 inhibition is beneficial in murine ischemia reperfusion injury.

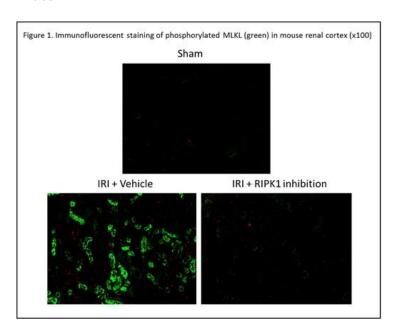
Kevin Gallagher¹, Allison Beal², John Bertin², Lorna Marson¹, Stephen Wigmore¹, Jeremy Hughes¹, James Ross¹, Ewen Harrison¹

Introduction: RIPK1 is a key driver of necroptosis. A non-specific RIPK1 inhibitor (Nec-1) is beneficial in murine ischemia reperfusion injury (IRI). It is not known whether Nec-1 effect is due to RIPK1 inhibition, whether it has direct effects on renal tubules or whether tubular epithelial cells (TECs) undergo necroptosis in IRI. We aimed to determine if a novel, specific RIPK1 inhibitor (GSK963a) is beneficial in murine IRI and to determine if TECs undergo necroptosis during IRI in-vivo.

Methods: Mice were given GSK963a or vehicle either 15 minutes before, or 15 minutes after 18 minutes of bilateral renal vascular clamp followed by 24 hours of reperfusion. Outputs included: Serum urea and creatinine; acute tubular necrosis (ATN) scoring, TUNEL staining and immunofluorescent (IF) staining of phosphorylated mixed lineage kinase like domain protein (pMLKL) (downstream of RIPK1, end effector of necroptosis).

Results: GSK963a given 15 minutes before reperfusion significantly reduced: mean (95% CI) serum creatinine (umol/L) 24 hours after reperfusion (Sham: 15.5 (7.7-23.4), Vehicle: 167 (139-194) vs GSK963a 97.4 (74.0-120.8) p=0.006 N=8-10); median (25th,75th) tubular necrosis score (Sham: 0/4 (0-0.75), Vehicle: 3/4 (2-3) vs GSK963a 1/4 (1-1.75) p=0.008) and mean number of TUNEL positive nuclei per field per kidney (Sham: 0.9 (0.4-1.4), Vehicle: 162 (75-250) vs GSK963a: 67.3 (12.4-122.2) p=0.03 N=6). Results were similar when drug was given 15 minutes after reperfusion. Phosphorylated MLKL was detected extensively in injured tubules at 24 hours, but not in sham, with significant reduction in pMLKL in RIPK1 inhibited animals (mean pixel intensity per field per kidney for pMLKL sham: 0.07 (0.004-0.13), Vehicle: 7.19 (4.11-10.26), GSK963a: 0.94 (0.07-1.81) N=4) p=<0.001) Figure 1.

Conclusion: IRI in mice is associated with extensive tubular MLKL phosphorylation suggesting necroptosis is occurring. MLKL phosphorylation and biochemical/histological evidence of kidney injury are significantly reduced by highly specific RIPK1 inhibition.



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Cardiovascular mortality following simultaneous pancreas and kidney transplantation: an analysis of the United Kingdom transplant registry

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Introduction: Patients with advanced type 1 diabetes and end stage renal failure are at increased risk of cardiovascular disease (CVD) mortality compared to the general population. Simultaneous pancreas and kidney transplantation (SPKT) offers survival benefit, but CVD mortality remains a concern. This study assessed the relationship between pre-transplant recipient variables and CVD mortality post-transplantation.

Methods: All patients with type 1 diabetes receiving SPKT nationally between 2001-2015 were included (n=1699). Pretransplant variables were related to CVD mortality using Cox regression. Cardiovascular mortality included all cardiac and cerebrovascular mortality events.

Results: Total mortality was 13.9% (n=237), 31.2% (74/237) of which were attributable to CVD. Patients experiencing fatal CVD were older (43 [interquartile range (IQR): 39-51] vs. 41 [IQR: 35-47], p=0.008) and were more likely to have a history of pretransplant cardiovascular events (20% vs. 6%, p<0.001) and amputations (12% vs. 5%, p=0.01). Each year increase in age conferred a 6% increase in CVD mortality risk (hazard ratio (HR): 1.06 95% confidence interval (CI): 1.03-1.10, p=0.001). In an age-adjusted model, patients with a history of a pre-transplant CVD event had 3-fold higher risk of CVD mortality (HR (95% CI): 3.6 (1.9-6.7), p<0.001); pre-transplant amputation conferred a 2-fold higher risk (HR (95% CI): 2.6 (1.2-5.5), p=0.014), and being unemployed conferred a 30% higher risk (HR (95% CI): 1.3 (1.006-1.8), p=0.046).

Discussion: A history of pre-transplant CVD events, amputations (a surrogate of peripheral vascular disease), and unemployed status (a surrogate for disease severity and social factors), are associated with increased risk of post-transplant CVD mortality after adjusting for age at transplantation. These factors should be considered alongside traditional risk assessment to facilitate identification of patients who may benefit from CVD pre-habilitation prior to SPKT. Studies of the prevalence of modifiable CVD risk factors before and after transplantation are called for.

Succinate accumulation accounts for greater transplant reperfusion injury induced by warm compared to cold ischaemia in mouse, pig and man

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Introduction: Recent murine evidence suggests mitochondrial succinate accumulation during ischaemia is the key metabolic pathway that generates reactive oxygen species (ROS) during reperfusion resulting in injury. We examined if this metabolic signature was conserved in mice, pigs and humans, and investigated whether its inhibition can prevent the greater detrimental impact of warm compared to cold ischaemia in transplantation.

Methods: Comprehensive metabolomic analysis of myocardial tissue exposed to warm and cold ischaemia was performed in mouse (whole hearts) [n=5-8], pig [n=5] and human hearts [n=4]. Under appropriate regulatory and ethical approval, apical heart tissue was procured immediately after exsanguination in pigs and human DBD donors. The impact of succinate dehydrogenase (SDH) inhibition by dimethyl malonate (DMM) on reperfusion injury was examined in a heterotopic mouse heart transplant model.

Results: Succinate accumulation relative to normoxic controls was much greater after 12 mins of warm ischaemia compared to 240 mins of cold ischaemia in mouse (11.7 ± 1.1 vs 6.3 ± 0.6 p=0.003; n=5), pig (5.9 ± 0.8 vs 1.7 ± 0.8 p=0.01; n=5) and human (8.0 ± 1.4 vs 3.2 ± 0.9 p=0.03; n=4) myocardium (Fig 1). DMM, administered at the onset of warm ischaemia, inhibited the accumulation of succinate during warm ischaemia in mice (431.6 ± 17.3 vs 242.9 ± 27.0 p=0.001; n=4). Administration of DMM to donor mouse hearts ameliorated myocardial injury after transplantation (24-hour serum troponin; 8.6 ± 1.9 vs 3.0 ± 0.4 p=0.03 [n=5-6]; Fig 2). Data are mean±SEM.

Discussion: Succinate accumulation is greater during warm compared to cold ischaemia and this metabolic signature is conserved across species. Greater accumulation of succinate underlies increased ischaemia reperfusion (IR) injury following DCD compared to DBD transplantation. Prevention of succinate accumulation by SDH inhibition is effective in ameliorating IR injury and is a promising therapeutic strategy to improve organ function in transplantation.

BTS/BLTG Symposium The Calne Williams Medal oral presentations 16:15, Thursday 15th March – Syndicates 3&4

CW01

The effect of normothermic machine perfusion after cold storage in liver transplantation: a multicentre prospective clinical trial

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Introduction: Normothermic machine perfusion (NMP) is a novel preservation method in liver transplantation. To date, most clinical studies have involved NMP for the entire preservation period, including transportation (continuous NMP). Clinical adoption of NMP may, however, be facilitated by normothermically preserving the liver retrieved and transported cold; simplifying logistics and reducing costs. This study aims to investigate the safety and feasibility of NMP following a period of SCS (post-SCS-NMP).

Methods: In this multi-centre, prospective clinical trial, 30 livers were transplanted. Livers were cold-stored after retrieval and transported to the recipient centre, where NMP was initiated. The primary endpoint was 30-day patient and graft survival. Secondary endpoints include: adverse events (Clavien-Dindo classification), peak serum aspartate aminotransferase (AST) (first 7 days post-transplant), early allograft dysfunction (EAD) and post-reperfusion syndrome (PRS). These were compared to each group of a multicentre RCT investigating the efficacy of continuous NMP versus SCS (n=104 NMP; n=82 SCS).

Results: Thirty-day graft and patient survival were 93% and 100%, respectively. Adverse events ≥grade IIIb severity occurred in 7 patients (23%). Mean peak serum AST in the pSCS-NMP group was 526.8±2.73U/L compared to 490.8±2.687U/L in the NMP control group (p=0.73) and 1007±2.859U/L in the SCS control group (p=0.004). EAD rates were similar in the pSCS-NMP and NMP groups (13% vs 11%, respectively) and were higher in the SCS group (33%; pSCS-NMP vs. SCS, p=0.056). Evidence of PRS was seen in 10% of pSCS-NMP livers and 11% of NMP livers. There was a significant reduction in PRS when comparing pSCS-NMP with SCS (10% vs 34%, p = 0.02).

Discussion: In this group of livers, pSCS-NMP was both feasible and safe. Early biochemical outcomes were similar to those observed with continuous NMP and a significant benefit was achieved compared to cold storage.

Assessing the time-varying impact of hepatocellular carcinoma on survival following liver transplantation

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Introduction: Historic studies have shown that patients with hepatocellular carcinoma (HCC) have favourable outcomes in the first 3 months following liver transplantation, but higher mortality thereafter. It had previously been argued that the introduction of the Milan criteria would reduce rates of tumour recurrence and negate this negative effect of HCC. We aimed to address this important research question by performing an updated analysis that identified the prognostic impact of HCC on mortality at different periods of follow-up time after liver transplantation.

Methods: We used the UK liver transplant registry to select a cohort of first-time adult recipients of elective liver transplants performed between 2007 and 2016. We compared the donor and recipient characteristics of HCC and non-HCC patients and used Kaplan-Meier methods to compare patient survival. We used Cox regression to examine the prognostic impact of HCC status on mortality at three separate periods of follow-up time: 0-90 days, 90 days-2 years and 2 years-5 years.

Results: 5780 first-time adult elective liver transplants were included. Patients transplanted for HCC had lower UKELD scores but were more likely to receive segmental grafts and grafts from circulatory death donors (P<0.05). No difference in 90-day mortality between HCC (n=1397) and non-HCC (n=4383) groups was identified (HR 0.82, 95% CI 0.58-1.15, p=0.25). HCC was associated with a statistically significant increased risk of mortality from 90 days-2 years (1.77, 1.32-2.38 and 1.55, P<0.001) and from 2 years - 5 years (1.58, 1.18-2.05, P<0.01). The effect of HCC was found to vary significantly across the three periods of follow-up time (p for interaction=0.0006).

Discussion: HCC remains a significant risk factor for mortality after 3 months of follow-up time. Despite the implementation of the Milan criteria we are still transplanting patients who are at risk of early tumour recurrence and death.

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Impact of donor hepatectomy time during organ procurement in donation after circulatory death liver transplantation; the United Kingdom experience

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Introduction: No data exists to evaluate the impact of hepatectomy time (HT) during donation after cardiac death (DCD) procurement on short and long-term outcomes following liver transplantation (LT). In this study we analyse the impact of the time from aortic perfusion to end of hepatectomy on outcomes following DCD LT across all UK transplant centers.

Methods: Using data requested from NHSBT, we identified 1112 adult patients receiving a first LT in the UK between 1 January 2001 and 31 August 2015 from a DCD donor. Primary end points were PNF and all cause graft survival. A cohort of DBD donor recipients (n=7221) in the same time period was included to allow comparison of long-term survival. Statistical methods included logistic regression and cox proportional hazard models.

Results: Incidence of PNF was 40 (4%) and in multivariate analysis only CIT >8 hrs. (HZ 2.186 (1.113-4.294, p=0.023) and HT > 60 mins (HZ 3.669 (1.363-9.873, p=0.01) were correlated with PNF. Overall 90 day, 1 yr., 3 yr. and 5 yr. graft survival in DCD LT was 91.2%, 86.5%, 80.9% and 77.7% (compared to a DBD cohort in the same period (n=7221) 94%, 91%, 86.6%, and 82.6% respectively (p<0.001)). In multivariate analysis the factors associated with poorer graft survival were HT >60 mins (or more specifically, \geq 53mins on a continuous spectrum), donor age >45 yrs., CIT> 8 hours and recipient previous abdominal surgery.

Discussion: The largest study to date to demonstrate a negative impact of prolonged HT on outcomes on DCD LT and although HT <u>></u>53 mins is not a contraindication for utilisation it should be taken into a multifactorial assessment with established prognostic donor factors such as age (>45yrs) and CIT (>8hrs) for an appropriately selected recipient.

Impact of regional organ sharing and allocation in the UK Northern Liver Alliance on waiting time to liver transplantation and waitlist survival

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Background: Currently in the UK, organ allocation for deceased-donor livers (DDLs) is centre-based. The Northern Liver Alliance (NLA) top-band is a supra-regional allocation system for patients at 3 UK liver transplant centres (Newcastle, Edinburgh and Leeds). NLA patients with a UKELD score >61 (top-band) are registered on a common waiting list (WL) and prioritised by UKELD score for DDL allocation. DDLs are shared between the 3 centres, with an organ 'payback' scheme ensuring no centre is disadvantaged. We aimed to investigate whether the NLA had improved WL survival and waiting time (WT) to transplantation, and what impact the scheme had on non-top-band patients.

Methods: Data was retrospectively extracted from the central NHSBT database from August 2013 to December 2016. The King's College and Cambridge liver units were used as control data. The Kaplan-Meier method was used to estimate WL survival and median WT to transplant, with the log-rank test used to make comparisons. The Cox proportional hazards model was used to ascertain the impact of waiting time on post-transplant survival in top-band patients, using data from all seven transplant centres.

Results: WL survival was no different at NLA centres compared to non-NLA centres for top-band patients (1-year survival 62.9 vs. 64.6%, respectively; p=0.999). WT was significantly lower at NLA centres compared to non-NLA centres for top-band patients (23 days vs. 99 days, respectively; p<0.001). WL survival for non-top-band patients was no different (117 vs. 192 days, respectively; p=0.999). WT was found to have a non-significant (p=0.712) effect on 3-year adjusted post-transplant survival.

Conclusions: The NLA did not improve WL survival despite a significantly shorter WT compared to non-NLA centres. However non-top-band patients did not experience inferior survival, demonstrating that prioritisation by severity does not adversely affect survival. The NLA achieved its aim of transplanting patients with the greatest need.

The assessment of liver quality during normothermic liver perfusion

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Background: Normothermic machine perfusion (NMP) may enable an objective assessment of liver quality to aid clinical decision making. However, there is little evidence as to which measures correlate best with outcome. This study aims to determine which NMP parameters may be predictive of post-transplant outcome.

Methods: As part of a RCT conducted by the Consortium for Organ Preservation in Europe, 120 NMP livers were transplanted. Biochemical analysis was performed on perfusate collected during NMP from livers with a post-transplant peak-AST <250 U/L (minimal preservation injury [MPI], n=28) and >1000 U/L (significant preservation injury [SPI], n=25). Bile production and post-reperfusion syndrome (PRS) were also compared.

Results: Groups were matched for donor and recipient characteristics and preservation time. There was a difference in baseline perfusate ALT (MPI 171U/L vs SPI 669U/L; p=0.005) and LDH (MPI 1073U/L vs SPI 1838U/L; p=0.01) between the two groups. These enzymes, along with GGT, also increased more rapidly during NMP in the SPI group (ALT +56U/L vs +461U/L, p<0.001; LDH +483U/L vs +980U/L, p=0.06; GGT +23U/L vs +104U/L, p=0.004). MPI livers experienced a drop in haemolysis index as NMP progressed in contrast to SPI livers where it rose (MPI -0.04U/L vs SPI +0.09U/L; p=0.03). Lactate clearance was similar in each group. Vhe MPI group showed superior bile production (MPI 13.1ml/hr vs SPI 7.8ml/hr; p=0.03) and lower rates of PRS (MPI 0/28 vs SPI 6/25; p=0.007).

Conclusion: A clear correlation exists between post-transplant outcome and the absolute values and trends in several biochemical parameters and bile production during NMP. These differences can be used to predict organ quality and potentially guide clinical decision making to ensure patients receive an appropriate organ for their clinical condition.

Can MRCP predict, and normothermic liver preservation prevent, ischaemic cholangiopathy?

<u>David Nasralla</u>¹, Carlo Ceresa¹, Hynek Mergental², Thamara Perera², Arvind Pallan³, Andrew Butler⁴, Sara Upponi⁵, Charles Imber⁶, Wayel Jassem⁷, John Karani⁸, Simon Knight¹, Rutger Ploeg¹, Constantin Coussios⁹, Peter Friend¹

¹Nuffield Department of Surgical Sciences, University of Oxford, Oxford, United Kingdom. ²Liver Unit, The Queen Elizabeth Hospital, Birmingham, United Kingdom. ³Department of Radiology, The Queen Elizabeth Hospital, Birmingham, United Kingdom. ⁴Addenbrooke's Hospital, Cambridge, United Kingdom. ⁵Department of Radiology, Addenbrooke's Hospital, Cambridge, United Kingdom. ⁶Royal Free Hospital, London, United Kingdom. ⁷Institute of Liver Studies, King's College Hospital, London, United Kingdom. ⁹Oxford Institute of Biomedical Engineering, University of Oxford, Oxford, United Kingdom.

Introduction: Increased utilisation of DCD livers is hampered by high rates of non-anastomotic biliary strictures (NAS) causing graft failure. NAS usually presents with deranged liver function prompting further radiological investigation. Early detection of NAS through protocol MRCP imaging at 6 months has been advocated but never investigated. Furthermore, it is unknown whether normothermic liver preservation (NMP) can prevent NAS and so improve DCD outcomes.

Methods: As part of a multinational RCT comparing NMP with conventional cold storage (SCS), all patients underwent a protocol MRCP at 6 months post-transplant to evaluate the biliary tree for strictures. Scans were reviewed by two independent, blinded radiologists. A system for grading biliary strictures was agreed to allow definitive categorisation of the presence and site of strictures.

Results: An MRCP was performed on 155 (81 NMP, 74 SCS) of the 222 transplanted trial patients. There was no significant difference in the rate of non-anastomotic strictures for DBD (NMP 7.4% (4/54) vs SCS 5.4% (3/55); p=0.678) or DCD (NMP 11.1% (3/27) vs SCS 26.3% (5/19); p=0.180) livers. Only one patient in each arm developed clinically relevant evidence of ischaemic cholangiopathy in the first year, both of whom were re-transplanted. There was no difference in the rate of anastomotic strictures for DBD (NMP 40.7% (22/54) vs SCS 41.8% (23/55); p=0.909) or DCD (NMP 48.1% (13/27) vs SCS 57.9% (11/19); p=0.515) livers.

Conclusion: The rate of NAS in NMP DCD livers was lower than SCS but did not reach statistical significance; the trial was not powered for this outcome. Prior to this study, the radiological incidence of both anastomotic and non-anastomotic strictures in asymptomatic patients was unknown. Apart from the two retransplanted patients, almost all others with radiological evidence of NAS had normal liver function at one year; this questions the clinical relevance of a protocol MRCP at six months.

Correlations between post-reperfusion biliary histopathology, the use of normothermic regional perfusion and the development of ischaemic cholangiopathy

Maithili Mehta¹, David J. Harrison², Gabriel C. Oniscu^{1,3}

Introduction: Ischemic cholangiopathy (IC) is a major complication of liver transplantation from donors after circulatory death (DCD). Normothermic regional perfusion (NRP) appears to reduce the incidence of IC. We investigated if histological changes seen in the biliary tree immediately post-reperfusion might herald the development of IC.

Methods: Two independent observers undertook a systematic analysis of donor gall bladder (GB) and common bile duct (CBD) to assess for differences in histological phenotype between (a) NRP and non-NRP cases and (b) recipients who developed IC and those who did not. H&E stained tissue samples of donor GB and CBD were scored according to a grading system published by Hansen *et al.* MRCP/ERCP diagnosis of IC was the primary outcome measure. Independent samples Mann-Whitney U tests were performed to assess for differences in histological scores between groups.

Results: 50 cases (38 DCD, 12 DCD-NRP) were studied. Eleven recipients (all standard DCD) developed radiologically confirmed IC (median follow-up:30.5 months). There were significantly less histological injuries in donor GB in the NRP group [mucosal loss (p<0.0005), mural necrosis (p=0.033), arteriolonecrosis (p=0.023) and total injury (p<0.0005)]. These differences persisted when comparing NRP with non-NRP transplants who did not develop IC. No differences reach statistical significance for donor CBD analysis. However, there was no significant difference in the tissue injury scores between the IC and non-IC groups in the full cohort and in the standard DCD (non-NRP) subgroup analysis.

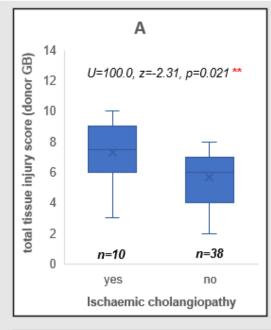
Discussion: The histological scores indicate that NRP ameliorates the ischaemic injury to cholangiocytes. However, ischaemia-related histological changes at the time of reperfusion did not correlate with the development of IC post-transplant, indicating that one or more complementary mechanisms are likely involved. A histological grading scale based on ischaemic injury alone may not be adequate to predict the development of IC.

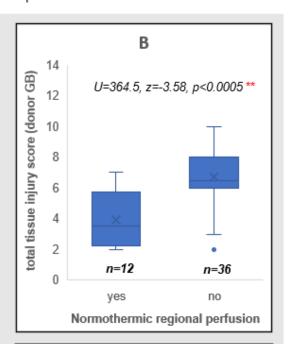
Image 1: The effect of normothermic regional perfusion (NRP) on the development of ischaemic cholangiopathy (IC) after DCD liver transplant [Fisher's exact test; p=0.46**]

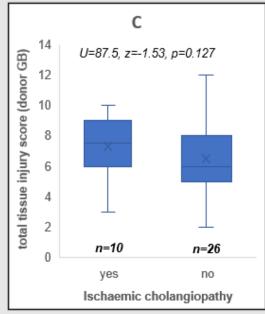
	IC	Non-IC	Total
NRP	0 (0.0%)	12 (100%)	12
non-NRP	11 (28.9%)	27 (71.1%)	38
Total	11	39	N=50 cases

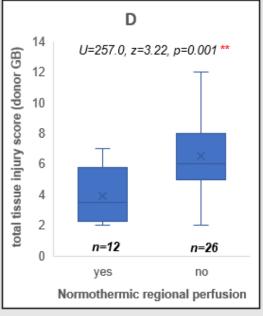
¹University of Edinburgh, Edinburgh, United Kingdom. ²University of St. Andrews, St. Andrews, United Kingdom. ³Royal Infirmary of Edinburgh, Edinburgh, United Kingdom.

Image 2: Graphical representation of differences in total tissue injury scores (donor gall bladder) between **A.** IC/non-IC groups, **B.** NRP/non-NRP groups, **C.** IC/non-IC groups within the subgroup of n=38 grafts that were not treated with NRP and **D.** NRP/non-NRP groups within the subgroup of n=39 patients who did not develop IC. Independent samples Mann-Whitney U tests were used, asymptotic p values reported.









Quality in Donation 14:00. Wednesday 14th March – The Auditorium

001

Impact of donor substance abuse on solid organ pancreas transplant outcomes

Emily R Thompson¹, Patrick Trotter², Ibrahim K Ibrahim¹, Lucy Bates¹, C Hopkinson³, Steve White¹, Derek M Manas¹, Colin H Wilson¹

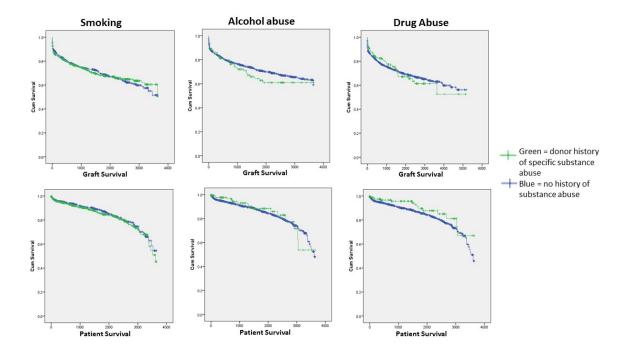
¹NIHR Blood and Transplant Research Unit, Institute of Transplantation, Freeman Hospital,, Newcastle upon Tyne, United Kingdom. ²NIHR Blood and Transplant Research Unit, Department of Surgery, University of Cambridge, Addenbrookes Hospital, Cambridge. United Kingdom. ³Statistics and Clinical Studies, NHS Blood and Transplant, Newcastle upon Tyne, United Kingdom.

Introduction: Substance abuse is unfortunately common in organ donors. Often these organs are declined for transplant, not only because of concerns around blood borne virus transmission but also because of perceived poor outcomes. In kidney transplantation, previous studies have demonstrated donor smoking significantly impacts transplant outcome, but IVDU or alcohol dependence does not(1). This study aims to clarify these issues in pancreas transplantation.

Methods: Retrospective data on all UK solid organ pancreas transplants from 1984-2015 was obtained from the NHSBT UK transplant registry. Unadjusted graft and patient survival were calculated using Kaplan-Meier (K-M) plots and compared using the log-rank test. Multivariate analysis was performed using Cox proportional hazards regression model. All reported adverse events of viral transmission to any transplant recipient from IVDU donors were also reviewed.

Results: Of 2317 analysed transplants, 1175 were categorised as substance misusers. Survival analysis using K-M plots revealed no significant impact of substance misuse on 10-year graft or patient survival. Multivariate analysis confirmed these variables were not associated with impaired graft of patient survival. Only traditional markers of poor outcome i.e. cold ischaemic time (p<0.001, HR 1.001 95%CI 1.001, 1.002), increasing donor age (p=0.045, HR 1.012 95%CI 1.000, 1.025), and increasing recipient BMI (p=0.038, HR 1.041 95%CI 1.002, 1.082) were found to significantly impact graft survival. Recipient age correlated with poor patient survival (p=0.015, HR 1.038 95%CI 1.007, 1.069). No identified viral transmissions to pancreas recipients from IVDU donors. There were 3 cases of unexpected HCV transmission in kidney/liver recipients.

Discussion: A history of donor substance misuse does not negatively impact 10-year graft or patient survival following pancreas transplantation, contrary to evidence in renal transplantation and widely held beliefs amongst transplant clinicians. In the UK, there were no cases of blood borne virus transmission in pancreas transplantation.



Transplantation of kidneys from DCD and DBD donors who died after ligature asphyxiation: the UK experience

Patrick Trotter^{1,2}, William Hulme², Matthew Robb², Christopher Watson¹, James Neuberger³, J A Bradley¹

¹University of Cambridge, Cambridge, United Kingdom. ²NHS Blood and Transplant, Bristol, United Kingdom. ³Queen Elizabeth Hospital, Birmingham, United Kingdom.

Introduction: Kidneys from donors who die after ligature asphyxiation are often used for transplantation but there is concern that the hypoxic injury following ligature asphyxiation may be associated with inferior transplant outcomes, particularly for recipients of donation after circulatory death (DCD) donor kidneys.

Methods: The UK transplant registry was used to identify all donors who died secondary to ligature asphyxiation and analyse transplant outcomes.

Results: Over the 14-year study period, 2.7% (n=521) of all potential UK organ donors died secondary to ligature asphyxiation (mostly suicide by hanging). Of these, 409 (78.5%) proceeded to donate kidneys for transplantation (46.9% DBD and 53.1% DCD donors). Compared to all other deceased kidney donors, those that died from ligature asphyxiation were significantly younger, more often male, and had less hypertension and cardiac disease. Donors after ligature asphyxiation provided kidneys for 650 kidney only transplants. 12-month eGFR was significantly better in recipients of kidneys from donors who died from ligature asphyxiation (both DCD and DBD). After adjustment for donor and recipient factors using multivariate linear regression, donor death from ligature asphyxiation was not an independent predictor of 12-month eGFR (p=0.625). Recipients of kidneys from donors who died following ligature asphyxiation (both DCD and DBD) had superior 5-year patient and death censored graft survival. After adjustment for other donor and recipient characteristics, donor death from ligature asphyxiation was not an independent predictor of 1 and 5-year patient survival or 1 year death censored graft survival, but was an independent predictor of 5-year death censored graft survival (HR 0.712 (0.513-0.990), p=0.042)).

Discussion: Donors who die following ligature asphyxiation represent a relatively small but important proportion of the overall deceased donor population. The use of kidneys from such donors is associated with excellent transplant outcomes and increased consideration should be given to their use, including those from DCD donors.

Paediatric transplantation 14:00. Wednesday 14th March – Syndicates 1&2

003

Improved renal allograft survival for pre-emptive paediatric renal transplant recipients in the United Kingdom

Matko Marlais¹, Kate Martin², <u>Stephen Marks</u>^{3,1}

¹UCL Great Ormond Street Institute of Child Health, London, United Kingdom. ²NHS Blood and Transplant, Bristol, United Kingdom. ³Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom.

Introduction: The aim of this study was to investigate whether being on dialysis at the time of renal transplantation affected renal allograft survival in paediatric renal transplant recipients (pRTR).

Methods: Data were obtained from the UK Transplant Registry (NHS Blood and Transplant) on all children (aged <18 years) who received a kidney only transplant between 1 January 2000 and 31 December 2015. Baseline demographic data were collected, including dialysis modality at the time of renal transplantation (none vs peritoneal dialysis vs haemodialysis). Kaplan-Meier estimates of 5-year renal allograft survival were calculated, as well as Cox regression modelling accounting for donor type. The relationship between time on dialysis and renal allograft survival was also examined.

Results: 2,038 pRTR were analysed: 607 (30%) were pre-emptively transplanted, 789 (39%) and 642 (32%) were on peritoneal dialysis and haemodialysis, respectively at the time of transplantation. 5-year renal allograft survival was significantly better in the pre-emptively transplanted group (90.6%) compared to those on peritoneal dialysis and haemodialysis (86.4% and 85.7% respectively; p = 0.02). After accounting for donor type, we found a significantly lower hazard of 5-year renal allograft failure in pre-emptively transplanted children (HR 0.742, p = 0.05). Time spent on dialysis pre-transplant was negatively correlated with renal allograft survival (p = 0.002). There was no significant difference in 5-year renal allograft survival between children who were on dialysis for <6 months and children transplanted pre-emptively (87.5% vs. 90.5%, p = 0.25).

Discussion: Children who are pre-emptively transplanted have improved 5-year renal allograft survival, compared to children on haemodialysis or peritoneal dialysis at the time of transplantation. Although increased time spent on dialysis was correlated with poorer renal allograft survival, we found no evidence that short periods of dialysis (<6 months) pre-transplant affected renal allograft survival in children.

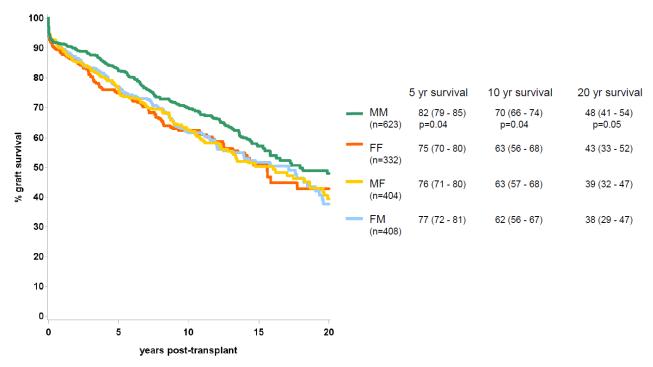
Superior renal allograft function with male deceased donors for paediatric renal transplant recipients

Nadeesha L Mudalige¹, Kate Martin², Stephen Marks^{1,3}

Introduction: Renal transplantation continues to improve the quality of life for children with end stage kidney disease and the policies surrounding allograft allocation have altered over time with the aim of improving patient and renal allograft survival. This study explored whether certain donor-recipient gender pairs are associated with a greater renal allograft survival than others.

Methods: A twenty year, retrospective survival analysis of all paediatric (<18 years of age), single kidney, donation following brain death (DBD) tranplant procedures performed in the United Kingdom between January 1996 and December 2016, from registry data held by the National Health Service Blood and Transplant service (NHSBT). Kaplan Meyer survival curves were synthesized for all donor:recipient gender combinations and analysis of variance to determine significant differences between groups. Renal allograft survival was defined as time from transplantation to graft failure, re-transplantation or patient death.

Results: Between January 1996 and December 2016, 1,767 single kidney, DCD, paediatric transplant procedures were performed. The majority of transplants took place from a male donor to male recipient (623; 35%), followed by female to male (408; 23%), male to female (404; 23%) and female to female (332; 19%). Survival analyses showed that male to male transplants were associated with superior renal allograft survival when compared to all other gender combinations (Figure 1), at five, ten and twenty years (82%, 70% and 48% respectively, p<0.05).



Discussion: A consistently superior renal allograft survival is observed for male to male deceased donor transplants at all time points following engraftment, which may be considered when preferentially allocating deceased donor grafts.

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Risk factors for developing post-transplant lymphoproliferative disorder in children after renal transplantation: a systematic review

Bente Reijtenbagh¹, <u>Sofie Simonis</u>², Huib de Jong¹, Nizam Mamode³

¹Erasmus Medisch Centrum, Rotterdam, Netherlands. ²Leiden Universitair Medisch Centrum, Leiden, Netherlands. ³Guy's Hospital, London, United Kingdom.

Introduction: Pediatric patients are at increased risk of post-transplant lymphoproliferative disorder (PTLD) after renal transplantation, but little data is available on causality. This review aims to identify risk factors for development of PTLD after pediatric renal transplantation.

Methods: A search of PubMed for articles containing data on the incidence of PTLD after pediatric renal transplantations was performed. Articles were included if they described children under 18 years undergoing kidney only transplantation, and one or more of the following risk factors were assessed: EBV viral load, seroconversion, immunosuppression and age.

Results: Of 24 articles identified, 16 did not meet the inclusion criteria. The remaining 8 studies included a total of 1388 children. The mean incidence of PTLD was 4,97%. Four studies considered EBV viral load and showed no significant association between viral load and development of PTLD. Mean viral load in patients who developed PTLD was 6236 copies/mL compared to 2698 copies/mL in patients who did not. Five studies considered seroconversion, but contained insufficient data to draw any conclusions. Five studies discussed age as a potential risk factor. Only two compared different age groups. McDonald et al. showed a significantly higher risk for patients in the 0-5yrs group compared to over 12yrs (HR=5.3, p=0.0017), whilst Smith et al. who showed a significantly higher PTLD incidence in adolescents (over12yrs) compared with those 0-5yrs (p=0.05). Finally, four studies evaluated immunosuppression as a potential risk factor, including tacrolimus, Cyclosporin, OKT3 and Azathioprine. Of these, only OKT3 therapy was identified as a risk factor for PTLD development.

Discussion: This review has found little evidence for specific risk factors for PTLD after renal transplantation in children. Although high viral loads, post-transplant seroconversion and powerful immunosuppression may increase the risks, there is insufficient data to predict which children will develop PTLD. Children without these risk factors remain at risk.

Oral presentations – 6 of the best 16:30, Wednesday 14th March – The Auditorium

006

Significance of basiliximab induction therapy in standard-risk renal transplant in tacrolimus era: a meta-analysis

Hatem Ali^{1,2}, Ajay Sharma^{2,3}, Ahmed Halawa^{2,4}

Introduction: Many studies proved that the use of basiliximab as induction therapy reduce the risk of acute rejection episodes in renal transplant patients on cyclosporine-based maintenance immunotherapy. Tacrolimus has overwhelmingly replaced cyclosporine in the maintenance immunosuppressive protocols in many transplant centres. The aim of our study and meta-analysis is to explore the effect of basiliximab induction therapy on rate of rejection, patient and graft survival in standard-risk renal transplant patients with tacrolimus based maintenance immunotherapy.

Methodology: We conducted a systematic review in pubmed, medline, embase and Cochrane. Inclusion criteria for our metaanalysis were all studies that compared basiliximab to placebo induction therapy in standard risk renal transplant recipients. Data collected were name of the first author, journal name, publication year, number of patients in basiliximab arm and in placebo arm, number of patients who had biopsy-proven rejection and graft survival in each arm. Random effects model was used for the meta-analysis.

Results: 389 abstracts were screened, of which 382 were excluded. 7 papers were included in the meta-analysis. Forest plot analysis for rate of rejection during the follow-up period, post-transplant showed no significant difference between both groups. Overall risk difference was -0.03(95%Cl: -0.09,0.02). Random-effect meta-analysis for patient and graft survival was done using forest plot analysis and showed no significant effect of basiliximab induction on patient or graft survival compared to placebo. Overall risk difference was -0.01 (95%Cl: -0.04,0.01) and 0.00 (95% Cl:0.00,0.01), respectively.3 of the included studies showed no effect of basiliximab on creatinine change .2 showed no effect on risk of CMV infection and one showed less risk of post-transplant diabetes in basiliximab group.

Discussion: Basliximab induction therapy has no significant effect on rate of rejection patient or graft survival in standard-risk renal transplant recipients with tacrolimus-based maintenance immunotherapy. More randomised-controlled studies are needed to address these.

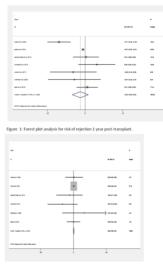


Figure 4: Forest plot analysis for graft survival 1 year post-transplant

¹Department of Renal Medicine, Royal Wolverhampton Hospitals NHS Foundation Trust, Wolverhampton, United Kingdom. ²Institute of Medical Science, University of Liverpool, Liverpool, United Kingdom. ³Transplantation Dept, Royal Liverpool University Hospital, Liverpool, United Kingdom. ⁴Sheffield Kidney Institute, Sheffield Teaching Hospitals, Sheffield, United Kingdom.

Have changes in the utilisation of livers donated following circulatory death affected survival in patients undergoing liver transplantation for hepatocellular carcinoma?

<u>David Wallace</u>^{1,2,3}, Kate Walker^{1,2}, Susan Charman^{1,2}, Abid Suddle³, Nigel Heaton³, Jan van der Meulen^{1,2}

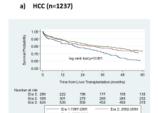
Introduction: The rising incidence of hepatocellular carcinoma (HCC) has placed a considerable strain on liver transplantation services. In response, donated livers following circulatory death (DCD) are increasingly being utilised as clinicians strive to transplant patients with HCC in an acceptable oncological time-frame. We aimed to identify how post-transplantation survival in patients with HCC has changed over successive eras of liver transplantation and to what extent changes in survival can be explained by changes in both donor and recipient characteristics.

Methods: We used the UK liver transplant registry to select a cohort of first-time adult recipients of elective liver transplants performed between 1997 and 2016. We stratified the cohort into 4 eras of transplantation a)1997-2001 b) 2002-2006 c) 2007-2011 and d) 2012-2016, and compared the change in the donor and recipient characteristics of HCC and non-HCC patients over eras. We used Kaplan-meier estimates to compare changes in 5-year patient survival and Cox regression to examine how, after adjustment for donor and recepient characteristics, the risk of undergoing liver transplantation for HCC successively changed from eras 1-3.

Results: 10,166 fist-time elective liver transplants were included. Across the entire study period, the utilisation of DCD livers disproportionately increased in HCC compared to non-HCC patients (32.7% vs 22.9%, p<0.05). 5-year patient survival improved from eras 1 to 3 in both HCC (59.9% to 73.2%) and non-HCC patients (74.8% to 83.4%, figure 1). Patient survival was consistently worse for HCC patients across all 3 eras of transplantation (log rank test p<0.05). This effect remained following adjustment for donor and recipient characteristics (table 1).

Discussion: Despite the increasing utilisation of DCD livers, survival for patients transplanted for HCC has improved considerably over last decade. However, in comparison to patients transplanted for non-HCC indications patients with HCC still have significantly worse long-term post-transplant outcomes.

Figure 1: 5-year patient survival for patients with HCC and non-HCC undergoing liver transplantation stratified by era (n=7009).



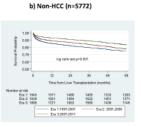


Table 1: Unadjusted and adjusted hazard ratios comparing liver transplantation for HCC vs non HCC indications over eras 1-3 (n=7009)

	Era 1 (1997-2001)	Era 2 (2002-2006)	Era 3 (2007-2011)
HCC with era	1.59 (1.35-1.88)	1.26 (1.06-1.51)	1.66 (1.40-1.98)
HCC with era +adjustment for patient characteristics	1.42 (1.19-1.70)	1.17 (0.97-1.41)	1.52 (1.23-1.81)

^{*}P=>0.05 for unadjusted and adjusted interaction of HCC status with era

¹Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom. ²Clinical Effectiveness Unit (CEU), Royal College of Surgeons of England, London, United Kingdom. ³Institute of Liver Studies, Kings College Hospital, London, United Kingdom.

Safety and efficacy of robot-assisted kidney transplantation

Kiran Sran, Ben Lindsey, Colin Forman, Peter Dupont, Ravi Barod, Neal Banga

Royal Free London NHS Foundation Trust, London, United Kingdom.

Introduction: Robot-assisted kidney transplantation (RAKT) is thought to offer the benefits of faster recovery and fewer wound complications than open kidney transplantation (OKT), and may ultimately improve access to transplantation for obese patients. Our centre began its RAKT programme one year ago, and currently has the largest series in the UK. We aimed to evaluate the safety and efficacy of this new procedure.

Methods: Data from RAKT recipients was compared in a 1:2 ratio to a control group of consecutive OKT recipients. All transplants were performed by the same surgeon. The primary outcome measure was graft function at 3 and 6 months post-transplantation. Secondary outcomes were implantation time, operative time, return to theatre, wound infection rate, and length of stay (LOS).

Results: We have performed RAKT in 8 patients. All patients received a live donor graft with single vessels, with no significant differences in donor or recipient characteristics between the two groups. Patients undergoing RAKT had significantly longer median implantation (65 vs 26 minutes) and operative (315 vs 180 minutes) times than OKT (p<0.0001). All grafts experienced primary function, with no difference between the groups in eGFR at 3 months (62 vs 57mls/min, p=0.76) or at 6 months (57 vs 57mls/min, p=0.95) post-transplant. One patient in the OKT group underwent re-operation for bleeding. There were no wound infections, and median LOS was 6 days in both groups. At the time of writing, graft and patient survival in both groups is 100%.

Conclusions: RAKT is a technically challenging procedure with a steep learning curve, resulting in longer implantation and operative times. Despite this, we have demonstrated equivalent graft outcomes in our initial cases to those from OKT. This was achieved through collaboration, specialist training and mentorship in robotic surgery, and the use of intracorporeal ice for graft cooling during implantation

Comparative mortality of live kidney donors in the UK: 15 year cohort study

<u>Nithya Krishnan</u>^{1,2}, Lisa Mumford³, Graham Lipkin⁴, Simon Fletcher¹, Indranil Dasgupta⁵, Paramjit Gill⁶, Ronan Ryan⁷, Neil Raymond¹

¹University Hospitals Coventry & Warwickshire NHS Trust, Coventry, United Kingdom. ²Faculty of Health & Life Sciences, Coventry University, Coventry, United Kingdom. ³ODT, NHSBT, Bristol, United Kingdom. ⁴Queen Elizabeth Hospital, Birmingham, United Kingdom. ⁵Primary Care, University of Warwick, United Kingdom. ⁷Primary Care, West Midalnds, United Kingdom.

With a move to increase live kidney donation numbers, understanding the risks and long-term outcomes for donors is essential.

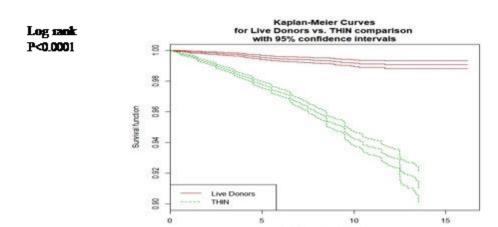
Aim: To investigate the all-cause mortality experience of U.K live kidney donors in comparison with healthy controls.

Methods: Ethics approval was in place to accrue data from data*base. Protocol reviewed and passed by Renal Registry projects advisory group, and independent scientific review committee, before release of the data. *Cohorts: A) Live Donors (LD):* Dataset obtained from UK Transplant Registry held by NHSBT, U.K. All live kidney donors from January 1st 2001 to 31st December, 2013 included and end date was 31st December 2016. *B) Comparative Cohort, The Health Improvement Network (THIN):* This is a large UK general practice database which contains anonymized longitudinal patient records from over 500 practices. Data from THIN was collected stratified by age, gender and year of entry, excluding a number of baseline conditions that would have been a contraindication to donation.

Results: Figure 1 shows a significant difference in mortality between the LD and the THIN cohort, with the LD group doing better. Cox Proportional hazard Modelling showed that the hazard ratio was significantly more for the THIN group even after adjustments for confounding variables. Further analyses were conducted to examine mortality for different age bands. This showed that there was no difference in 18-29 years age group, but statistically significant differences emerged with longer durations of follow-up in the other age groups; 30-44 years (P= 0.01), 45-59 years (P<0.001) and >60 years (P<0.001).

Conclusions: There was no increased risk of mortality in the LD group compared to a healthy cohort on analysis of a 15-year UK database.

Figure 1: All cause Mortality Between LD and THIN cohort



En-bloc kidney transplantation from infant and neonatal donors provide acceptable graft and patient outcome and a potential new donor pool

Imeshi Wijetunga, Adam Barlow, Clare Ecuyer, Adrienne Seitz, Sonsoles Martinez-Lopez, Vivek Upasani, Lutz Hostert, Richard Baker, Niaz Ahmad

St James's University Hospital, Leeds, United Kingdom.

Introduction: Over recent years there has been an increase in the use of en-bloc kidney transplants (EKTs) from small paediatric donors. We report outcomes of all EKTs performed at our centre, including those from neonatal donors.

Methods: All data was retrieved from a prospectively completed database and corroborated with NHSBT registry data. Survival was calculated using the Kaplan-Meier method.

Results: Between February 2005 and June 2017, 36 EKT were performed.

*median	0d-2m	2m-2yr	2yr-5yr	Overall
	(n=16)	(n=13)	(n=7)	(n=36)
Donor age (days)*	7	234	1451	98 (0-2081)
Donor weight (kg)*	3.2	7	16	4.75 (1.9-17.8)
Recipient Age (yr)*	29	38	27	31 (15-62)
Recipient wt (kg)*	54.7	61	56.9	56.1 (41.2-82.8)
Graft Loss (<90d) (n)	4	0	1	5
PNF (n)	1	0	0	1
1yr Graft Survival	69%	100%	86%	83%
5yr Graft Survival	69%	100%	48%	71%
3m Creatinine*	177.5	121	127	147
6m Creatinine*	113	95	107	106
12 m Creatinine*	89	80	91.5	87
3m PCR*	114.75	105.4	34.3	86.45
6m PCR*	96.9	20.95	32.1	36.05
12m PCR*	18.4	16.65	13.3	14.9
cRF after graft loss*	93.5	N/A	49.5	60.5

There was one recipient death from pneumonia 3 months post-transplant.

Conclusion: This abstract reports the outcome from the largest series of EKT from small paediatric donors in the UK including transplant of kidneys from neonatal donors not previously reported. Overall, very good outcomes can be achieved from EKT from donors less than 5 years of age. Transplant from donors under 2 months of age is associated with an increased risk of early graft loss, primarily due to thrombosis. Surviving grafts have excellent function at one year. Refinement in procurement, preservation, implantation technique and post transplant management is expected to improve outcome from these kidneys and will also provide expansion of the donor pool.

Does gene transcript analysis in renal transplant biopsies assist in the distinction of antibody-mediated rejection from glomerulonephritis?

<u>Barbora Salcman</u>¹, Candice Roufosse², Michelle Willicombe³, Terry Cook³, Adam McLean³, Jack Galliford³, Kathy Dominy²

Introduction: Glomerulonephritis (GN) is an important non-rejection cause of renal failure characterized by inflammation of the glomeruli of the kidney. Morphologically, *de novo* or recurrent GN can have the same features as alloimmune transplant glomerulitis (g), which is most often related to antibody-mediated rejection (AMR). Establishing the distinction between these two diagnoses is important for patient management. Gene expression analysis for markers of AMR is a new feature of the AMR diagnosis, so we investigated whether it distinguishes AMR from GN.

Methods: 241 renal transplant biopsies with RNA available for qRT-PCR were graded using Banff 2015 classification (non-AMR/GN controls n=135; AMR n=76, GN n=20). Gene expression analysis was carried out through qRT-PCR for 6 AMR-related transcripts (*DARC, PECAM1, KLRF1, MYBL1, FGFBP2, SH2D1b*) and results were analysed using ΔΔCT method and afterwards by calculation of the geometric mean of the transcripts. Kruskal-Wallis test was used to assess the significance.

Results: When comparing controls, AMR, GN and AMR+ GN there was a significant difference between the control and AMR groups (p=<0.0001) and between AMR and GN (p=<0.0001). In a subgroup analysis of only selected patients glomerular inflammation (g>0) (AMR n=52; GN n=9; AMR+GN n=7), a significant difference was observed between AMR and GN groups (p=0.0159). There wasn't any statistical significance between AMR+GN and other groups, possibly due to insufficient amount of samples in this group as only limited number of patients had this diagnosis.

Discussion: We show that AMR-related gene expression is different in samples with AMR or GN, including when glomerular inflammation is present. This suggests a different pathophysiology of glomerular inflammation and may represent a useful diagnostic tool for the differential diagnosis between these 2 entities.

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Clinical oral presentations 09:00. Thursday 15th March – The Auditorium

012

A 10 year experience of dual kidney transplantation in a single UK centre

Ibrahim Rajput, Abdul Hakeem, Shahid Farid, Muhammad Jameel, Niaz Ahmed, Omar Masood

St. James's University Hospital, Leeds, United Kingdom.

Introduction: Bridging the disparity between the kidney waiting list and donor poor continues to pose challenges globally. For highly sensitised patients and older recipients the wait is contributing to a high waiting list mortality. The UK has seen a significant rise in DCD transplants and specialist centres have made increasing efforts to widen their donor acceptance criteria. Fast track and aggressive screening policies have paved the way for techniques such as Dual Kidney Transplantation (DKT). First described by Remuzzi in 1996 there has been significant debate around solitary vs dual graft implants from marginal donors. Our centre has over 10 years of experience in DKT, and this work summarises our overall experience to date.

Methods: We analysed all DKTs over a 10 year period from 2007, specifically looking at recipient and donor characteristics, initial graft outcome and 30 day creatinine. Both grafts were placed in an Ipsilateral manner. Immunosuppression remained as standard. There was a Day 0 biopsy at time of implant and an USS on day 1.

Results: During the 10 year period a total of 62 DKTs were performed. There were 41 male recipients and 21 female. Median recipient age was 65 years (48-78). There were 47 DCD and 15 DBD paired grafts. Median donor age was 73 (43-83). Primary function was present in 65% of patients. There was 1 case of primary non function (PNF). The remaining 34% of patients experienced DGF between 2 and 22 days (median 6 days). 30 day creatinine ranged between 73 μ mols/L to 547 μ mols/L (median of 160 μ mols/L). Early and 5 year graft outcome is comparable to conventional solitary kidney transplant.

Conclusion: Dual kidney transplants provide a feasible option for previously discarded grafts giving outcomes comparable to solitary grafts in carefully matched donor recipient pairs.

Disease-specific differences and outcomes from listing for lung transplantation in the UK

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¹Papworth Hospital, Cambridge, United Kingdom. ²NHS Blood and Transplant, Bristol, United Kingdom. ³Wythenshawe Hospital, Manchester, United Kingdom. ⁴Harefield Hospital, London, United Kingdom. ⁵Freeman Hospital, Newcastle, United Kingdom. ⁶Queen Elizabeth Hospital, Birmingham, United Kingdom.

Introduction: Demand for lung transplantation exceeds the availability of donor organs. Patients who are likely to have the longest duration and higher risk of death on the waiting list should be prioritised. We set out to examine factors influencing outcomes whilst on the lung transplant waiting list in the UK.

Methods: Waiting list registration data between January 2004 and March 2014 at NHS Blood and Transplant for adult lung-only registrations were analysed. Outcomes (transplanted, still awaiting, removed or died) were evaluated against lung disease category, blood group and height.

Results: From 2,213 patient registrations, chronic obstructive pulmonary disease (COPD) comprised 28.4%, pulmonary fibrosis (PF) 26.2%, cystic fibrosis (CF) 25.4% and other lung pathologies 20.1%. At 3 years after listing, COPD patients were more likely to receive a transplant (78%) followed by CF (61%) and other lung disease (59%). PF patients were less likely to be transplanted (48%) than any other group (p<0.001) and have the highest waiting list mortality (28% and 37% at 1 and 3 years respectively). Shorter adults (<161 cm) had a lower probability of transplant at 3 years compared to taller patients (>174 cm) (52% vs 69%, p<0.001) and this pattern is seen in all disease categories and blood groups. At 3 years, 70% blood group A patients were transplanted compared to other blood groups (56-58%). Patients with blood group O have the lowest probability of transplantation and highest waiting list mortality. Nevertheless, 18% of blood group O donor lungs were given to non-blood group O recipients.

Discussion: The way donor lungs were allocated in the UK resulted in discrepancies between the risk profile and probability of lung transplantation. A new lung allocation scheme has been introduced in 2017 to prioritise patients most at risk with the aim of reducing waiting list mortality.

Comparative morbidity outcomes in live kidney donors in the UK: 15 year cohort study

<u>Nithya Krishnan</u>^{1,2}, Lisa Mumford³, Graham Lipkin⁴, Simon Fletcher¹, Indranil Dasgupta⁵, Paramjit Gill⁶, Ronan Ryan⁷, Neil Raymond¹

With a move to increase live kidney donation numbers, understanding the risks and long term outcomes for donors is essential.

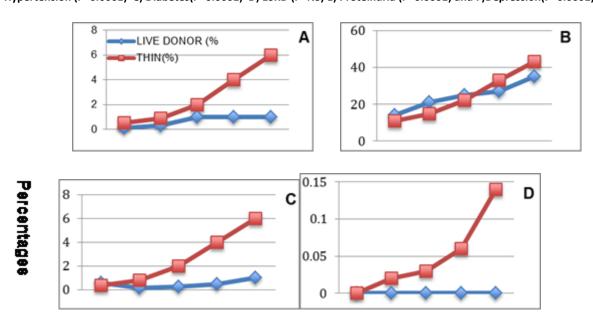
Aim: To investigate longer term morbidity outcomes of live kidney donors (LD) compared to healthy controls.

Methods: Ethics approval was in place to accrue data. Protocol reviewed and passed by Renal Registry projects advisory group, and independent scientific review committee. <u>Cohorts: A) Live Donors (LD):</u> Dataset obtained from UK Transplant Registry held by NHSBT, U.K. All live kidney donors from January 1st 2001 to 31st December, 2013 included; end date 31st December 2016. <u>B) Comparative Cohort, The Health Improvement Network (THIN):</u> This is a large UK general practice database containing anonymized longitudinal patient records. Data from THIN was collected stratified by age, gender and year of entry and excluding a number of baseline conditions that would have been a contraindication to donation.

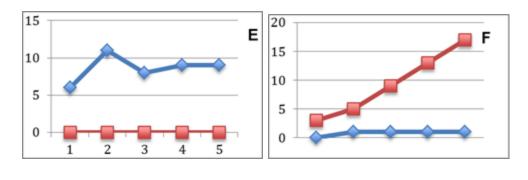
Results: Figure 1 shows significant increase in cardiovascular disease, diabetes and depression in the THIN cohort. Hypertension, though higher in the LD group initially, after seven years was significantly lower. No cases of ESRD in the LD group whereas 17 cases in THIN (P=0.01). Analysing eGFR <30, there were 8 cases in the LD group when compared to 94 in THIN (P<0.001).

Conclusions: Though hypertension was significantly more common in the LD group in the early years when compared with a healthy matched cohort, the prevalence of hypertension after about seven years was lower in the LD group. In this analyses live kidney donors seemed to have better long-term health outcomes than matched controls.

Figure 1: Morbidity outcomes of live kidney donors in comparison with THIN cohort - A) Cardiovascular disease (P<0.0001) B) Hypertension (P<0.0001) C) Diabetes(P<0.0001) D) ESRD (P=NS) E) Proteinuria (P<0.0001) and F)Depression(P<0.0001)



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1 2 5 10 15 years 1 2 5 10 15 years

A comparison of inflammatory profiles in donor lungs following donation after brain-death (DBD) and donation after circulatory death (DCD)

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Introduction: Brainstem death is associated with haemodynamic instability and an acute inflammatory response in donor lungs. Previous studies have linked this inflammatory response with an increased risk of primary graft dysfunction and early mortality post-transplantation. It is thus postulated that DBD donors express higher levels of acute inflammation than lungs from DCD donors, eventhough objective supporting evidence is lacking. In this study, the inflammatory profile of lungs from both DBD and DCD donors undergoing *ex-vivo* lung perfusion (EVLP) was evaluated to investigate this hypothesis.

Methods: Bronchoalveolar lavage (BAL) and perfusate samples collected from donor lungs undergoing EVLP as part of the DEVELOP-UK study were analyzed using a multi-array. Cytokine levels (Interleukin-1 β , IL-6, IL-8, TNF- α and IL-10) were compared between DBD and DCD lungs using Mann-Whitney U tests.

Results: Longitudinal perfusate samples from 46 (35 DBD and 11 DCD) and pre-EVLP BAL from 40 (31 DBD and 9 DCD) donor lungs were available. There were no differences in BAL levels between DBD and DCD lungs. At 15 minutes into EVLP there was, however, a significant difference in IL-1 β levels between DBD and DCD lungs: median (DBD)=0.06pg/ml (IQR 0.02-1.54), median(DCD)=0.74pg/ml (IQR 0.01-5.70), p=<0.01. Perfusate IL-1 β levels remained significantly higher in DCD lungs at the 2-hour time-point. There were no significant differences in other perfusate cytokine levels.

Discussion: There was no evidence that DCD lungs had decreased inflammation compared to DBD lungs in BAL or perfusate. In fact, there was a significant early increase in IL-1 β levels measured in the perfusate of DCD lungs when compared to DBD. This suggests that either pre-existing lung inflammation or events surrounding death upregulate inflammation in DCD donors. Whether warm-ischaemic insults in DCD donors contribute to the increased IL-1 β observed during EVLP requires further evaluation.

Recipient APOL1 genotype and allograft outcomes in live kidney transplantation

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¹Kidney and Transplant Centre, Imperial College Healthcare NHS Trust, London, United Kingdom. ²Histocompatibility and Immunogenetics Laboratory, Imperial College Healthcare NHS Trust, London, United Kingdom

Introduction: Apolipoprotein-L1 (APOL1) risk variants have emerged as a predictor of renal disease in individuals of African Ancestry (AA). The effect of APOL1 risk variants on the Living Kidney Transplant Recipients (KTR) has been rarely reported. We investigated the effect of APOL1 genotype on allograft outcomes.

Methods: We reviewed prospectively collected data on 220 KTR (141 male, mean age 46.7, 18-73 years). Genomic DNA was extracted from stored blood samples and three *APOL1* single nucleotide polymorphisms (SNPs) were amplified using primers. The product was sequenced using the forward primer on the ABI 3130xl. The variants typed (rs73885319 and rs60910145) are missense mutations in the last exon of the APOL1 gene (S342G and I384M) and (rs71785313), a six base-pair deletion leading to the deletion of two amino acids (delN388/Y389) in the last exon of the APOL1 gene. Sequences were evaluated using Mutation Surveyor software.

Results: 220 KTR were included, 77 Asian (48 male, mean age 45.9, 20-69 years), 66 AA (37 male, mean age 47.7, 20-71 years), and 77 Caucasian (47 male, mean age 46.65, 18-74 years), with a mean follow up 69 ± 27 months. Two APOL1 risk alleles were found in 28 (42.4%) AA, 1 (1.3%) Asian and none of the Caucasian KTR's. (p<0.001) In the AA cohort, Kaplan Meier analysis showed no significant difference in allograft survival in KTR'S with \geq 2 and 0-1 risk alleles. (log rank p=0.49) However KTR with \geq 2 risk alleles were found to have lower eGFR at 6m (54.7 \pm 18.1 $_{\odot}$ vs 45.3 \pm 15.3, p=0.03), 1y (56,7 \pm 17.5 vs 44 \pm 17.4, p=0.008) and 3y (51.5 \pm 21.7 vs 40.9 \pm 17.1, p=0.04).

Discussion: In this single center study, with medium term follow up, the presence of APOL1 risk alleles did not affect allograft loss, but KTR with ≥2 risk alleles appear to have lower eGFR for the first 3 years post transplant.

Causes of renal allograft failure in the United Kingdom

Hannah Burton¹, Lydia Lyamu Perisanidou², Retha Steenkamp², Becci Evans², Lisa Bradbury³, Fergus Caskey^{2,4,5}, Rachel Hilton¹

¹Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom. ²UK Renal Registry, Bristol, United Kingdom. ³NHS Blood and Transplant, Bristol, United Kingdom. ⁴School of Population Health Sciences, University of Bristol, Bristol, United Kingdom. ⁵North Bristol NHS Trust, Bristol, United Kingdom

Introduction: Most renal transplant recipients outlive their allografts. Improving long-term allograft survival remains a major unmet need in transplantation. To address this, better understanding of the causes of long-term allograft loss is required. We present outcome data for UK kidney recipients transplanted from 2000-2013. This is the largest cohort of renal allograft losses reported worldwide and the first such study from the UK.

Methods: The study population included incident renal allograft recipients from 1/1/2000-31/12/2013, aged ≥18 when transplanted, who received a single organ (first transplant only). Data were provided by the UK Renal Registry (UKRR) and NHSBT.

Results: 22,730 recipients met the inclusion criteria, with median follow-up 5 years. 23.7% allografts failed over the study period. Of 5,389 failed allografts, 40.8% were due to death with a functioning graft (DWFG), and the second most common cause of graft failure was alloimmune pathology (25% of all grafts lost). Other recorded causes were surgical (4.9%); recurrent primary disease (3.5%); non-viable kidney (2.7%); infection (1.7%); and various other pathologies (8.2%). No cause was recorded for 12.7%.

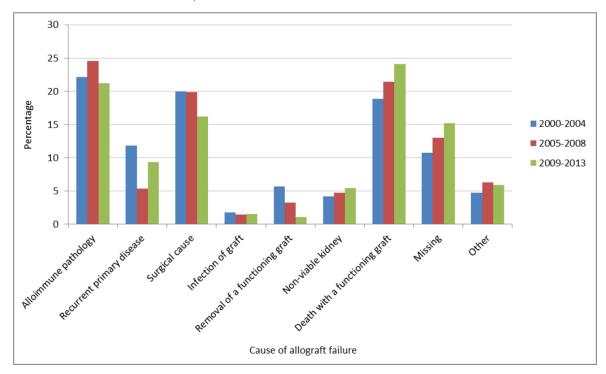
Table 1 compares demographics for patients with surviving or failed allografts.

Table 1 Patient demographics for total follow-up time

Demographics	Total N=22,730	Surviving % or median (IQR)/mean (SD) N=17,341	Failed % or median (IQR)/mean (SD) N=5,389
Age at transplantation			
<40 years	6,585	30.1	25.4
40-54 years	8,473	39.3	30.8
≥55 years	7,672	30.6	43.8
Overall (Mean (SD))	22,730	47.3 (13.3)	50.7 (14.4)
Recipient gender			
Male	13,978	61.3	62.3
Female	8,752	38.8	37.7
Recipient ethnicity			
Asian	2,268	10.1	9.7
Black	1,273	5.5	5.9
Other	469	2.2	1.5
White	18,714	82.2	82.9
Missing	6	0.0	0.0
Pre-transplant modality			
Haemodialysis	12,406	52.6	60.9
Peritoneal dialysis	6,226	27.0	28.6
Pre-emptive transplant	4,063	20.2	10.4
Unknown	35	0.2	0.2
Time on dialysis			
<1 year	8,070	38.8	24.8
1-3 years	7,252	31.3	33.9
>3 years	7,408	29.9	41.3
Overall (Median (IQR))	22,730	1.6 (0.3-3.5)	2.4 (1.0-4.5)
Primary renal disease			
Diabetes	3,266	13.5	17.3
Glomerulonephritis	4,970	22.0	21.5
Hypertension	1,317	5.5	6.8
Missing	633	2.8	2.6
Other (high risk)	1,339	5.8	6.2
Other (low risk)	2,098	9.5	8.3
Polycystic disease	3,326	15.7	11.2
Pyelonephritis	2,259	9.9	10.0
Renal vascular disease	291	1.2	1.6
Uncertain	3,231	14.1	14.6
Donor type			
DBD	10,824	44.0	59.3
DCD	4,423	19.7	18.6
Live	7,483	36.3	22.2
Donor age			
<40 years	6,443	30.1	22.7
40-54 years	9,268	41.1	39.7
≥55 years	7,008	28.7	37.6
Missing	11	0.1	0.0
Overall (Mean (SD))	22,719	46.2 (14.8)	49.6 (14.6)
HLA mismatch	1	l	l
000	2,535	11.2	11.1
ODR & 0/1B	6,120	25.9	30.4
0DR & 2B or 1DR & 0/1B	9,606	42.5	41.6
1DR & 2B or 2DR	4,460	20.5	17.0
Missing	9	0.1	0.0
Cold ischaemic time (hours)	1	1	l
Overall (Median (IQR))	21,892	12.3 (3.5–16.9)	15.1 (9.8–19.3)
Missing	838	I .	

The proportion of allografts failing in the first two years has fallen from 12.5% of transplants performed from 2000-2004, to 9.8% of transplants performed from 2009-2013. Figure 1 depicts how causes of allograft loss have also changed over transplant eras.

Figure 1. Percentage distribution of causes of allograft failure across different transplant eras adjusted for age group (40–54 years), gender (male), primary renal disease (glomerulonephritis) and ethnicity (white) for two years follow-up.



Discussion: This detailed analysis of outcomes in a large cohort of UK kidney transplant recipients reveals the changing causes of allograft failure in the era of modern immunosuppression. DWFG remains the leading cause of graft loss beyond six months, but there are now fewer failures due to alloimmune pathology and surgical causes. Further work is required to shed more light on the causes of death in transplant recipients to identify ways to improve their long-term survival.

Impact of symptomatic UTI on long-term renal transplant function

Rhana Zakri, Rohit Srinivasan, Katie Wong, Theo Kassimatis, Ellie Asgari, Jonathon Olsburgh

Guy's & St Thomas' NHS Trust, London, United Kingdom

Introduction: Urinary tract infection (UTI) affects 25-40% of renal transplant (RTx) recipients in the first year. UTI, particularly pyelonephritis, may cause rejection, sepsis and allograft loss. We investigated the incidence of UTIs and effect of UTI on 5 year transplant function.

Methods: A retrospective analysis of 610 adult RTx performed at our unit between 2010 – 2012. 213 patients followed-up at our hospital for at least 5 yrs were included. n=6 excluded for primary non-function, n=1 following early graft nephrectomy.

Results: Mean age: 47.3 yrs. Male:female 129:77 (62.6%:37.3%). Overall 43% (n= 88/206) suffered 1≤ UTI during the study period, 58% of which were female. There were n=442 positive urine cultures. Commonly offending bacteria included *E-coli, Klebsiella* and *Enterococcus*. Of n=88 with 'UTI', 14% were ABU, 12% cystitis, 17% pyelonephritis. Of n=25 with Cystitis as worst clinical episode, n=14 had recurrence. Of n=35 with Pyelonephritis, n=11 had recurrent pyelonephritis. There was a statistically significant change in 5 yr eGFR from baseline of 19.9mL/min, 20.9mL/min, 18.7mL/min respectively for pts with pyelonephritis, cystitis and ABU. Linear regression analysis against change in eGFR showed total number of UTIs to be significant. For each UTI 'hit', a 1.7% decrease in eGFR was shown. At 5 years, 171 transplants were functioning, 24 patients were on dialysis,12 had died with functioning graft, 1 was transferred. Diabetes significantly shortened overall graft survival at 5 yrs. Pts with pyelonephritis did have a shorter graft survival but at 5yrs this was not statistically significant.

Discussion: A high incidence of cystitis and pyelonephritis, particularly in women, was noted during first 5 years post RTx. Symptomatic UTI appears to significantly adversely affect long term graft function but ABU does not. This data emphasises the importance of identifying risk groups, prevention and early treatment of symptomatic UTI in RTx.

Ethics, law, psycho-social issues & public policy oral presentations 09:00. Thursday 15th March – Syndicates 1&2

019

Socioeconomic deprivation is associated with lower rates of pre-emptive kidney transplantation

<u>Keith Gillis</u>¹, Jennifer Lees¹, Maximilian Ralston², Siobhan McManus², Marc Clancy², James Traynor², Patrick Mark¹

 1 University of Glasgow, Glasgow, United Kingdom. 2 Glasgow Renal and Transplant Unit, Glasgow, United Kingdom

Introduction: Modality of initial renal replacement therapy (RRT) for chronic kidney disease (CKD) has long-term implications, and is influenced by medical and non-medical factors. We investigated effect of socioeconomic status on receiving pre-emptive kidney transplantation (PET).

Methods: A database of adults with CKD in a Scottish health board from 2006-2017 was analysed. Multiple logistic regression was performed to determine predictors of PET. Competing risks survival analysis was performed grouping by decile of Scottish Index of Multiple Deprivation (SIMD, 1=most deprived).

Results: 7765 patients had follow-up of 6.6±7.0years; 1298 required RRT; 113 received PET (64 live donors). Patients from SIMD≤3 had greater risk of death (p=0.006) but not RRT (p=0.6). Patients receiving PET had higher SIMD (5±7 vs 4±5; p=0.003), were referred to clinic younger (36.5±19.5 vs 58.2±24.6years; p<0.001) with higher eGFR (39.7±39.8 vs 30.5±26.3mlmin; p=0.001), lower proteinuria (75.5±150.2 vs 163.8±330.3mg/mmol; p<0.001) and lower BP (138/82±32/17 vs 150/82±34/18mmHg; p<0.001); There was lower prevalence of cardiovascular disease (6 vs 22%; p<0.001), malignancy (3 vs 12%; p=0.004) and diabetes (15 vs 37%; p<0.001). RRT commenced at higher eGFR in PET (9.3±5.7 vs 7.0±3.8ml/min/1.73m²; p<0.001). Live donation was less likely with SIMD≤3 (64 vs 45%; p=0.004). SIMD, diabetes, cardiovascular disease, referral age and proteinuria were independent predictors of PET (R^2 =0.22, p<0.001).

Discussion: Each decile increase in SIMD was associated with 14% greater likelihood of receiving PET and this was not explained by competing risk of death. Further work is required to explore if this effect is specific to kidney transplantation or wider CKD care in patients of lower socioeconomic status.

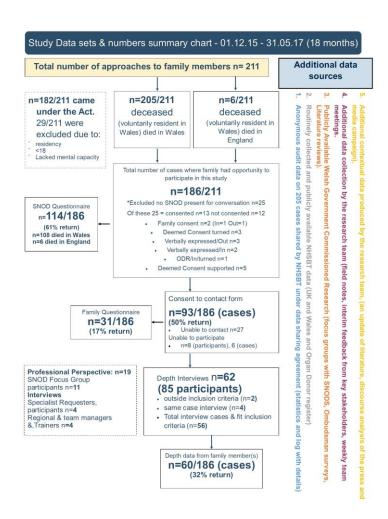
Evaluation of family attitudes, actions, decisions and experiences following implementation of deemed consent and the Human Transplantation Act (Wales) 2013

Jane Noyes¹, Karen Morgan², Phillip Walton³, Abigail Roberts⁴, <u>Leah Mc</u>¹, Michael Stephens⁵

¹School of Social Sciences, Bangor University, Bangor, United Kingdom. ²Major Health Conditions Policy Team, Directorate of Health Policy, Health and Social Services Group, Welsh Government, Cardiff, United Kingdom. ³Department of Organ Donation, NHS Blood and Transplant, Cardiff, United Kingdom. ⁴NHS Blood and Transplant, North West Regional Office, Liverpool, United Kingdom. ⁵Department of Nephrology and Transplantation, Cardiff and Vale University Health Board, University Hospital of Wales, Cardiff, United Kingdom

Introduction: On 01.12.15 Wales introduced a 'soft opt-out' system of organ donation.

Methods: A co-productive, mixed-methods study partnered with NHS Blood and Transplant (NHSBT) and patient and public representatives. Data were collected on 211 approaches between 01.012.15-31.05.17 (18 months) including; all 205 approaches to family members of potential organ donors in Wales, and a sample of 6 Welsh residents who died in English hospitals. 182/211 deceased patients came under the Act. Sixty-two in-depth interviews were conducted with 85 family members of 58 patients who were potential/actual organ donors, and 2 focus group or individual interviews with 19 NHS BT professionals. (Fig1). Organ donor register activity was monitored.



Results: Welsh Consent rates increased by around 10% to 61%; 64% when family consent was removed. This is now higher than England and has reversed an unexplained drop to 48.5% before implementation. However, family member(s) still overrode the patients organ donation decision 31/205 times. It is not always negative personal organ donation views that override a decision: health systems issues affected support for organ donation. 46/205 cases were deemed with a consent rate of 61%. The Act provided a useful framework but family members did not fully understand deemed consent. The media campaign did not focus on the changed role of the family. Family member(s) did not understand that they were no longer the decision maker about organ donation. Only 6% of the population have thus far opted out on the Organ Donor Register and this was less than anticipated (10%).

Discussion: The media campaign was not memorable and mostly worked to change behaviours but had gaps. More work is needed to inform the family member(s) about their changed role. As a result of this study Welsh Government commissioned a new campaign launched on 01.11.17. (Fig.2)

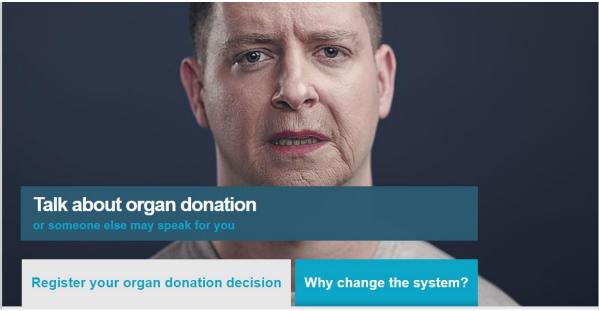


Fig.2

An economic analysis of the UK pancreas allocation scheme

Kerry Burke¹, Stephen Birch^{2,3}, Titus Augustine¹

¹The Renal and Pancreas Transplantation Unit, Manchester Royal Infirmary, Manchester, United Kingdom. ²Centre for Health Economics, University of Manchester, Manchester, United Kingdom. ³Department of Health Research Methods, Evidence and Impact, McMaster University, Canada, Canada

Introduction: Economics provides input to decisions concerning the best use of available resources. In transplantation, limitations include organ availability and competing organ demands. This is particularly evident in beta cell replacement. An analytical framework is presented for the allocation of a fixed supply of pancreata to be shared between solid pancreas and islet transplants according to national allocation criteria.

Methods: We consider the mean number of organs retrieved per solid pancreas and islet transplant, and the number of transplants per patient. Using retrieval allocation data from NHSBT, we estimate the rate of transformation (or trade-off) between procedures.

Results: Between 01/04/08 and 31/03/2016, 3294 pancreata were retrieved for solid organ and islet cell transplantation. 2551 went into the solid organ pathway, with 1606 transplants (62.95% conversion). 743 went into the islet pathway, with 183 transplants (24.62% conversion). With each patient requiring two islet transplants, 12.5 patients can be treated. In the context of an available supply of 100 pancreata, around 25 islet transplants could be performed. For solid pancreata, the same organ supply would allow 63 transplants. So for every islet recipient, the same organs could be used on average for 5 solid pancreas transplant recipients. The mean outcome per islet patient is freedom from hypoglycaemia unawareness, and for solid organ transplant it is freedom from insulin. A cost analysis found islet transplants to be more expensive than solid pancreata per patient.

Discussion: The allocation of a restricted supply of organs presents many clinical, economic and ethical challenges. These estimates identify the trade-offs involved in organs allocation. While clinical priorities are paramount in allocation policies, economic estimates provide an indication of the 'price' or opportunity cost of considerations that can help inform decisions makers, aimed at the efficient use of organs and the equitable treatment of different patient groups.

Primary school students: an untapped resource to increase awareness of organ donation?

Roberta Bullingham¹, Rachel Hung², Gareth Morgan², Bimbi Fernando²

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Introduction: NHSBT *Taking Organ Transplantation to 2020* (2013) highlights the importance of changing public attitude and behavior in organ donation (OD). Evidence shows that public education increases willingness to donate and decrease opposition. However, there are few studies evaluating interventions focusing on school education. We sought to educate primary school children on OD with the principle aim of stimulating discussion of the subject within their families.

Methods: A team of 2 patients, a transplant surgeon, 2 junior doctors and a nurse conducted a series of workshops across 5 primary schools around North London each year from 2013 to 2017. Year 5 and 6 primary school students were included in the study group. Pre and post-workshop questionnaires were conducted on the students and a post-workshop questionnaire was given to teachers and parents.

Results: A total of 506 students attended the workshops during the study period, with 50% female students. The ages (years) of the children were 9(8%), 10(32%), and 11(60%). 92% of students found the workshop to be valuable and 61% found it an easy topic to discuss with their family or friends. 96% of teachers and parents agreed that OD is an important topic and 78% agreed that it was an appropriate subject to be discussed with primary school students. Before the workshop, only 40% of parents had discussed OD with their children compared with 69% following the workshop.

Conclusion: Our data shows that majority of parents and teachers consider OD an important and appropriate subject to be discussed with primary school students. Educating students about OD successfully led to further discussion of the topic with their family suggesting that this is an effective way of raising awareness of OD and ultimately may increase the number of potential donors.

Engaging teenage students in transplantation ethics and organ donation via an interactive tutorial

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Introduction: England is considering implementing opt-out organ donation. This has the potential to increase donation rates but places a greater emphasis on the public to have formed an opinion prior to the act of donation; where their consent is presumed. Despite this, most school leavers have never had a facilitated conversation about transplantation ethics or had the opportunity to interact with individuals with experience of the process. To address this, we commenced a pilot educational program for teenagers delivered by members of a NORS team.

Methods: An interactive tutorial was designed and presented at various schools in the south of England and students aged 16-18yrs were invited. Attitudes were assessed via a mix of multiple choice and free text answers given in response to pre- and post-questionnaires.

Results: 67 young adults (64 females) participated in the school tutorials. Within our cohort, 22% reported prior registration on the Organ Donor Register, yet 96% would consider joining. 65% had spoken to their family about organ donation, but only 26% agreed with the current model of familial consent. Prior to the start of the session, surprisingly, 53% (n = 26) would have considered monetary procurement of an organ for transplantation. Following the tutorial attitudes had changed in 42% (n = 20). Qualitative feedback highlighted an increased awareness of the UK NHS transplant pathway, the ethical decisions faced by transplanting teams and the current requirement for next of kin consent. 95% of follow-up questionnaire respondents (n=22) had spoken to family and friends regarding tutorial during the intervening week.

Discussion: We have shown that a small, cost-effective tutorial can stimulate a wider discussion at home and at school in almost all participants, and is well received by students and teachers. Qualitative feedback highlighted an improved awareness of the donation pathway, sophisticated ethical reasoning and interest in consent.

Barriers to pre-emptive kidney transplant listing – a single centre experience

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Introduction: Pre-emptive transplantation provides the best long term outcomes for patients with kidney failure. For patients who do not have potential live donors, early assessment and activation on the waiting list is required to achieve transplantation before starting dialysis.

Methods: We undertook a cross sectional analysis of all patients in our pre-dialysis clinic who were under the age of 65 with an eGFR persistently under 15ml/min, as this group were most likely to be suitable for kidney transplantation and should be active on the waiting list at this level of kidney function. Transplant status and reasons for not being active on the transplant list were reviewed.

Results: The pre-dialysis service looked after 624 patients, of which 157 were aged under 65 with an eGFR persistently under 15ml/min. Fifteen patients had an absolute contra-indication or did not want transplantation. Of the remaining 142 patients, 136 (95.8%) had been assessed by their nephrologist regarding transplant suitability, 107 (75%) had been referred to the pre-transplant assessment nurse, 85 (60%) had been reviewed by a transplant clinician in the assessment clinic and 44 (31%) were active on the transplant waiting list. Ninety-eight patients were not active on the transplant waiting list. The main reasons were: 25 patients (26%) were obese, 24 patients (25%) were thought to be non-concordant with therapy or had not attended assessment clinic/investigations, 12 (12%) had been assessed as fit for transplantation when their eGFR was above 15 but had not been activated by their nephrologist when the eGFR had deteriorated, 11 (11%) were awaiting investigations to assesses suitability and 9 patients (9%) were waiting to be seen in assessment clinic.

Discussion: Obesity and poor concordance remain key barriers to pre-emptive kidney transplantation. Activation of suitable patients as their GFR deteriorates is an easy win to improving long term patient outcomes.

A significant proportion of kidney transplant candidates have poor health literacy and access health information in non-traditional formats

Joanne Henry^{1,2}, Sacha De Serres^{3,4}, Shashi Hirani², Ciara N. Magee^{1,5}

Introduction: Transplant candidates receive a significant amount of information during work-up, which, at our institution, is provided during face-to-face sessions, transplant education evenings and annual review clinics, with printed information provided for reference. Nonetheless, retention of this information is poor, and can lead to non-concordance with treatment and adverse outcomes. We examined the demographics of our transplant candidate population, with particular reference to health literacy scores and information-seeking behaviour.

Methods: A service evaluation questionnaire was completed by listed transplant candidates, alongside performance of a rapid estimate of adult literacy in medicine (REALM-R) based on word recognition.

Results: 61 patients participated, with a mean age of 52 (range 24-75). 41% (25) had previously undergone kidney transplantation. 41% (25) were black, 26% (16) were white and 15% (9) asian; 8% (5) identified with multiple ethnic groups and 10% (6) as other. 46% (28) reported English as a second language; 53% (32) scored at risk of poor health literacy (Range 2-6, mean 4.46). Education levels varied from less than completion of secondary school (5%) to university qualifications (30%). Digital natives (individuals born after 1980) represented 13%, while 87% (53) owned a smartphone/tablet and 54% (33) availed of free WiFi during dialysis. 60% reported often searching the Internet to learn about their condition. 70% had never attended a transplant education evening, while only 15% (9) had read all of the written information provided. 74% requested to see the printed material as an online digital publication with videos and screen reader function. Crucially, those with lower REALM-R scores were significantly less likely to read the printed material (p=0.004).

Discussion: Our data indicate a critical need to produce transplant-specific patient information aimed at lower health literacy levels and in different formats, in efforts to efficiently and robustly disseminate important information prior to transplantation.

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O27 & O29 Withdrawn

028

A novel approach in real-time monitoring of renal allograft perfusion in an ex-vivo normothermic perfusion human kidney model system –a translational interface

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Introduction: Monitoring of renal perfusion in real-time transplantation may provide valuable insight into sub-clinically relevant haemodynamic changes in tissue oxygenation of the renal allograft which necessitates early intervention for graft salvage. We describe a potential novel solution to this problem using ex-vivo normothermic perfusion (EVNP) of discarded human kidneys and a reflectance probe to monitor allograft perfusion in real time.

Methods: EVNP was performed on 5 discarded human kidneys using a blood (packed cell) based perfusate solution based on a clinically approved protocol¹. During EVNP, a reflectance probe was placed upon the kidney at 4 points: hilum, superior, lateral and inferior margins, and reflectance data was recorded at key times during the perfusion process. The process was repeated using continuous measurements by attaching a custom-built probe to the surface of the kidney and recording reflectance data in real time. Estimation of O₂ saturation was achieved by comparing the recorded data to known haemoglobin species spectra.

Results: Table 1 shows O_2 saturation estimates of a perfused kidney at various EVNP pump speed rates. Estimated O_2 saturation drops sharply between the 50% and 25% pump rates. Figure 1 shows the raw reflectance data corresponding to the presented O_2 saturation estimates. Similar spectral variations (characteristic of haemoglobin species) have been observed in the continuously recorded data.

Table 1 Kidney O₂ saturation estimates at various perfusion rates

EVNP pump rate	O ₂ saturation
100%	40%
75%	40%
50%	40%
25%	30%
0%	27%

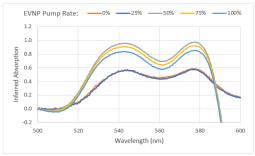


Figure 1 Spectral data of perfused kidney at various EVNP pump rates

Conclusion: This initial study proves promising in identifying and monitoring perfusion within an EVNP human kidney model using reflectance probes. We have shown the potential of this work in identifying haemodynamic changes within the kidney which may have clinical significance in early graft salvage interventions.

References: 1. Hosgood SA, Saeb-Parsy K, Hamed MO, Nicholson ML. Am J Transplant. 2016 Nov;16(11):3282-3285.

IgM HLA DSAs do not alter the outcomes of renal allograft rejection

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Introduction: Whilst IgG HLA DSAs are associated with renal allograft rejection and graft loss, the role of IgM HLA DSAs is controversial. In this study we investigate the significance of de novo IgM HLA DSAs in patients with T-Cell mediated rejection [TCMR], acute antibody mediated rejection [aAMR] and chronic antibody mediated rejection [cAMR].

Methods: 1667 CDC/FCXM negative renal transplant recipients receiving a steroid sparing, tacrolimus based regimen with monoclonal antibody induction were studied. Four patient cohorts were investigated; 50 with TCMR, 50 with aAMR and 57 with cAMR. Patients were screened at the time of biopsy for IgG and IgM HLA DSAs and compared with 50 control, unsensitised renal transplant recipients with normal surveillance biopsies. The diagnosis of rejection was based on Banff 2015 criteria. Graft survival was compared in each cohort and categorised as; IgG-/IgM-, IgG+/IgM-, IgG-/IgM+ and IgG+/IgM+.

Results: The incidence of IgM DSAs in the aAMR group was 10/50 (20%), 5/50 (10%) in the TCR group, 18/57 (32%) in the cAMR group and 6/50 (12%) in the normal controls.

Figure 1 shows that graft survival in the presence of an IgM DSA was not inferior in the aAMR/TCR groups when compared to controls and only significantly inferior in those groups with an IgG DSA (p=0.005).

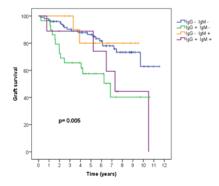
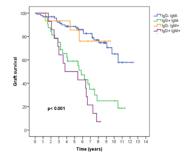


Figure 2 shows that graft survival in the presence of an IgM DSA was not inferior in the cAMR/TCR when compared to controls and only significantly inferior in those groups with an IgG DSA (p<0.001).



Discussion: This study demonstrates that the presence of an IgM DSA alone or in association with an IgG DSA does not result in inferior outcomes. It is the presence of an IgG DSA in allograft rejection which significantly reduces graft survival.

Human neutrophil antibodies are associated with severe early rejection in kidney transplant recipients

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Introduction: Non-HLA antibodies have a range of effects on transplant outcome. The effects of donor specific antibody (DSA) to Human neutrophil antigens (HNA) has not been documented. HNA-3 is expressed on many cell types including the kidney. 5% of Caucasian's are homozygous for HNA-3b and at risk of allosensitisation to HNA-3a. We report experience in four patients undergoing kidney transplant with pre-formed HNA-3a DSA.

Methods: All patients are Caucasoid females, parous, undergoing first transplant in 3 different UK centres. Each had a positive pre-transplant donor T and B cell flow cytometric crossmatch (FCXM). Autologous FCXMs were negative in all cases. Recipients and donors were HNA genotyped and recipients tested for HNA-3a and HLA antibodies.

Results: HNA-3a IgG Ab was detected in all recipients. HNA genotyping by PCR-SBT showed all recipients were HNA-3b3b. All donors expressed HNA-3a. No recipients had HLA-DSA at the time of transplant.

<u>Patient 1</u> Deceased donor (DD) transplant 2006, ATG induction therapy, severe vascular rejection in first 2 weeks, currently stable graft function

<u>Patient 2</u> Living kidney donor transplant 2013, ATG induction therapy, good initial function, rise in proteinuria over 3 years, eGFR now 28, biopsy pending.

<u>Patient 3</u> DD transplant 2016 received basiliximab, tac/MMF/pred immunosuppression, acute antibody mediated rejection day 5 post-transplant treated with ATG, graft failed after 10 months.

<u>Patient 4</u> DD transplant September 2017, basiliximab, tac/MMF/pred immunosuppression. eGFR currently 34, biopsy considered.

Discussion: Antibodies to HNA-3a cause a positive FCXM in allosensitised HNA-3b homozygous individuals. A positive FCXM will occur with the majority of donors as 95% of individuals express HNA-3a. The pathological significance of HNA-3a antibodies should be carefully considered prior to kidney transplantation. Despite ATG induction, two patients had severe early rejection and one has probable chronic transplant glomerulopathy.

Quality in transplantation presentations 16:15. Thursday 15th March – The Auditorium

032

Outcomes of recipients of a kidney transplant who have been suspended from the national kidney transplant waiting list (NKTWL)

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Introduction: A significantly increasing proportion of patients activated on the NKTWL end up being suspended. It is not known if the event of a suspension is associated with survival after transplantation. In this study, we aim to identify the association between suspension from NKTWL and post-transplantation outcomes.

Methods: We linked the UK Transplant Registry to Office for National Statistics mortality data and identified all patients who had undergone a deceased donor kidney transplant between 1/1/2000 and 31/12/2010. We categorised patients by whether they had been suspended for a continuous period of 30 days or more during their entire registration until transplant. We then stratified both cohorts by donor type (DBD/DCD) and produced Kaplan-Meier estimates to examine patient and graft survival rates. Cox proportional hazards regression models were also developed to investigate the effect of suspension after risk adjustment for donor and recipient factors.

Results: A total of 12,238 deceased donor kidney transplants were included. On unadjusted analysis, 5-year graft survival showed no statistically significant difference between the suspended (n=3285) and non-suspended (n=8937) groups either on direct comparison (log rank test p=0.08) or when stratified by donor type (log-rank test p=0.30). Following case-mix adjustment, patients who experienced suspension from the waiting list had a statistically significantly worse graft survival (HR 1.18 95% CI: 1.05-1.32). In the unadjusted analysis, 5-year patient survival was also significantly worse for suspended patients, both on stratification of donor type (log rank test p<0.01, figure 1), and following case-mix adjustment (HR 1.21, 1.08-1.37).

Discussion: The event of suspension is associated with worse outcomes when analysing survival after transplantation. In patients who have experienced a prolonged suspension event, enhancing their fitness for transplantation and optimising organ utilisation is paramount. Earlier prioritisation of patients at risk of suspension should be carefully considered.

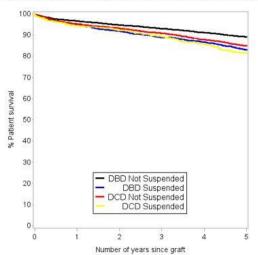


Figure 1: Patient survival following transplantation stratified by suspension event and donor type (n=12,230)

Predictors of outcomes in a HLA incompatible renal transplant cohort

<u>Trijntje Rennie</u>¹, Richard Battle², David Turner², Paul Phelan¹, Wendy Metcalfe¹, Lorna Henderson¹

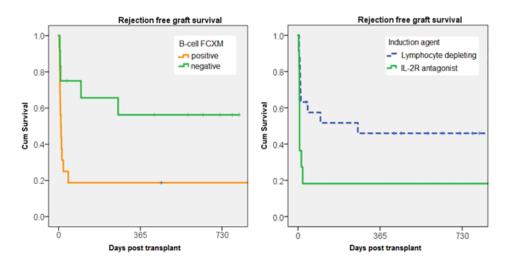
Introduction: Kidney transplantation in the presence of donor-specific HLA antibodies is an option for difficult to match patients. Various treatment regimens are available and predicting the risk of rejection and/or worse outcomes remains a challenge. We reviewed HLAi transplants outcomes 2011-2017.

Methods: Patients with current or historic DSA defined by Luminex were included. Pre-transplant recipient characteristics (age, gender, donor source, previous transplants, T and B-cell flow cytometry crossmatch (FCXM), cumulative MFI, induction and desensitisation details) were analysed retrospectively. Mortality data, eGFR, histological diagnosis of T-cell Mediated Rejection (TCMR) and Antibody-Mediated Rejection (AMR) were collected.

Results: Thirty patients underwent HLAi transplant; mean age 45 years; 57% female, 70% re-transplants. All were CDC-crossmatch negative, 68% were FCXM positive of which 89% B-cell FCXM+. Median cumulative MFI at transplant was 3018 (IQR 1210-6669). Eleven out of thirteen living donor recipients were desensitised with plasma-exchange. All transplant recipients received induction therapy with IL-2R antagonist (IL2Ra, n=11) or lymphocyte depleting agent (LDa, n=19). Mean follow up was 2.5 (SD±1.4) years. Fifteen patients developed AMR and five TCMR at a mean of 28 (SD±67) and 77 (SD±112) days. Effect of AMR on eGFR is shown in the table. BFCXM+ was associated with increased risk of AMR (p<0.001). Rejection-free graft survival at 1 year was 19% in BFCXM+ and 57% in BFCXM- recipients (p<0.05), 18% versus 45% following IL2Ra and LDa induction (p<0.05). Graft survival at 1 year was 78% in patients with AMR, compared to 100% without AMR (p=0.05).

Discussion: B-cell positive FCXM and IL-2R antagonist induction were associated with increased risk of AMR, inferior graft survival and reduced eGFR following HLAi transplantation. Despite 50% AMR rate, overall graft survival was 89% with mean eGFR of 47ml/min/1.73m² at 1 year.

		Time post transplant					
		3 months 6 months 12 months					
		(n=28) (n=25) (n=25					
eGFR,	Whole cohort	49 (23)	51 (26)	47 (27)			
ml/min/1.73m ² ;	AMR	38 (23)*	37 (23)*	31 (23)*			
mean (SD)	No AMR	59 (18)*	61 (23)*	62 (22)*			



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Skin cancer awareness and compliance with photo protection in long-term kidney transplant patients:a single centre cohort analysis

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Introduction: Long-term kidney transplant recipients (LKT) are up to 200 times more likely to develop non-melanoma skin cancer (NMSC) than age-matched general populations. Underlying mechanisms affecting development of NMSC include Fitzpatrick skin type (FST 1-6) and UV Light exposure. Primary prevention of NMSC by reducing UV sun exposure and using appropriate photo protection is recommended.

Aims: (i) catalogue FST and prevalence of NMSC in all LKT attending our Annual Review Transplant Clinic (ARTC), (ii) evaluate levels of skin cancer awareness and compliance with photoprotection in this cohort.

Methods: Between 01/09/16-31/08017 all LKT attending our ARTC completed screening measures including: Sun Photoprotection, Skin Cancer Awareness Questionnaire (SCAQ).

Results: There were N=307 screening encounters. N=184(60%) were male and N=123(40%) were female. Mean age was 53.2 years (range 22-81years). Mean GFR was 49mL/min (range 5-116mL/min). N=80(26%) patients had at least one NMSC. N=280(91.1%) LKT received advice about protecting skin from sunlight. Of those N=103(36.9%) remember having advice before their transplant, N=118(42.1%) said they had no advice prior to transplantation. N=261(85%) LKT reported receiving skincare advice after their first transplant. 100% of patients with FST1, but only 75% of patients with FST6 reported receiving advice about protecting skin. 92.4% of patients with FST1 usually/always avoid sun exposure in contrast to only 30.8% of FST6 patients. Sun exposure avoidance correlated with receiving skin protection advice. N=258(83.9%) LKT reported using sunscreen, however only N=33(10.8%) applied sunscreen daily, and N=107 (55.4%) applied sunscreen only when it was sunny. 100% of patients with FST1 used sunscreen in contrast to only 41.7% of patients with FST6.

Conclusion: NMSC is a significant cause of morbidity in LKT. Nearly all LKT attending our ARTC received advice about protecting skin from sunlight. However skin cancer awareness and compliance with photoprotection varies considerably with FST.

Pancreas & islets presentations 16:15, Thursday 15th March – Syndicates 1&2

035

Peri-transplant glycaemic control as a predictor of pancreas transplant survival

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Introduction: The impact of peri-transplant glycaemic control on outcomes after pancreas transplantation is unknown. Our aims were to relate peri-transplant glycaemic control to survival and improve our understanding of peri-transplant dysglycaemia by describing its relationship with inflammation.

Methods: Peri-transplant glycaemic control profiles over the first 5 days postoperatively were determined by the area under the curve (AUC) of daily means and the coefficient of variation (CV). Serial blood samples were obtained at multiple time points over the first 3 days post-operatively to measure levels of circulating inflammatory mediators (TNFα, IL6, IL10, and CRP). Covariate adjusted Cox regression determined whether AUC and CV predicted graft survival and linear regression assessed relationships between inflammatory mediators and glucose levels. Survival models were adjusted for donor variables: insulin requirement; donors after circulatory death status and body mass index.

Results: Between 2010 and 2015, we collected 7606 glucose readings from 125 pancreas transplant recipients, and inflammatory mediator data in a subgroup (n=45). Median (IQR) for glucose AUC: 32 (30-35) mmol.day/L and glucose CV: 96 (81-111) %. During a median follow-up of 3.6 years, graft failure occurred in 36 (29%) recipients. Technical graft failures within 5 days were excluded (n=12). Glucose AUC predicted graft loss (adjusted HR (95%CI): 1.16 (1.05-1.28) p=0.004). Glucose CV also predicted graft loss (adjusted HR (95%CI): 0.96 (0.93-0.99) p=0.002). No significant relationships between inflammatory mediators (TNFα, IL6, IL10, and CRP) and glucose levels nor survival were identified.

Conclusion: Peri-transplant hyperglycaemia and/or variability could be a cause of graft loss through glucotoxicity or it could be a consequence of early graft dysfunction - predicting later graft loss. Intervention studies could assess whether better glycaemic control in pancreas transplant recipients can improve graft survival.

Alemtuzumab versus basiliximab based immunosuppression regimes: incidence of de-novo donor specific anti-human leucocyte antigen (HLA) antibodies (DSA) in simultaneous pancreas kidney (SPK) transplant patients

Aditya Kanwar¹, Manushi Vyas¹, Rohan Thakkar¹, Aimen Amer¹, Giorgio Alessandri¹, Ibrahim Ibrahim¹, John Moir¹, Jennifer Logue¹, James Shaw², Jeremy French¹, Colin Wilson¹, Gourab Sen¹, David Talbot¹, Alison Brown³, Derek Manas¹, Vaughan Carter⁴. Steven White¹

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Introduction: De-novo Donor Specific Human Leucocyte Antigen(HLA) Antibodies (DSA) are detrimental to organ transplants. We aim to compare two different Alemtuzumab versus Basiliximab regimes with regard to the development of DSA and their long-term outcomes in SPK patients.

Methods: A retrospective analysis between 2003 – June 2016. Alemtuzumab based regime(steroid free) was used from 2008 onwards. DSA were measured as early(within 2 years) and late(>2 years post-transplantation). HLA antibody testing was performed as per clinical need using a Luminex 200 flow cytometer. Data was analysed using Microsoft Excel 2011 and SPSS23. Chi-square test was used to compare the groups.

Results: A total of 83 SPK transplants were performed Alemtuzumab(n=53) and Basiliximab(n=30). For early DSA, 20 patients were tested in the Basiliximab group; none developed DSA. In contrast, 34% patients(14 out of 41 tested) in the Alemtuzumab group developed early DSA(p=0.009). Of those 14 patients, 3(21%) lost their kidney, 6(43%) lost their pancreas and 3(21%) eventually died. For late DSA, 18 patients were tested in the Basiliximab group and 3(17%) were found to be positive. 2/3 patients suffered pancreas graft loss, 1 lost the kidney and 1 died(post-transplant lymphoproliferative disorder). In the Alemtuzumab group, 12(41%) out of 29 tested developed DSA(p=0.077). Out of those 12 patients, 4(33%) kidneys and 5(42%) pancreas were lost and 3(25%) deaths were recorded. 11(92%) out of the 12 who were positive for late DSA, had early DSA as well.

Conclusion: Patients on an Alemtuzumab based regime had a significantly higher incidence of early DSA. A higher proportion continued to develop late DSA. The presence of DSA was associated with very high rates of both pancreas and kidney graft loss.

Quality of life after simultaneous pancreas-kidney transplantation

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Introduction: A Simultaneous Pancreas-Kidney transplant (SPK) may be offered to individuals with type 1 diabetes and diabetic nephropathy. SPK is associated with a significant risk of morbidity, however can be life changing for those with a successful transplant. The aim of this study was to compare quality of life outcomes in SPK recipients compared to recipients of kidney transplants alone.

Methods: A questionnaire was sent to deceased and live donor transplant kidney recipients (DDR and LDR, respectively) transplanted between January 2013 and December 2016 and SPK recipients transplanted between January 2013 and June 2017. The questionnaire included validated measures of life satisfaction, mood, distress and health-related quality of life (HRQoL). Participants were additionally asked about benefit, expectations, regret and whether their life had changed for the better since the transplant.

Results: 115 responses were received (18 SPK, 34 DDR, 63 LDR). The average time since transplantation was 27.2 months (SD 11.932). There was a statistically significant difference in age between SPK and DDR (47.5 years vs. 57.0 years; p=0.009). There were no significant differences in life satisfaction (p=0.115), distress (p=0.592), mood (p=0.896) or HRQoL (p=0.180) between the 3 groups. There were also no significant differences in perceived benefit or regret. Expectations had been met equally between the different groups and there was no significant difference in perceived life change.

Discussion: This study has demonstrated that quality of life outcomes after successful SPK are comparable to those after both live and deceased donor transplantation. Quality of life may therefore provide a valuable role in the selection of potential candidates for listing. More sophisticated studies exploring the psychosocial issues inherent to SPK are warranted due to the lack of available data. Specific focus should be on those with suboptimal clinical outcomes to truly ascertain the level psychosocial morbidity within this group of patients.

MODERATED POSTERS

WEDNESDAY 14TH MARCH

18:30

THE EXHIBITION HALL

P001 - P048 &P056

Do we need to worry about EBV DNAemia in the late post-transplant period?

Kanika Daga², Muir Morton¹, Paul Klapper², Michael Picton¹, Pamela Vallely²

Background: Despite detectable Epstein-Barr virus (EBV) in blood, kidney transplant patients (KTR) may have no apparent clinical consequence. This study aims to explore the clinical relevance of EBV DNAemia in the late post-transplant period.

Methods: This observational study recruited 60 KTRs, with a history of previous undetectable (UVL) (n=19), transient/low (LVL) (n=20), and high (HVL) (n=21) whole blood (WB) EBV levels. Patients were matched for age and time from transplant. Symptom enquiry, plasma DNA, cervical lymphadenopathy (on ultrasound), and lymphocyte subsets were assessed and clinical outcomes were determined at long-term follow-up.

Results: There was no significant difference in symptoms between groups at recruitment. HVL patients had higher anti-VCA antibody levels (p=0.03) and more individuals with ≥2 cervical nodes >5mm than other groups (p=0.049). Plasma DNA was detectable in those with WB DNAemia ≥log 3.47 copies/ml, and was associated with lower CD4:8 ratios (p=0.041). CD19 numbers, while low in 66% of patients, were not significantly different between EBV groups. Mycophenolate usage was lowest in the HVL group. UVL patients had lower tacrolimus and ciclosporin trough levels (p=0.03).

Median follow-up time was 6 years with no difference in patient or graft survival between groups. HVL patients had the only case of PTLD, higher rates of cancer, skin cancer, death and admissions, but lower diabetes incidence during follow-up. Numerically, plasma-positive patients had higher mortality and malignancy rates than plasma-negative patients.

Lymphocytes $<1x10^9$ /L, low CD3 and CD19 numbers were associated with higher mortality (p=0.01), but not cancer. Low B-cell counts protected from diabetes development (p=0.005).

Conclusions: In this exploratory study, EBV patterns had no clear impact on graft or patient survival. Chronic high whole blood and plasma viraemia may predict outcomes such as cancer development. Our study also identifies associations between lymphopenia and B-cell numbers with clinical outcomes post-transplant.

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BK virus nephropathy - a single centre experience over an 11-year period

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Introduction: BK polyoma virus is a significant cause of graft dysfunction after kidney transplantation. Although guidelines suggest monitoring for BK viraemia, this has not been adopted widely. Our unit has historically not screened for BK viraemia routinely except for HLAi and ABOi recipients. In this retrospective review, we studied the outcomes of BK virus infection over an eleven year period.

Methods: Sixty-seven patients were diagnosed with BK viraemia or biopsy-proven BK virus nephropathy (BKVN) between 2006 and 2017 (1306 patients received kidney transplants during this period; crude incidence rate 5.1%). BK DNA PCR blood test was done in the event of unexplained rise in S. creatinine and at the time of all allograft biopsies. BK PCR log value > 4 was considered significant.

Results: Sixty-six of 67 patients were taking tacrolimus and mycophenolate mofetil (MMF) at the time of BK diagnosis. Median time from transplant to significant viraemia was 5.1 months (2.3-33.1), with viraemia levels ranging from log 1.97 to log 9.53. Reducing or stopping MMF cleared the viraemia in 61% of patients and reduced to low levels in 31%. Five patients (8%) were treated with varying combinations of ciprofloxacin, leflunomide, IV immunoglobulins and switching to ciclosporin. Death-censored graft loss occurred in 13 patients - 7 attributed to rejection and 1 to BKVN. S.creatinine level at BK diagnosis but not peak viraemia level, predicted graft loss (HR 1.1 per 10 units creatinine rise, p=0.01). 5-year graft survival rate was 83% (unit average 90%).

Conclusions: Despite testing for BK viraemia "for-cause" only, graft survival after BKVN was satisfactory although lower than average. A proposed screening strategy to identify BK viraemia at an earlier stage may improve graft outcomes.

The role of KIR2DS4 polymorphisms in BKV and acute rejection following renal transplantation

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Introduction: Natural Killer (NK) cells have been implicated in the pathogenesis of rejection, and their activation may be modulated by engagement of Killer cell Immunoglobulin-like Receptors (KIRs). The KIR gene is highly polymorphic and the inhibitory KIRs are activated in response to self HLA ('missing-self hypothesis'). Polymorphisms in KIR genes have been associated differential outcomes in infection and pregnancy. To date, the impact of KIR genotype on immune responses in renal transplantation has not been fully explored. We aimed to interrogate activating KIR2DS4 polymorphisms in kidney transplant recipients and to determine whether variation in this gene was associated with susceptibility to BK viraemia (BKV) or acute rejection.

Methods: Genomic DNA was obtained from n=854 kidney transplant recipients at a single centre between 2008-2014 and KIR2DS4 polymorphisms analysed via sequence specific primer polymerase chain reaction (SSP PCR).

Results: 1072 renal transplants were performed at our unit between 2008-2014, of which 157 (14.6%) developed BKV viraemia, 145 (13.5%) developed acute rejection (both cellular and antibody mediated) and 35 (3.2%) renal recipients developed both BKV and acute rejection. DNA was available or could be extracted from n=854 of these recipients. The KIR2DS4 full length polymorphism was more common in non-white renal recipients (25.3% vs. 12.9%), whereas the 22-base pair deletion variant was more commonly observed in the white renal recipient population (55.3% vs. 43.0%). No KIR2DS4 polymorphism was found to be significantly associated with BK viraemia (p=0.282) or with acute rejection (p=0.824).

Conclusions: KIR2DS4 polymorphisms do not significantly influence susceptibility to BKV or acute rejection in renal transplant recipients. However, the KIR locus is one of the most complex regions in the human of genome and we are currently exploring how other KIR polymorphisms influence transplant outcomes.

Association between donor:recipient BK viral serostatus and risk of BK viraemia post-transplantation

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Introduction: Development of BK nephropathy is a potentially devastating event associated with graft loss. In contrast to other clinically important viruses (e.g., CMV), donor/recipient BK serostatus is not routinely established. It is therefore unclear whether active infection post-transplantation is donor-derived or due to re-activation of latent virus. We investigated the BK serostatus of UK organ donors and examined the association of donor/recipient serostatus mismatch with development of BK viraemia post-transplantation.

Methods: Serum samples from 95 kidney donors, matched to 101 organs transplanted in our unit, were obtained from the QuOD biobank; 10 recipients of these organs had developed BK viraemia (>100 viral copies/ml). Donor serum was tested for BK IgG and viral DNA. Recipient clinical data, including development of BK viraemia, time to/duration of viraemia, and peak viral load, were collected. Pre-transplant serum samples from 26 matched recipients, 5 with documented BK viraemia, were similarly analyzed and linked to donor serostatus.

Results: Of 95 donors evaluated, only 46(48.4%) were seropositive for BK, none with detectable viraemia. 10/47(21.3%) patients who received kidneys from BK seropositive donors developed BK viraemia, versus 6/54(11.1%) patients who received kidneys from seronegative donors. The mean peak viral load was 100-fold higher in recipients of a kidney from a seropositive versus a seronegative donor (428331 vs 3293 copies/ml). Similar rates of BK seropositivity (14/26;53.8%) were seen in recipients pre-transplant. 4(33.3%) seronegative recipients developed viraemia compared to 1(7.1%) of seropositive recipients; 4/5(80%) were seronegative pre-transplant, all 5 received a kidney from a seropositive donor.

Conclusion: In our pilot study, BK viraemia rates were higher in seronegative recipients, and in patients who received kidneys from seropositive donors. Our data suggest that determining the donor/recipient serotype mismatch may be a useful tool for stratifying the risk of BK disease.

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Outcomes for live kidney donation: the Leeds experience

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Introduction: We aimed to analyse outcomes for live kidney transplant donors

Methods: NHS blood and transplant collects live kidney donor follow-up data including estimated GFR (eGFR), blood pressure (BP), proteinuria, antihypertensive medication and survival. We analysed outcomes at 1, 5 and 10 years post-donation and expressed results as summary statistics for all live kidney donors in Leeds since 2007.

Results: Of 653 donors, 28 had donated within the last year. We had data for 495 patients at 1 year, 256 patients at 5 years and 98 patients at 10 years. Mean age at donation was 45.8. 32 (4.9%) were altruistic donors and the remaining 621 (95.1%) were either living-related or non-related donors. Mean eGFR was >60ml/min/1.73m2 at all time-points following donation (table 1, figure1). Systolic BP was greater than 140mmHg in approximately 1 in 3 donors (32.1% at 1 year; 36.6% at 5 years, 34.8% at 10 years) with 5.7% at 1 year, 7.5% at 5 years and 6.2% at 10 years being prescribed anti-hypertensives (table 1, figure2). Only one donor died, 5-10 years following donation.

Discussion: These data suggest that, kidney function is well-preserved following living donation, with a low prevalence of chronic kidney disease. Although around a third of patients have documented hypertension, the use of anti-hypertensives is low.

Table 1: Live donor follow up data

Years post	Field	Mean	Minimum	Maximum	
transplant					
1 (n=495)	eGFR	60	34	>90	
	Systolic BP (mmHg)	129	80	191	
	Diastolic BP	76	50	125	
	Haematuria (%)	9.1			
	Proteinuria (%)	7.1			
	Antihypertensives (%)	5.7			
5 (n=256)	eGFR	64	35	>90	
	Systolic BP (mmHg)	130	92	185	
	Diastolic BP	77	52	109	
	Haematuria (%)	7.8			
	Proteinuria (%)	4.7			
	Antihypertensives (%)	7.5			
10 (n=98)	eGFR	68	42	>90	
	Systolic BP (mmHg)	134	100	181	
	Diastolic BP	78	54	104	
	Haematuria (%)	3.1			
	Proteinuria (%)	3.1			
	Antihypertensives (%)	6.2			

Figure 1:

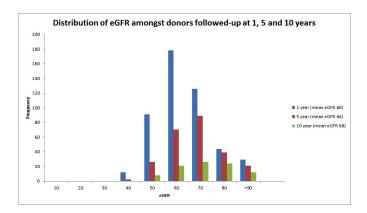
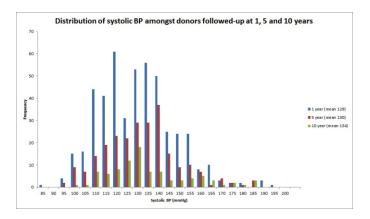


Figure 2:



Incidence, recurrence and survival post chemotherapy in renal transplant recipients with post transplant lymphoproliferative disorder: single center study

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is the third most common malignancy complicating solid organ transplantation. Degree of T cell suppression, pre-transplant malignancy, EBV serostatus and time post-transplant have been implicated as risk factors. We studied incidence, time of onset, type and site, survival post chemotherapy and rate of recurrence in our population of stable renal transplant recipients.

Methods: Single, centre retrospective study of renal transplant recipients (n=450) over a 30 year period.

Results:

Туре	Episodes	Chemotherapy
Polymorphic	3	Local resection only
Diffuse large B cell lymphoma	14	RCHOP/RVP + RCHOP/RCEOP
Large anaplastic T cell lymphoma	1	Local resection + CHOP
High grade NHL	5	RCHOP/R-EPOCH
Hodgkin's lymphoma	2	ABVD

Table 1: Type of PTLD and type of chemotherapy

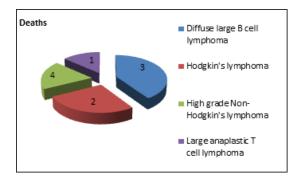


Figure 1: Distribution of PTLD in deaths

- 1. 20 patients developed PTLD at varying sites and times of onset.
- 2. 16% developed PTLD in the first year.
- 3. Median time of onset was 15 years post-transplant (range 0.3-26 years).
- 4. There were 25 episodes in the 30 year period, out of which 3 were recurrences.
- 5. Diffuse large B cell lymphoma was most common type (56%) and large anaplastic T cell lymphoma was least common (5%).
- 6. Site of development was along gastrointestinal tract in 85% of patients.
- 7. Extra nodal PTLD was found in 3 cases and involved CNS, heart and lung.
- 8. There were 7 deaths in total (33.33%) and poor survival was associated with older age of recipient, longer duration of transplant and type of PTLD.
- 9. Mean survival post chemotherapy was 44 months.

Conclusions: Patients remain at risk of developing PTLD irrespective of duration post-transplant. Due to varied sites of distribution, clinicians should have a low index of suspicion for diagnosis. Prognosis remains poor with aggressive forms although post chemotherapy, survival is better. Longer study period is needed to determine long term survival rates in the population studied.

Renal transplantation in sickle cell disease with and without exchange transfusion: a single centre experience

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Introduction: Renal transplantation offers the best outcome for sickle cell disease (SCD) patients with End Stage Renal Disease, although outcomes are poorer than in other groups. Regular exchange blood transfusions (EBT) improve fitness for transplantation and may reduce the risk of SCD-related allograft dysfunction. However, concerns over alloimmunisation with EBT potentially limit its widespread implementation.

Methods: Data were collected retrospectively on all SCD patients transplanted over 20 years and followed up at our unit.

Results: 10 SCD patients underwent renal transplantation between 1997 and 2017 (6 DBD, 2 DCD and 2 LD transplants). 5-year patient and graft survival was 80% and 50% respectively. 1 patient was on an EBT programme prior to transplantation. 6 patients were on an EBT programme post-transplantation. The median number of units of blood transfused/year in patients on an EBT programme was 30, as compared to a median of 8 units/year in patients not on an EBT programme. Median eGFR at 1 year and 5 years among those on an EBT programme was 39 and 18 mL/min/1.73m² respectively, as compared to 27 and 12 mL/min/1.73m² among those not on an EBT programme. Median cRF was 27% in patients not on an EBT programme and 18% in patients on an EBT programme. 2 patients developed *de novo* donor specific antibodies post-transplantation, one prior to starting on an EBT programme (with 3 previous pregnancies), and one 8 years after starting on an EBT programme. Incidence of biopsy-proven rejection was 50% in both groups.

Discussion: In this inevitably small cohort transplant outcomes were superior in SCD patients on an EBT programme to those not on such a programme, without any evidence of increased alloimmunisation or rejection. These results suggest that EBT programmes should be adopted more widely when transplanting SCD patients.

Short, long and ultra long-term patient and graft survival following kidney transplantation is progressively improving: the Irish experience

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Introduction: It is often quoted that while short term graft survival in kidney transplantation has improved in recent years it has not translated into a commensurate improvement in long term and ultra-long term patient or graft survival.

Methods: We analysed patient and graft survival for all adult first deceased donor kidney transplant recipients in Ireland with Kaplan-Meier methods. Of 5,000 kidney transplants over 52 yrs with 99% complete registry, N=3260 recipients were included in this study.

Results: See Table 1 and Table 2.

Discussion: Ireland has experienced a progressive improvement in both early, long and ultra-long term patient and graft survival following kidney transplantation.

Table 1: Recipient survival over the last 40 years.

Era	Number		Year post transplant % Survival							
transplanted	of	1	5	10	15	20	25	30	35	40
	recipients	%	%	%	%	%	%	%	%	%
2011 - 2015	548	98								
2006 - 2010	524	99	91							
2001 - 2005	481	96	90	79						
1996 - 2000	456	96	87	79	68					
1991 - 1995	481	94	83	68	54	44				
1986 - 1990	369	94	83	67	51	39	30			
1981 - 1985	195	90	78	69	53	44	38	30		
1976 - 1980	129	73	59	50	40	31	21	19	12	
1971 - 1975	77	51	39	31	24	17	16	15	13	11

Table 2: Uncensored graft survival over the last 40 years.

Era	Number	Year post transplant								
transplanted	of		% Survival							
	recipients	1	5	10	15	20	25	30	35	40
		%	%	%	%	%	%	%	%	%
2011 - 2015	548	97								
2006 - 2010	524	96	88							
2001 - 2005	481	93	83	67						
1996 - 2000	456	88	74	58	45					
1991 - 1995	481	86	69	48	34	26				
1986 - 1990	369	86	66	44	28	19	13			
1981 - 1985	195	68	55	44	33	26	21	15		
1976 - 1980	129	59	46	35	27	19	11	9	7	
1971 - 1975	77	38	26	17	10	7	5	4	3	3

Obesity and kidney transplantation: a single centre experience using a steroid sparing regimen

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Introduction: The question whether or not obese end stage renal disease patients should lose weight before being transplanted is a matter of debate. Aim of this study was to investigate the effect of obesity in kidney transplant recipients (KTR) treated with a steroid sparing regimen.

Methods: Data was prospectively collected on consecutive single organ KTR transplanted between 2014 and 2016. The patients were stratified according to their body mass index (BMI) using the WHO classification. As a measure of allograft function MDRD eGFR was used at 3, 6 12 and 24 months post-transplant.

Results: We included 370KTR: 125 female, median 52.7 years (range, 19-77 years), followed up for 30.25± 10.3 months (0-45 months). In total 154 KTR (41.6%) were underweight or of normal BMI at transplant, while 146 (39.5%) were overweight, and 70 (18.9%) were classified as obese [50 (13.5%) class 1, 11 (3%) class 2, 9 (2.4%) class 3]. Overweight and obese KTR had a higher incidence of pre-transplant diabetes (p=0.006), but no difference was found in new onset hyperglycemia post-transplant (p=0.18). There was also no difference in post-transplant hospital length of stay (p=0.48). Obese and overweight KTR had a significantly lower eGFR than underweight and normal BMI KTR at 3, 6 months, and at 2 years post-transplant. However, the rate of eGFR decline did not differ when BMI groups were compared, (p=0.55). Overall, 27 patients lost their grafts and 24 patients died during follow-up. Kaplan Meier analysis showed no difference in allograft loss between the different BMI groups (log rank p=0.8).

Conclusion: Overweight and obese patients were shown not to have inferior outcomes regarding renal function. We believe the steroid sparing regimen minimises the negative effect of obesity in patients and graft survival and our policy does not include a BMI cut off to waitlist end stage renal disease population

Outcomes of robot-assisted radical prostatectomy before and after renal transplant

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Introduction: Prostate cancer (CaP) is the second commonest male cancer and men over 40 with end-stage renal disease (ESRD) could have both diagnoses. Guidelines for renal transplantation (RT) suggest that CaP should be treated before RT and immune-suppression may affect CaP behaviour. We report our outcomes of robot-assisted radical prostatectomy (RARP) in this group.

Methods: A review of males over 40 with ESRD being considered for or having undergone RT since 2010 was conducted. Prior to activation on the RT list and annually post-RT, men over 50 and those over 40 with risk factors, have a PSA test, MRI and transperineal prostate biopsy if indicated. Those diagnosed with localised prostate cancer and RARP were included. Patient demographics, prostate-cancer disease features and outcomes are reported. Prior to RARP attempt was made to stent the RT-ureter to reduce injury.

Results: Between 2010-2017, 16 men (median age 58) with ESRD diagnosed with CaP underwent RARP: 6 prior to RT; 10 after. Mean blood loss was 323mls and mean operating time was 191 minutes. One patient suffered an intra-operative partial RT-ureteric injury. There were no Clavian-Dindo 3 or above complications. Final histology revealed median Gleason score 7 and no patient had GS 6. T-stage was T2b to T3b and no patient had a positive margin but one was node positive. 14/16 men have undetectable PSA at a median of 15 months' follow-up. In the 6 pre-RT men, 1 has successfully undergone RT, 4 are active on the waiting-list whilst one was excluded due to T3bN+ pathology and detectable PSA post RARP. RARP did not impact on creatinine or eGFR.

Discussion: Management of localised prostate cancer in ESRD prior to and after RT is complex and challenging. In our series, RARP has proven to be a feasible, safe and oncologically-effective allowing appropriate ESRD patients to progress to RT.

PSA surveillance in renal transplant recipients

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Introduction: PSA screening remains controversial with different outcomes reported on risks, costs and effect on cancerspecific mortality. High-risk groups, such as renal transplant recipients (RTR) however may benefit from screening, as immunosuppression increases the risk of developing malignancy. Between 2013-17, we implemented annual PSA screening for all male RTR, over 50 years or between 40-50 with CaP risk-factors, 5 years after transplant. We report outcomes of screening.

Methods: Prospective data was collected for all male RTR who underwent PSA screening between January 2013 and October 2017. If PSA was raised and remained elevated, MRI was performed, followed by transperineal (TP) biopsy if appropriate. Outcome measures were adherence to our screening protocol, incidence of CaP, disease features and management.

Results: 299 RTR underwent PSA testing (mean age 56 years) including 67 men out of the protocol (37 under 40, and 30 aged between 40-50 years without risk-factors). After repeat PSA test, none of these men required MRI or biopsy and were excluded from further analysis. Mean age for the screening population was 60 (range 40-86). 42 underwent annual PSA screening, 71 were screened 3-4 times in the 5-year period and 119 patients had PSA test 1-2 times. 26 patients over 40 had a raised PSA and 13 required an MRI. Following this, 11 patients underwent TP biopsy. 9 prostate cancers were identified (mean age at diagnosis 67; mean PSA 14ug/L); 8 were Gleason 7 or above. The patient with Gleason 6 CaP is on active surveillance. 4 patients underwent radical prostatectomy (with undetectable PSA); 1 had brachytherapy and 3 received hormones and radiotherapy.

Conclusions: PSA screening in RTR is appropriate due to a higher incidence of prostate cancer compared with age-matched UK population and higher grade disease. Patients were managed rapidly, potentially improving quality of life and overall survival.

A survey of the variation in practice in kidney transplantation across the UK: is standardisation necessary?

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Introduction: NHSBT has recently proposed standardising the tariff for kidney transplantation in the UK. The ATTOM study demonstrated variation in practice in listing patients for transplantation, but vagaries in patient management around the time of transplantation have not been investigated. The aim of this survey was to investigate national variation in practice in the peri-transplant period.

Method: A questionnaire addressing several aspects of deceased donor kidney transplantation was distributed to all 23 renal transplant units in the UK.

Results: 78% (18/23) of the centres responded to the survey. The salient findings are summarised in the table below.

Treatment	Number of Centres	% of Total
Back-up policy		
Routinely called in	2	11.11%
Virtual Crossmatch		
>75%	7	38.89
50-75%	3	16.67%
Theatre access		
24-hour transplant theatre	1	6.25%
Day-time transplant theatre	2	12.5%
Emergency theatre	13	81.25%
Hypothermic Perfusion	11	68.75%
Indications :		
Long cold ischaemia	4	36.3%
Trial	3	27.27%
DCD kidneys	1	6.25%
<u>Antibiotics</u>		
Co-amoxiclav	11	61.1%
Meropenem	2	11.11%
Amikacin	1	5.6%
Flucloxacillin & ertapenem		
	1	5.6%
Cefuroxime	1	5.6%
Ciprofloxacin	1	5.6%
Induction Agent		
Basiliximab	13	72.2%

Alemtuzumab	3	16.6%
Day-Zero biopsy		
Routine	9	56.25%
<u>Mannitol</u>		
Routinely given intra-operatively	4	33%
<u>Ureteric Stent Insertion</u>		
Routine	12	75%
Preferential	4	25%
Baseline imaging	13	72.2%
Doppler	10	76.9%
Transcan	3	23.1%
Length of hospital stay(days)		
4-6	8	44.44%
		38.89%
7-10	7	
-		

Discussion: These results highlight the disparity in practice in the peri-transplant period across the UK. Previous work from our unit has suggested that current tariffs do not accurately reflect the actual cost of kidney transplantation. As per NHSBT data, there is no gross difference in outcomes across centres. Therefore, standardising practice by adopting the most cost-effective options at various stages in the peri-transplant period may be the necessary first step before implementing a uniform tariff for kidney transplantation across the country.

Renal transplantation into resting ileal conduits or augmented bladders. Short and long term results in adults and children in two centres

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Introduction: Kidney transplantation in patients with urinary diversions are relatively uncommon. We report outcomes of renal transplantation drained into resting ileal conduits and augmented bladders in two large centres in both adult and paediatric recipients.

Methods: Retrospective analysis between 1980 and 2016 of recipients transplanted into diversions compared to the overall population transplanted during the same period. Primary endpoints were patient and graft survival at 1, 5, and 10 years. In addition rates of rejection, pyelonephritis, surgical complications were analysed.

Results: In a combined transplant group of 5311, there were 81 patients (65 adults and 16 paediatric) with 93 transplants draining into neobladders. In adults, graft survival at 1, 5 and 10 years was 95.6%, 68.9%, 47.5% vs 88.8%, 72.2%, 47.95%. Overall patient survival was 97.8%, 88.9%, 75% vs 95.6%, 86.5%, 68.8% at 1 year, 5 years and 10 years in patients with augmented bladders and ileal conduits versus the overall population. In the neo-bladder group, the rates of ureteral stenosis, pyelonephritis and rejection were 21.53%, 69.2%, 23.07% in adult patients vs 0%, 43.75%, and 43.75% in children. The Clavien Dindo score in the neo-bladder group was 1.76 (min = 1, max = 5) in adult patients and 1.06 (min = 1-max = 2) in children graft survival at 1 year, 5 years and 10 years was 94%, 88%, 64% vs 88%, 78%, 69% respectively in patients with modified bladder versus the overall paediatric population transplanted.

Conclusion: Renal transplantation in patients with augmented bladders or resting ileal conduits shows similar results in patient and graft survival when compared to transplantation into recipients with normal bladders. Postoperative complications are acceptable considering the complexity of these patients and does not affect outcomes. The risk of ureteral stenosis and pyelonephritis is higher but does not increase the risk of graft dysfunction.

Mismatching kidney size increases kidney allograft recipient mortality in a national population cohort analysis

Adam Arshad¹, James Hodson², Jay Nath³, Adnan Sharif³

Introduction: Kidneys from small donors may be at increased risk for graft failure if they are transplanted into larger recipients. However, the effect of mismatching kidney size on patient survival and graft function has not been clearly reported.

Methods: Data from the UK Transplant Registry was analysed for all patients receiving deceased donor kidney transplants (Jan 2003 - Jan 2015). We used weight as a marker for kidney size, and defined the following mismatch categories (calculated donor weight/recipient weight*100): [1] <75% (small donor/big recipient), [2] 75%-125% (same donor/recipient) and [3] >125% (big donor/small recipient). Risk-adjusted outcomes were assessed by multivariable analysis factoring for donor, recipient and transplantation variables using either general linear (creatinine), logistic regression (delayed graft function) or Cox regression models (patient and graft survival).

Results: Outcomes for 11,720 transplants were analysed, with weight mismatch stratified into three groups; [1] <75% (n=1,608), 75%-125% (n=7,247) and >125% (n=2,865). In multivariate analysis (with group [2] our reference), \log_{10} transformed general liner models demonstrated 1-year creatinine was higher in group [1] (fold difference 1.07 (95% CI 1.05-1.09), p<0.001) and lower in group [3] (fold difference 0.93 (95% CI 0.91-0.94), p<0.001). No significant difference in graft survival (death-censored or overall) or delayed graft function was identified between the mismatch groups. Surprisingly, we identified group [3] to be associated with an increased adjusted risk for recipient mortality (hazard ratio 1.21 (95% CI 1.05-1.40), p=0.009).

Discussion: As expected, mismatching donor/recipient kidney size in transplantation influences 1-year creatinine. However, our observation of increased recipient mortality after receiving a larger donor kidney is novel and not previously reported. While we can speculate on possible mechanisms, we suggest further investigation into this association given potential methodological limitations with the current analysis (e.g. confounding/missing data).

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The effect of donor nephrectomy in the older living kidney donor: single centre experience

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Background: Living kidney donor transplantation is the best treatment for ESRD and considered safe for the donor. We aimed to investigate short and medium-term outcomes of older donors post-donation.

Methods: We prospectively collected data on 579 consecutive live donors in Imperial College Transplant Center during 2002-2015. Donors were categorized as older(≥ 60years) or younger(<60years). We analyzed data for kidney function [24hr Creatinine-Clearance(CrCl) and CKD-EPI], proteinuria (24h-urine protein) and blood pressure control. Loss of GFR≥5ml/min/1.73m² per year was defined as progressive CKD. Hypertension was defined as BP>140/90mmHg on ≥2 separate occasions.

Results: A total of 579 (334 female) donors were included. Mean age at donation was 46.8±13 years. 44 (8.4%) donors were over 60 and followed-up for 38.18±26.7 months. Older donors had significantly lower CrCl (ml/min) pre-donation (mean 99 Vs 111, p=0.01) and the difference remained significant at 1 year (mean 68 Vs 84, p=0.01), 3 years (70 Vs 87), p=0.1) but not at 5 years (80 Vs 92,p=0.27). When CKD-EPIeGFR was used this difference persisted at 5 years (72 Vs 78, p=0.03). GFR<60ml/min/1.73m² at the end of follow up was more prevalent in older donors both with CrCl and CKD-EPIeGFR (p=0.013, p<0.001 respectively). However, there was no difference in progressive function deterioration between the two groups (p=0.4, p=0.3 respectively). Moreover, there was no difference in proteinuria between the groups (p=0.127). Although older donors were more likely to be hypertensive pre-donation, there was no significant difference in developing post-donation hypertension between the groups (p=0.19).

Conclusions: Donor nephrectomy in the elderly appears to be safe. As expected, our study shows that older donors have lower pre- and post-donation CrCl and CKD-EPleGFR, however this is not accompanied by more prevalent progressive kidney disease, proteinuria or post-donation hypertension.

Pre-donation body mass index associations with outcomes in living kidney donors: a single centre experience

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Background: Living kidney donor (LD) eligibility criteria have expanded as a result of excellent donor outcomes and increasing organ demand. However, considerable variability exists between transplant centres for the acceptable pre-donation BMI. We investigated short and medium-term outcomes of LD according to BMI pre-donation.

Methods: We prospectively collected data on 579 consecutive LD in Imperial College Renal and Transplant Center during 2002-2015. Donors were stratified according to WHO-BMI (Kg/m²) classification as: Underweight (U=16-18.5), Normal (N=18.5-25), Overweight(O=25-30), Moderately Obese(MO=30-35) and Severely Obese(SO>35). We analysed data for kidney function [using Creatinine-Clearance(CrCl) and CKD-EPI], proteinuria(24h-urine protein) and Hypertension. Loss of GFR≥5ml/min/1.73m² per year was defined as progressive CKD.

Results: A total of 579(334 female) donors were included. Full dataset was obtained for 549 donors. The number of patients per WHO category were: U=9(1.6%), N=178(32.4%), O=225(41%), MO=103(18.8%), SO=34(6.2%). CKD3 prevalence at the end of follow up was not different between donor groups based on CrCl(p=0.36). When CKDEPI-eGFR was utilized, there were more overweight and obese donors with CKD3(p=0.04). There was no difference in progressive function deterioration between the two groups with CRCL(p=0.3), while obese donors had more progressive kidney function deterioration as per CKDEPI-eGFR (p=0.015). Moreover, there was no difference in proteinuria between the groups(p=0.7). Although overweight and obese donors were more likely to be hypertensive pre-donation(p=0.04), there was no significant difference in developing post donation hypertension between the groups(p=0.67).

Conclusion: Donor nephrectomy in the overweight and obese is not accompanied by more prevalent post-donation proteinuria or hypertension. However, we showed conflicting results regarding kidney function and progressive deterioration at the end of follow up, a finding which requires further investigation and raises questions regarding the most appropriate kidney function evaluation test post donation.

Post-transplant lymphoproliferative disorder, a single centre experience

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is one of the most serious complications of chronic immunosuppression after an organ transplant and the second most common malignancy after skin cancer in adult kidney transplant recipients.

Methods: The aim of our study was to assess the incidence and the management of PTLD in our kidney transplant centre.

Results: Over a 30-years period, of the 1855 transplants that were performed and followed-up in our department, 53 patients developed PTLD (2.9%). Among them, 45 had diffuse large B cell lymphoma. This was mainly after the first transplant, (n=37, 82%) and in patients who received only kidney (n=38 (84%)). The majority (61%) were EBV seronegative at the time of transplantation. The patients developed PTLD in a median of 107 months [0-306] after the transplantation. Only 11 of them (25%) developed early PTLD (less than one year after the transplantation). Clinical presentation was abdominal symptoms for 63% the patients. The median EBV load was 2.9 logs, but 5 patients had a negative EBV load. All patients had reduction of their immunosuppression and 29 (64%) also received chemotherapy. Fifteen percent (n=7) of the patients developed an episode of rejection after the treatment of the PTLD. Overall 4% of patients had a recurrence of PTLD during the same transplant. Thirty-six patients (80%) survived after their PTLD. The median follow-up time was 5 years and 24 patients (53%) reached this five-years follow-up. Among them, 75% of patients (n=18) had a functioning kidney and 2 were re-transplanted.

Discussion: PTLD is a rare disease that responds well to reduction of immunosuppression with both good kidney and patient survival. Although it occurs more often in EBV seronegative patients, it needs to be suspected in all transplant patients particularly in patients with abdominal symptoms even if the EBV load is negative.

Large volume intraoperative fluid use in small (

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Introduction: With advances in surgical and medical transplantation, progressively younger children are being transplanted. There is no consensus and little evidence on the optimal intraoperative fluid volume/type and inotropic support in small recipients (<20kg). This retrospective cohort study provides insight into the differences in intraoperative fluid and inotropic support use between small and large recipients (>20kg).

Methods: Patients transplanted between 2014-2017 were identified from a local transplant database at the UK's largest paediatric transplant Centre. Small recipients were compared to randomly selected large recipients. We compared the volume of fluid required (mean percentage of dry weight), type of fluid used and inotropes required intra-operatively between the groups. Student's T-test and Fisher's test were used for analysis. Further analysis on <20kg group assessed the impact of intraoperative management on post-operative outcomes: length of PICU admission and dependence on inotropic support post-operatively.

Results: Twenty-five small recipients (mean weight 14.9kg, SD2.7kg) were compared with twenty-five large recipients (mean weight 48.6kg, SD 21.9). Small recipients received significantly higher volumes of fluid than large recipients (mean 15.4%(SD7.5%) vs. 6.8% (SD2.4%), p<0.001) and received significantly more colloids intra-operatively (73.9% vs. 26.1%, p=0.001). Mean fluid requirement for small recipients was 154ml/kg (range 63.7-333.3ml/kg) compared with 67.5ml/kg (range 32.6-114.3ml/kg) for large recipients. 96% of small recipients required intraoperative inotropes compared with 83% of large recipients (not statistically significant, p=0.142). Mean stay on PICU for small recipients was 66.3hours (SD110.2 hours) with mean dependence on inotropic support being 24.5hours (SD 19.6 hours). Death-censored graft survival was 100% at 1 year (1 patient died from sepsis 8 months post-transplant).

Discussion: This data suggests that small recipients require larger volumes of intra-operative fluid and more colloids than large recipients. It also confirms that high fluid volumes and colloids are well tolerated by this group with excellent post-operative outcomes.

The benefit of dedicated low clearance transplant clinics for patients with failing kidney allografts

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Introduction: Recipients with failing kidney transplants (RFKT) require tailored care from a transplant and low clearance perspective. The British Transplant Society recommends the use of dedicated low clearance transplant clinics (LCTC) to manage these patients, however there is limited evidence as to their benefit versus general transplant clinics. To investigate this further, this retrospective study compared the management of two groups of kidney transplant recipient at a large transplant centre; patients managed in a dedicated LCTC versus similar patients in the general transplant clinic.

Methods: All transplant patients with an eGFR ≤20ml/min over a six-month period were included in the analysis. All transplant patients are followed up in two general transplant clinics, but one transfers RFKT into a dedicated LCTC while the other manages RFKT within the general clinic. We compared the following parameters; renal replacement therapy counselling, hepatitis B vaccination, clinical and biochemical parameters. Statistical analysis was undertaken with SPSS (version 24).

Results: Data for 141 patients was analysed (61 in LCTC, 80 in general transplant clinic). There was no significant difference in eGFR (p=0.120) or age (p=0.200) between the LCTC and general transplant clinic cohorts. A significantly greater proportion of LCTC versus general transplant patients had received documented discussions regarding their preferred modality of dialysis (98.3% versus 54.3% respectively, p<0.001), hepatitis vaccine status (65% versus 17.3% respectively, p<0.001) and retransplantation status (80% versus 58% respectively, p=0.006). No significant difference was noted between patients in blood pressure, haemoglobin, bicarbonate, phosphate or parathyroid hormone checks.

Discussion: Our data supports the use of dedicated LCTC to focus attention on renal replacement therapy counselling for RFKT patients. Further work is warranted to investigate if such clinics prolong graft longevity or improve patient satisfaction.

Bone health after kidney transplantation: a single centre audit

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Introduction: Kidney transplant recipients are at a higher risk of osteoporosis due to the prevalence of long term glucocorticoid use as part of immunosuppressive regimes. Furthermore they may have pre-existing renal bone disease and deterioration in bone health as graft function declines.

Methods: We conducted a retrospective audit of 221 renal transplant recipients, looking at audit standards set out by the renal association's clinical guideline in post-operative care in kidney transplant recipients. Data on Bone Densomitry (DXA) scans, risk factors for osteoporosis, biochemical markers of bone health and use of medications such as bisphosphonates and calcimimetics was recorded. DXA scan data including T-Scores and FRAX scores was used to look at bone mineral density and estimate the 10 year risk of osteoporotic fractures. The data was analysed and stratified according to the stage of CKD.

Results: Patients across stages of CKD 2T-5T were found to have evidence of osteopenia or osteoporosis at the femoral neck based on T-Score on DXA. The average risk of a major osteoporotic fracture (MOF) was 9.6%, however 5% of patients were found to have a MOF risk >20%. Based on recommendations from DXA scans 15% of patients were on bisphosphonates while another 9.5.% were on a drug holiday. Calcimimetics were required in 3% of patients for hyperparathyroidism. In the osteoporotic group, 6 patients were at CKD Stage 4T/5T and were on a bisphosphonate.

Discussion: We identified that low BMD is common in this group and the use of bisphosphonates often indicated although not always recommended. The usefulness of DXA for patients with eGFR <30ml/min is debated. Assessing bone health in this group of patients is therefore difficult given the lack of consensus on how best to monitor and assess bone mineral density. Bone specific ALP and bone biopsy may be required to guide treatment.

Cochrane meta-analysis; hypothermic machine perfusion prevents delayed graft function in DBD and DCD kidney transplant

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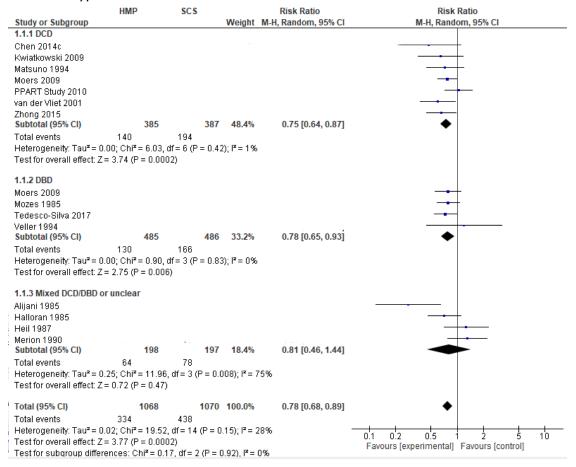
Introduction: There remains a lack of consensus as to whether hypothermic machine perfusion (HMP) is superior to static cold storage (SCS), especially in DBD transplantation. This review aimed to examine the effect of HMP versus SCS by meta-analysing the evidence from randomised controlled trials (RCTs).

Methods: We searched the Cochrane Kidney and Transplant Specialised Register using terms relevant to this review. All RCTs and quasi-RCTs were included in our meta-analysis. Two authors reviewed the identified studies. The primary outcome of interest was the incidence of delayed graft function (DGF), with primary non-function (PNF) and cost-effectiveness as secondary outcomes. A subgroup analysis was performed comparing results from donors after circulatory death (DCD) versus donors after brain stem death (DBD). Statistical analyses were performed using the random effects model and results expressed as relative risk (RR).

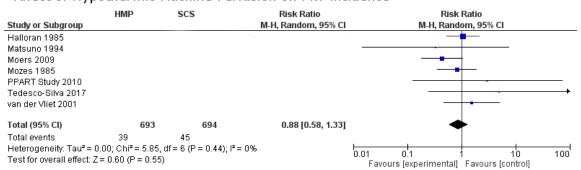
Results: 14 RCTs (2138 patients) were included in our primary analysis. Overall, there was a significant reduction in the incidence of DGF when HMP was used; RR 0.78 (0.68-0.89, P=0.0002). In subgroup analysis, HMP significantly reduced DGF in the DCD group (772 patients from 7 studies); RR 0.75 (0.64-0.87, P=0.0002), as well as in the DBD group (971 patients from 4 studies); RR 0.78 (0.65-0.93, P=0.006). The number of perfusions required to prevent one episode of DGF was 7 and 14 in DCD and DBD grafts respectively. Seven studies (1387 patients) reported PNF rates, but meta-analysis failed to demonstrate a difference between storage methods; 0.88 (0.58-1.33, P=0.55). Two studies performed economic evaluation, both reported cost savings with HMP.

Discussion: Hypothermic machine perfusion does reduce the incidence of DGF in recipients of DCD and DBD kidneys. This is the first meta-analysis to report a significant effect in DBD kidneys. Further trials comparing cold storage and HMP are not required in kidney transplantation.

Affect of Hypothermic Machine Perfusion on DGF incidence



Affect of Hypothermic Machine Perfusion on PNF incidence



Normothermic perfusion depletes inflammatory leukocytes in human donor kidneys

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Introduction: Passenger leukocytes that migrate from donor kidneys present alloantigen to the central immune system and this can stimulate acute rejection. This paired study aimed to elucidate the effect of removing passenger leukocytes during a period of *ex-vivo* normothermic perfusion (NP).

Methods: Five pairs of human discard kidneys underwent one hour of NP with a red cell based perfusate at 36°C. One kidney from each pair had a leukocyte filter incorporated into the perfusion circuit (WCF) and the other acted as a control. Renal blood flow (RBF) was measured throughout EVNP and total urine output recorded. Tissue samples were taken at the start and end of EVNP for RNAseq analysis. Leukocytes were isolated from the filter and analysed by flow cytometry.

Results: There was no significant difference in the level of RBF (Control, 63.5±30.8ml/min/100g vs WCF, 72.2±65.9ml/min/100g; P=0.797) or in the total amount of urine produced between the groups (Control, 188±154ml vs WCF, 168 ±146ml; P=0.837). Over 700 genes were up-regulated in both groups after EVNP. Gene ontology analysis showed an increase in inflammatory pathways. However, there was no significant difference between the groups. A large population of leukocytes were captured by the filter. Forty percent of CD45+ live cells were CD3+ T cells. Neutrophils (CD15+) and B cells (CD19+) were also observed, at 17% and 5% respectively.

Conclusions: Passenger leukocytes can be removed during NP by targeted filtration. This technique has therapeutic potential to reduce the immunogenicity of transplanted kidneys.

Normothermic machine perfusion parameters correlate with early allograft function in DBD and DCD kidney transplants

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Introduction: Normothermic machine perfusion (NMP) is a new technique that utilises extracorporeal circulation technology to assess and re-condition kidneys prior to transplantation. This study is the first comparison of NMP for kidney transplants from brain death donors (DBD) and circulatory death donors (DCD).

Patients and methods: Immediately prior to transplantation, kidneys underwent 60 minutes of NMP using an oxygenated red cell-based solution at 36°C. During NMP kidneys were scored from 1 (highest quality) to 5 (lowest quality) according to macroscopic perfusion, renal blood flow and urine output. NMP score was correlated with clinical outcome in DBD and DCD kidneys.

Results: 28 DBD and 38 DCD kidney transplants were performed after NMP. Donor and recipient demographics were similar between groups. NMP scores were as follows: DBD group - score 1 (n=19), score 2 (n=4), score 3 (n=5); DCD Group score 1 (n=15), score 2 (n=14), score 3 (n=9); (χ^2 =5.22, P = 0.07). The delayed graft function rate was 2/28 (7%) in DBD kidneys and 14/38 (37%) in DCD kidneys (P = 0.008). There was one primary non-function (PNF) in the DCD group due to renal vein thrombosis 7 days post-transplant. NMP score was negatively correlated with improved early allograft function measured by recipient serum creatinine at day 7 (r^2 = 0.179 P=0.0009) and one-month post-transplant (r^2 = 0.121 P=0.006).

Conclusion: DCD kidneys had poorer quality scores during NMP and this was reflected in a higher rate of DGF. NMP can be used to predict early renal allograft graft function.

Twenty-four hour normothermic perfusion of discarded human kidneys with urine recirculation

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Introduction: Normothermic kidney perfusion for 24 hours or longer could offer significant clinical advantages. It would enable clinicians to investigate the condition of the renal parenchyma before deciding for implantation.

Methods: We established a normothermic kidney perfusion prototype, with the objective of perfusing human kidneys for 24 hours. Urine produced during perfusion was recirculated.

Results: Ten clinically-declined kidneys were perfused, five from donors after brain stem death (DBD), five from donors after circulatory death (DCD). Median cold ischemia time prior to perfusion was 37.4±18.1 hours in DBDs and 41.2±16.22 hours in DCDs. There was evidence of stable and physiological functional parameters, including arterial flow, pressure, pO₂, pCO₂ and pH. There was effective urine production in both DCDs and DBDs (596.3±138.3ml vs. 543.1±195.4ml). Arterial flow was comparable in both groups, 365±37.6 ml/min in DCDs and 305.3±53.3 ml/min in DBDs. Physiological mean arterial pressures were maintained; 70.9±49 mmHg in DCDs and 84.3±7.1 mmHg in DBDs. In DCDs, pH during 24 hours of perfusion was higher than in DBDs; 7.58±0.1 vs. 7.28±0.04, p=0.02. All kidneys showed evidence of glucose consumption. Biomarkers, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), liver-type fatty acid-binding protein (L-FABP) and lactate dehydrogenase (LDH) were detected in the perfusate. Histologically, the presence of donor lesions and baseline conditions (IFTA, arterial fibroelastosis or arteriolar hyalinosis) was not associated with the development of acute tubular injury after NMP. In all but one kidney, the baseline tubular condition was preserved or improved.

Discussion: Normothermic machine perfusion (NMP) for of human kidneys for 24 hours with urine recirculation appears to be feasible and allows biomarker measurement. Clinical translational studies are now needed to demonstrate the clinical utility of this technology.

How should we manage positive cultures from renal transplant transport perfusion fluid?

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Introduction: In August 2016, NHSBT recommended routine microbiological testing of transplant perfusion fluid (TPF) from all abdominal organs. There is little evidence regarding significance and management of positive cultures. Following loss of a renal transplant as a result of Candida infection, we reviewed our practice.

Methods: Prospective follow up of recipients of renal and pancreas transplants at Freeman Hospital between September 2016 - October 2017 with culture-positive TPF. We asked all UK renal transplant units about their management of culture-positive TPF.

Results:

- 38 culture-positive TPF from 35 renal, 2 SPK, 1 PAK transplants 33 UKT donors
- 15/38 (40%) positive cultures were Candida 12 UKT donors
- All isolated Candida fluconazole-susceptible in vitro (11 C. albicans, 3 C. glabrata and 1 C. dubliniensis)
- 4 weeks oral fluconazole given in 13/15 (87%)

Infective complications in 2 renal transplants with C. albicans in TPF:

- Identical C. albicans isolated at transplant nephrectomy at 10/52 for mycotic aneurysm and graft fungal nephritis. Patient was **not** treated with antifungals
- C. albicans isolated from perinephric haematoma 13 days post-transplant, despite fluconazole from day 4

Feedback from 4 other UK units demonstrated variable isolation rate and management of culture-positive TPF:

- Birmingham ~10% Candida: variable duration of treatment
- Cardiff: treatment 14 days or longer
- Portsmouth <10% Candida; do not routinely treat Candida
- Royal Free ~2% Candida: treat for 6 weeks

Discussion: Routine cultures of TPF show our Candida isolation rate is significantly higher than the 3.7% previously reported¹. We now give 4 weeks antifungals when Candida isolated; defending no treatment is difficult in cases that subsequently develop serious infective complications such as mycotic aneurysm. The clinical significance of non-fungal isolates from TPF is debatable. Further guidance is necessary to facilitate a rational approach to managing culture-positive TPF across the UK.

References: Singh et al: Am J Transplantation 2012; 12: 2414–2428.

Cold pulsatile machine perfusion versus static cold storage in kidneys from donation after circulatory death: a multi-centre randomised controlled trial

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Introduction: Delayed graft function affects around half of all recipients of donation after circulatory death (DCD) kidneys in the UK and has a significant impact on recipient morbidity, hospital stay and costs. The benefits of cold pulsatile machine perfusion for storage and transportation of deceased donor kidneys are disputed. We conducted a randomised trial to compare outcomes of kidneys stored with machine perfusion (MP) versus cold static storage (CS). This is the largest UK randomised trial evaluating the use of machine perfusion in deceased donor kidneys.

Methods: This was an open, paired, multi-centre, randomised controlled trial that recruited recipients of DCD kidneys between May 2011 and April 2016. Comparison was made on an 'intention to treat' basis between the two kidneys from each donor and the primary outcome was delayed graft function (DGF).

Results: 102 patients were recruited into the study. Median donor age was 60 years (IQR 48-67), recipient age was 57 years (IQR 47-65) and cold ischaemia time was 13.8 hours (IQR 11.2-17.0) and well-matched across the trial groups. DGF was equally common 31/51 (60.8%) in both CS and MP groups. There were no significant differences between CS and MP for 'dialysis-free at 28 days' (CS 45/51(88.2%) vs MP 44/51(86.3%), p= 0.77), primary non-function (CS 1/51(2%) vs MP 0/51(0%), p= 1), slow graft function (41/51(80.3%) vs 39/51(76.5%), p= 0.63), one year death-censored graft survival (CS 94% vs MP 94%, p= 0.95), and one year patient survival (CS 95.9% vs MP 95.3%, p= 0.92). Per protocol analysis did not demonstrate a significant difference between the groups. This study is underpowered and concluded early due to difficulty recruiting patients.

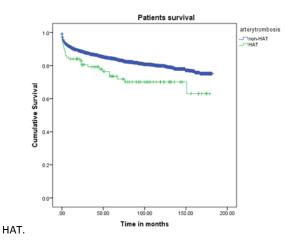
Discussion: Within the limitations of the study, there is no evidence that machine perfusion improves outcomes for recipients of DCD donor kidneys.

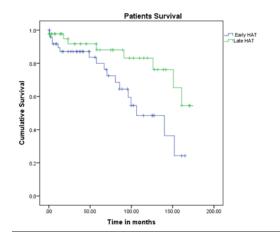
Early and late hepatic artery thrombosis after liver transplantation: single-centre experience

<u>Yogesh Puri</u>¹, Chiara Mazzarelli^{2,1}, Wayel Jassem¹, Parthi Shrinivasan¹, Andreas Prachalias¹, Krishna Menon¹, Hector Vilca-Melendez¹, Mohammad Rela¹, Nigel Heaton¹

Introduction and methods: A retrospective analysis of adult and pediatric liver transplantation at our centre between January 2000 and December 2014 identified 3036 patients who were divided into 2 cohorts: those with evidence of Hepatic Artery Thrombosis (HAT) (n=96), and those without (n=2940). HAT patients were categorized respectively in early (e-HAT) or late HAT (l-HAT), early within 28 days of transplant.

Results: The overall incidence of HAT was 3.1%. 51 had e-HAT while 45 had an I-HAT. The most common presentation of HAT was graft dysfunction, followed by incidental finding and biliary problems. No statistical difference was noted between the HAT and non-HAT groups in terms of sex, recipient age, history of the previous transplant and primary indication for liver transplant. Previous abdominal operation (p=0.037), younger donor age (p=0.092), use of split graft (p=0.097) and Cytomegalovirus (CMV) mismatch (p=0.005) impacted on HAT occurrence. The use of plasma or platelet transfusion pre-surgery was associated with HAT (p=0.028 and p=0.007). Patients with HAT had a higher risk of portal vein thrombosis (p=0.013) and biliary complications after transplant (p=0.008) compared to the non-HAT cohort. HAT was associated with longer hospital stay (p=0.004), mechanical ventilation (p=0.005) and major septic events (p=0.098). In multivariate analysis, only the CMV mismatch was an independent factor for HAT. Median patient survival for non-HAT and HAT patients were respectively 61.5 vs 57.5 months (p=0.012). Graft survival for HAT patients was 80%, 79.1% and 72.5 % at 1,3 and 5 years. Paediatric recipients were at greater risk of e-HAT, while the presence of co-morbidities was associated with I-HAT.





Conclusion: HAT influences patient's survival and morbidity and CMV mismatch appears to be an independent risk factor of the Median Survival e-HAT vs I-HAT 106.2 vs 174.4 (p=0.022)

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Effects of the gut-liver axis on ischemia-mediated hepatocellular carcinoma recurrence in the mouse liver

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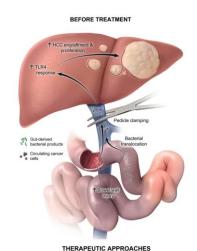
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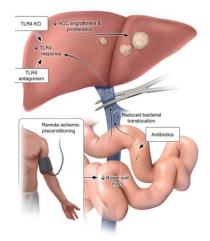
Introduction: There is growing evidence that liver graft ischemia-reperfusion (I/R) is a risk factor for hepatocellular carcinoma (HCC) recurrence, but the involved mechanisms are unclear. Here, we tested the hypothesis that mesenteric congestion due to portal blood flow interruption induces endotoxin-mediated Toll-Like Receptor 4 (TLR4) engagement, resulting in elevated liver cancer burden. We also assessed the role of remote ischemic preconditioning (RIPC) in this context.

Methods: *C57BI/6j* mice were exposed to standardized models of liver I/R injury and RIPC, by occluding hepatic and femoral blood vessels. HCC was induced by injecting RIL-175 cells in the portal vein. We further evaluated the impact of the gut-liver axis (LPS-*Tlr4* pathway) in this context, by studying mice with enhanced (LPS infusion) or defective (*Tlr4* -/- knockout mice, gut sterilization, *Tlr4* antagonist) *Tlr4* responses.

Results: Portal triad clamping provokes upstream mesenteric venous engorgement, increased bacterial translocation, resulting in aggravated tumor burden. RIPC prevented this mechanism by preserving intestinal integrity and reducing bacterial translocation, thereby mitigating HCC recurrence. In further mechanistic experiments, we show that these observations are linked to the LPS- *Tlr4* pathway, as testified by the high and low tumor burden displayed by mice with enhanced, or defective, *Tlr4* response, respectively.

Conclusions: Modulation of the gut-liver axis and of the LPS- *Tlr4* response by RIPC, gut-sterilization and *Tlr4* antagonism represent potential therapeutic targets to prevent ischemia-reperfusion lesions, and to alleviate HCC recurrence after liver transplantation and resection.





The success of Kaffes stent insertions for post liver transplant anastomotic strictures

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Introduction: Biliary anastomotic strictures (AS) occur in around 30% of patients following liver transplantation and are treated by endoscopic dilatation and plastic stent (PS) insertion. However, AS frequently recur and patients require multiple procedures. The Kaffes stent (KS, Taewoong Medical) is a removable, covered metal stent designed to be deployed across AS.

Methods: To examine outcomes in patients with AS, we compared a recent cohort of patients treated using KS with a historical cohort of patients who received PS.

Results: The 22 patients (12 females) treated by KS had mean age 55 (range 22-69) years; 11 patients had DBD and 11 DCD grafts; mean cold ischaemia time was 9.6 ± 3.3 hours. Four patients had failed previous treatment with PS. To date, 16 patients have had KS removed. The 69 patients (20 female) treated by PS were similar, mean age 51 (range 28-79) years; 47 patients had DBD and 22 DCD grafts; mean cold ischaemia time was 8.9 ± 3.1 hours.

AS resolved after one deployment of KS in 14 out of 16 patients (88%) compared to 26 out of 69 patients (38%) receiving their first PS (Relative Risk of persistent stricture (KS vs PS) =0.2, 95% CI 0.05-0.74; P=0.016; number to treat by KS for one benefit =2, 95% CI 1.3-4.0). There were no complications, including stent migration, after KS compared to 6 (8.4%) in the PS group (3 cholangitis, 2 pancreatitis, and 1 bleeding). All KS were removed successfully, although 1 stent needed 2 attempts because of wire migration. Following initial ERCP, PS patients required more supplemental ERCPs (mean 2.71 vs 1.13 more; p<0.01) and 32% required biliary reconstruction.

Discussion: Our data indicate that the KS is a promising method for managing post-transplant AS because the majority of strictures are treated by deployment of a single stent at first ERCP.

Alemtuzumab versus basiliximab as an induction therapy for renal allograft transplantation: 5-year outcome of a single centre

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Introduction: We compared alemtuzumab to basiliximab as an induction therapy. Our Objectives were to study the renal graft survival, acute rejection rate, cytomegalovirus (CMV) infection, post-transplant lymphoproliferative disease (PTLD), diabetes mellitus (PTDM) and skin cancer in the two groups.

Method: A retrospective study of 101 patients over a period of 12 months from April 2011. The cohort was divided in two groups based on their immunosuppression induction therapy as alemtuzumab (n=50), and basiliximab (n=50). Patients excluded (n=1) as lost to follow up. Campath and Simulect where used in high immunological and standard immunological risk recipients respectively. The maintenance immunosuppression was tacrolimus and mycophenolate without steroid.

Results: The overall graft survival among the cohort was 92%. Total graft loss was 8% of which 6% in the alemtuzumab group vs 2% in the basiliximab group. The causes of graft loss were graft thrombosis 2%, polyomavirus associated nephropathy 2%, acute graft rejection 1%, chronic graft rejection 1%, recurrence of membranous glomerulonephritis 1%, and hypercalcaemia 1%. The rate of biopsy-confirmed acute rejection was lower in the alemtuzumab 8% vs 18% in the basiliximab group. The graft loss secondary to acute rejection was 0% vs 2%, chronic rejection was seen in 2% vs 0% in the two groups, respectively. CMV viremia was higher in the campath 46% vs 24% in the simulect group, and PTLD was 6% vs 0% in the two groups respectively. The rate of post-transplant diabetes mellitus was higher in the alemtuzumab group 10% vs 2%. Skin cancer occurred in the alemtuzumab group only in 4% of recipients.

Conclusion: The 5-year follow-up results showed that, there were no significant difference between both groups in graft survival, and graft loss due to rejection was seen in 2% of each group. Overall, the campath group had higher rate of PTLD, PTDM, CMV and post-transplant skin cancer.

Generic ciclosporin, supervised switch programme for established renal transplant recipients from Neoral-ciclosporin to Vanguoral-ciclosporin.

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Introduction: Generic ciclosporin is not new to the market. However previous brands did not meet the revised European Medicines Agency (EMA) drug bioequivalence guideline for narrow therapeutic index drugs which have applied from 2010. Vanquoral-ciclosporin by Teva does meet the tightened bioequivalence acceptance interval. A pharmacy led supervised switch for all renal transplant recipients on Neoral-ciclosporin was implemented as a cost improvement programme.

Methods: Patients were identified via electronic records. A letter was sent, describing the generic switch programme and explained this was an NHS cost saving initiative. Patients in clinic were pre-identified. Once Vanquoral commenced, the patient notified us of two dates (switch and "check" ciclosporin level) to ensure results reviewed. All patient data was logged on a secure, password protected electronic database. Four pre-switch ciclosporin and creatinine levels were recorded in addition to prospective levels post switching.

Results: A total of 157 Neoral patients were identified. 22 patients were not switched for various reasons. As of September 2017, 89/135(66%) patients have been evaluated. Chi-squared test analysis on all pre and post switch ciclosporin levels demonstrated with 85% confidence that the interpatient variability was similar between the two products. Intrapatient variability, patients who had pre-switch levels (mean L4-L0 and L0) within 20% limit were then compared to assess post-switch level(s) variability, there was no significant difference.

Intrapatient CyA level variability ≤ 20% (80-125%	%)
Vanquoral L1 –L2 cf mean Neoral (L-4 to L0)	61/89(69%)
Vanquoral L1 cf Neoral L0	55/89(62%)
Neoral (L-4 to L0) cf mean Neoral	47/89 (53%)

No rejection episodes have occurred, no difference in serum creatinine or ciclosporin levels compared to baseline. Two patients switched back to Neoral due to non-specific vague symptoms.

Discussion: Preliminary results and clinical impression of this switch programme have not demonstrated any safety concerns. The post-switch "check" level was precautionary and offered reassurance to patients that they were being switched in a controlled environment. The cost efficiency savings generated will be reinvested back into clinical services to further enhance quality of care.

Polypharmacy in renal transplant recipients

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Introduction: Polypharmacy and medication complexity are risk factors for non-adherence in chronic diseases. This study is the first longitudinal analysis of medication complexity in patients pre/post transplantation.

Methods: Retrospective analysis of incident transplant recipients in a single centre, 2014. Data source: prospectively managed electronic patient and prescribing record. Exclusions: any of death, graft failure or transfer in the first year. Immunosuppression (IS): modified Symphony regime. Medication burden was assessed (0, 1, 6, 12 months) and complexity was calculated using a validated tool (Medication Regimen Complexity Index, MCRI).

Results: 53 patients (68% male, 30% LD, 15% regraft) with a mean age 51 ± 14 and Charlson Comorbidity Index (CCI) 2.8 ± 1.0 were analysed (all data are mean \pm SD):

,	0 (pre-txp)	1 month	6 months	12 months	
Total medications	8.7 ± 3.9	11.6 ± 2.9	9.6 ± 2.6	9.4 ± 3.2	
Total pill burden	16.7 ± 9.3	27.5 ± 8.2 16.9 ± 5.2		16.3 ± 7.2	
IS medications		2.8 ± 0.5	2.7 ± 0.5	2.7 ± 0.5	
IS pill burden		11.2 ± 2.6	7.4 ± 2.4	7.0 ± 2.4	
CV pill burden	4.0 ± 3.0			3.0 ± 1.4	
CKD-MBD* pill burden	4.4 ± 3.3			0.9 ± 0.9	
MRCI	20.6 ± 10.2			25.8 ± 8.6	

^{*}Chronic Kidney Disease-Metabolic Bone Disease

The MRCI was high pre-transplant and significantly higher at 12 months (p<0.001). The pill burden peaked at 1 month due to higher IS burden, CMV/PCP prophylaxis and drugs for symptom control. The MRCI at 12 months was significantly higher in DM (p=0.014) and CCI>2 (p=0.005) but was not associated with age, gender, CMV serostatus, DR mismatch, donor type or pre-transplant HD. If once daily tacrolimus had been used, the potential reduction in MRCI was negligible (-1.4, p=0.38).

Discussion: The MRCI in CKD5 and transplant patients is exceptionally high. Published mean MRCI for other chronic diseases include DM 6.3 and HIV 4.9. This study does not provide direct evidence of a link between MRCI and non-adherence in transplantation but evidence in other diseases makes this likely. Studies are needed to link medication complexity to graft outcome and to devise interventions to reduce MRCI.

Improving understanding of heath beliefs and immunosuppression adherence in long-term kidney transplant patients through pharmacist-led consultation and medicines optimisation

Hayley Wells¹, Sharon Frame¹, Amy Carroll¹, Anna Simpson², Antonia Cronin^{1,2}

Introduction: Health beliefs in long-term (>7 years) kidney transplant patients (LKT) have been associated with immunosuppression (IS) non-adherence resulting in poorer transplant outcomes. The purpose of this study was to (i) identify the extent of IS non-adherence in a cohort of LKT; (ii) investigate the influence of health beliefs on IS adherence; and (iii) explore the potential of pharmacist-led consultation and medicines optimisation (MO) in this setting.

Methods: All LKT attending Transplant Clinic between 01/09/16 and 30/08/17 completed screening questionnaires, including adapted versions of (i) Medicines Adherence Report Scale (MARS) and (ii) Beliefs About Medicines Questionnaire (BMQ). All LKT were offered either face-to-face or telephone consultation with a renal pharmacist.

Results: 289 LKT were screened. Their mean age was 53.2 years (range 22-81 years). 116 (40%) were female. 263 (91%) screened were taking at least 2 IS medications. 268 completed MARS and BMQ with 251 (94%) patients agreeing their health depended on IS. However 66 (25%) patients worried about taking IS and 81 (30%) reported unpleasant side-effects. 155 (58%) patients admitted forgetting IS, 20 (7.5%) avoiding IS, and 15 (6%) deciding to omit IS. There were n=135 pharmacist consultations (99 face-to-face, 36 telephone) resulting in MO in 88 (65%) patients. 43 (32%) patients were given repeat or amended IS prescriptions. 28 (21%) patients had in-depth IS adherence discussion. Of these, 10 had prescription or timing of administration changes. 40 (30%) patients were offered other medicines advice, including vaccination and dosette box provision.

Discussion: Understanding about the importance of IS in this LKT cohort was good. However, a significant proportion is non-adherent. Our findings demonstrate considerable scope for a pharmacist-led MO consultation and intervention service focussing on adherence. Analysis to identify associations between health beliefs, IS adherence and MO are underway and will inform service implementation.

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Short digital videos aimed at kidney transplant candidates with low health literacy educate regardless of educational level

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Introduction: Previous work in our department revealed a significant disconnect between patient preferences for digital information platforms and the predominantly traditional formats currently offered, indicating insufficient institutional adaptation to the digital age. It is also evident that a significant proportion of patients are at risk of low health literacy, and likely to be failed by traditional programs.

Method: Short digital videos featuring healthcare professionals were created for kidney transplant candidates on living donation, the kidney offer and transplant medications; for living donation and the kidney offer, a paired video was made with a corresponding patient testimonial. An online questionnaire, wherein videos were embedded, was completed by 61 actively-listed transplant candidates while receiving haemodialysis; all patients had received previous transplant information in clinical sessions or via attendance at a transplant education seminar. Patients were asked knowledge-based questions before and after watching the 5 short videos to assess understanding of key messages from healthcare professionals.

Results: Patients with lower health literacy levels were significantly less likely to read printed patient information (p<0.004) and more likely to find videos helpful (p<0.001). Statistically significant improvements in self-assessed patient knowledge (p<0.001) and mean correct answers for all questions were seen following the videos (p<0.001). Patients reported consistently positive responses to questions regarding the quality of each video (length, speed, pace and interest), while the patient testimonial videos evoked a strong emotional connection and reported synergy with the paired healthcare professional videos.

Discussion: We created an education intervention aimed at lower health literacy levels and achieved improvements in knowledge and patient engagement regardless of education level. Short digital videos are an effective medium to receive health messages, and allow access and refreshment of knowledge at a time and place convenient for patients.

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Quality improvement methodology to improve patient experience and transforming transplant service delivery

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Introduction: Living donor kidney transplants that represented 30 % of the total kidney transplant programme fell by 3% in 2016-2017 nationally. Locally, there was 10% fall from the preceding year. We applied quality improvement (QI) methodology to review local policies, identify areas of improvement and streamline protocols for evaluation of potential recipients and donors.

Methods: We analysed transplant records, PROTON system and ODT website for collecting data on referral to listing times, number of suspended patients and transplant status.

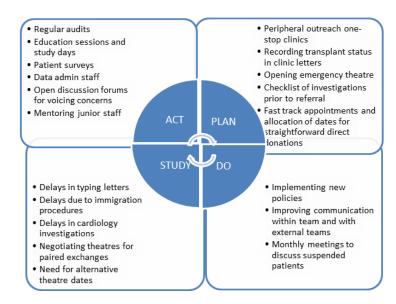


Figure 1: QI methodology in transplant evaluation

Results: By applying multiple PDSA cycles and LEAN methodology with the aim of transforming healthcare through perfect patient experience, we demonstrated achievement as follows:

Before PDSA (2016-2017)

- 1. Number of hospital visits- 6
- 2. Median time from referral to listing 38 weeks
- 3. Number of suspended patients on the waiting list-59

Specific interventions:

- 1. One stop clinic- Legal interview and r eviews by Transplant co-ordinator, Nephrologist, Surgeon and Anaesthetist in 1 day
- 2. Investigations booked on day of referral and co-ordinated to happen on same day
- 3. Regular MDT meetings in-centre and with referring centres to manage patients on suspended list

After PDSA (Apr 2017 to current date)

- 1. Number of hospital visits-2
- 2. Median time from referral to listing- 20 weeks
- 3. Number of suspended patients on the list- 42

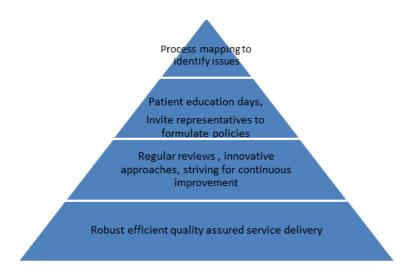


Figure 2: Application of innovative patient centred approach to achieve transformation in service

Discussion: It is possible to transform transplant service delivery through multidisciplinary concerted team effort and embedding new policies. Patient experience and safety is at the heart of healthcare services. For improving quality and efficiency, measure of patient experience is paramount. We have demonstrated improvement through measurement of outcomes in terms of median time from referral to listing, reducing number of suspended patients on waiting list and minimising hospital visits which enhanced patient experience and improved patient journey.

Living donor kidney transplantation in black, Asian and minority ethnic patients; a single centre cross sectional cohort study

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Introduction: Black, Asian and minority ethnic groups (BAME) constitute 11% of UK population yet represent 30% of the national kidney transplant waiting list. Initiatives to address this disparity are underway including promotion of living donor kidney transplantation (LDKT) in BAME. Currently approximately one third of all kidney in the UK are from living donors. The purpose of this study was to (i) assess BAME representation in our large ethnically diverse LDKT cohort, (ii) identify strategies to promote LD in BAME.

Method: We undertook a retrospective cross sectional cohort study of live related (LR) and unrelated (LU) KT between 1/1/10 and 1/8/15.

Results: N=537 LDKT took place. 62% of recipients were male. Mean age at transplant was 45.2Yrs. Mean living donor age was 45.0Yrs. 79.9% of recipients were white. Of the BAME recipient group 9.9% were Black, 5.8% Asian, 0.74% mixed race, 1.3% Chinese/Oriental, 2.4% other.

Table 1: Distribution of	Ethnic Group						
LU & LR KT in each ethnic group	White	Black	Asian	Mixed	Chinese	Other	
LU KT	45%	34%	45%	50%	57%	23%	
Pooled	n=8	n=2	n=1	-	_	n=1	
Altruistic	n=26	n=4	n=2	-	-	-	
Spouse	n=84	n=7	n=7	n=1	n=3	_	
Partner	n=27	n=1	-	n=1	n=1	-	
Other	n=48	n=4	n=4	-	-	n=2	
LR KT	55%	66%	55%	50%	43%	77%	
Sibling	n=104	n=17	n=6	n=1	-	n=5	
Parent	n=60	n=2	n=3	n=1	n=1	n=2	
Son/daughter	n=49	n=8	n=6	-	n=2	n=3	
Other	n=23	n=8	n=2	-	-	-	

Conclusion: According to national figures our unit performs more BAME LDKT than average. Nevertheless our data highlight that BAME are significantly underrepresented on our LDKT programme. Except for Chinese recipients LD were most likely to be a related sibling. In contrast to Caucasians noone in the 'other' group (majority Middle Eastern) received a transplant from spouse/partner. Understanding intercultural differences may help address BAME representation and guide policy to promote LD in BAME.

Experience of (relinquishing) anonymity in the UK

Emma Massey¹, Mathilde Pronk¹, Dorthe Slaats¹, <u>Lisa Burnapp</u>²

Introduction: Anonymous living kidney donation is carried out in a few European countries such as the UK, the Netherlands and Sweden. The UK differs from other countries in that the donor and recipient may meet one another after the operation. However, there is little evidence on how this policy and meetings after donation are experienced. The aim of this questionnaire study was to investigate the experience of anonymity among donors and recipients in the UK.

Methods: A self-report questionnaire with return envelope was sent to anonymous donors and recipients via post. Potential participants had given/received a kidney via the living kidney sharing schemes or through non-directed donation. Questions were specifically developed for this survey. Satisfaction with (relinquished) anonymity was rated on a scale of 1-7. As data were not normally distributed, medians are presented.

Results: 211 recipients and 355 donors returned the questionnaire. Anonymity had been relinquished among 25 (1%) recipients and 29 (8%) donors, after surgery. Five recipients had met their donor. Among the non-anonymous group, recipients were content that they were not anonymous (mdn=7, range 1-7), and the experience of contact/meetings was positive (mdn=7, range 6-7). Similarly, donors were content that they were not anonymous (mdn=7, range 3-7) and experienced contact/meetings positively although experiences were more mixed (mdn=7, range 3-7). Recipients who remained anonymous were generally content with anonymity after surgery (mdn=7, range 1-7), however, 70 (39%) report that they would have liked to have had some contact with the donor to express their gratitude. Similarly, donors who remained anonymous were generally content (mdn=7, range 1-7), however, 116 (36%) would have liked to have had contact out of curiosity regarding the outcome.

Discussion: Although not widely utilised, findings of this exploratory study support the option of voluntary contact and the potential to meet after anonymous living donor transplantation.

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Why are we declining kidney offers and what can be done to improve kidney utilisation?

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Introduction: Despite recent increases in registration for organ donation, waiting list time for renal transplant remains around three years, with considerable variation between centres. We set out to analyse the reasons for declining kidneys offered to our centre and develop a standardised procedure for monitoring organ turn-down, in an effort to improve organ utilisation.

Methods: A retrospective analysis of a consecutive cohort of all declined kidneys for adult recipients January 2016 to November 2017 was performed. Data were collected from an electronic database and paper records. As no standard adult proforma for declining kidneys exists, reasons for decline were sorted into categories based on the national paediatric form. Once categorised, a form was designed more relevant to the adult population, which is being used locally to record decline reasons prospectively.

Results: During the study period there were 557 offers, 347 (62%) of which were declined. The top reasons were:

- 1. Donor medical reasons (n=147, 42%), of which 49 (31%) were virology, 31 (19%) malignancy and 19 (12%) diabetes.
- 2. DCD donor not aystolic within required time frame (n=40, 12%).
- 3. Donor age (n=36, 10%), with median age mismatch of 28 years.
- 4. Recipient refusal (n=30, 9%), of which 17 (57%) recipients refused ECD transplant.
- 5. Low eGFR (n=29, 8%); with current documentation it was often difficult to determine whether this was acute or chronic.

Discussion: Analysis of reasons for kidney decline led to creation of a user-friendly proforma (figure 1), to be used alongside EOS documentation to ensure accurate, standardised and comprehensive record-keeping. Going forward we are instigating a monthly turn-down meeting so that decline decisions become accountable, and we can start to identify areas to work on to improve uptake, such as educating donors about ECD kidneys. There may be scope to extend use of our form to other centres, allowing multi-centre comparison and improvement.

REASONS FOR DECLINE OF KIDNEYS FOR ADULT PATIENTS Figure 1							
OFFER DETAILS			Donor Case Number				
Date of offer			Hospital Code				
080 000			Recipient M	IRN I			
REASON(S) FOR DECLINE OF KIDNEYS							
Please record as many re	esons es nece	ssary by ticking the app	ropriste box(e	s) and include further inf	formation below		
Donor Reasons							
Acute renal failure		Donor not asystolic		Virology (or high real behaviour record all details)			
Chronic renal failure		within 3 hours Donor arrested		Infection			
Record creatinine: Admission Current	_	5010101010	\Box	(record (etals)			
GP		Donor > 75 yrs		Haematological	\neg \mid		
En bloc offer				malignancy			
Organ damaged		Age mismetch Record age gap		Renal malignancy			
Cold ischaemic time	П	Donor BMI		Other malignancy (reunt death)	\Box		
Time Warm ischaemic time	П	Diabetes	\Box	Vescular disease	\sqcap		
Time	H	Hypertension		(record details) Other medical reason	H 1		
Poor perfusion	\Box	- Appendix and	\Box	(record details)			
Recipient Reasons							
Acute infection		Recipient unavailable		Unable to X-match			
Recipient refused	\Box	(word death) Recipient unfit	\Box	X-match positive	\exists		
Live donor being	H	(record details) Recipient siready	\exists		_		
worked up		transplanted					
Centre Reasons							
Centre siresdy		No beds/staff/		Second offer – other			
transplanting Centre criteria not	\exists	theatre/time		centre accepted	_		
achieved	ш						
Other Reasons							
Transport difficulties		Other					
Additional Details							
Kidney declined by: Transplant Co-ordinator Transplant Surgeon Renal Physician							

Correlation between differential kidney volume and split renal function in prospective living kidney donors

<u>Usman Hayat</u>¹, Anthony Fenton², Rob Jones², Graham Lipkin²

Introduction: Prospective living kidney donors undergo radiological assessment of renal anatomy and a DMSA scan to measure split renal function (SRF). We assessed the relationship between differential kidney volume and SRF, to determine whether abnormal SRF might be determined by renal imaging.

Methods: Data were retrospectively collected on 123 prospective living kidney donors. Kidney and cortical volumes were measured on CT using semi-automated kidney and cortex boundary delineation. Percentage differential kidney volume (DKV) and differential cortical volume (DCV) were calculated and their correlation with SRF on DMSA assessed using Pearson's correlation coefficient. Sensitivity, specificity, and ROC curve analyses were used to assess the ability of DKV and DCV to detect abnormal SRF (defined as a >10% difference).

Results: The cohort was 59% female, mean age was 43 years, and mean GFR was 94 mL/min/1.73m². Twenty-five (20%) had a >10% difference in SRF on DMSA.

DKV had a moderate correlation with SRF (r=0.667, P<0.0001) and an AUC of 0.826 (95% CI 0.726-0.926). The commonly-used arbitrary cut-off of a DKV >10% had a sensitivity of only 32% (14 to 50%) and specificity of 97% (94 to 100%). The ROC curve-derived optimal DKV cut-off of 6.2% had a sensitivity of 68% (50 to 86%), and specificity of 85% (78 to 92%). DCV also had a moderate correlation with SRF (r=0.692, P<0.0001), an AUC of 0.824 (0.723-0.926), and at the optimal cut-off of 5.2% has a sensitivity of 84% (70% to 98%) and specificity of 72% (64% to 81%).

Discussion: DKV and DCV are moderately correlated with SRF, but do not have sufficient sensitivity and specificity to be considered an alternative to performing DMSA to detect abnormal SRF. In particular, the commonly-used DKV cut-off of >10% demonstrated poor sensitivity.

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The hidden burden of abnormal renal histology in living kidney donors

<u>Ailish Nimmo</u>¹, Gabriel Oniscu², Paul Phelan², John Terrace², Chris Bellamy³, Lorna Henderson²

Introduction: Recent evidence suggests living kidney donors (LD) are at increased risk of end stage renal disease despite rigorous screening. Predicting those at risk remains a challenge in the absence of clinical disease at donation. We investigated the prevalence of donor disease in early post-implantation renal biopsies.

Methods: Biopsies carried out within 20 days from transplant in living donor kidney recipients transplanted from January 2012 to June 2017 were identified. Histologic variables were extracted from pathology reports and scored for glomerulosclerosis ≥ 1 (gs), interstitial fibrosis and tubular atrophy ≥ 1 (IFTA), arteriolar hyalinosis ≥ 1 (ah) and vascular fibrous intimal thickening \geq (cv). Donor characteristics associated with risk of CKD were collected. This included; BMI, hypertension and smoking status.

Results: Early post-implantation biopsy was carried out in 65 of 185 LD. Indication for biopsy was either unexplained rise in creatinine (sCr) or baseline sCr higher than expected in the majority of patients. There was a higher number of female donors and donors with a smoking history compared to LD without biopsies. Donor characteristics were otherwise similar (Table 1). The prevalence of any histological abnormality was 60% (11% gs, 20% IFTA, 41% ah, 35% cv). 18 biopsies (28%) had at least 1 histological abnormality, 13 (20%) 2 abnormalities, 5 (7.7%) 3 abnormalities and 3 (4.6%) 4 abnormalities. Fifty-two LD were paired with their recipient's biopsy. The presence of ah or $cv \ge 1$ was observed in a high proportion of LD irrespective of risk factors (Table 2). Nine LD with no risk factors had at least one histological abnormality and five had ≥ 2 .

Discussion: Abnormal histology was detected in a high proportion of early post transplant biopsies from LD screened and accepted for donation according to BTS guidelines. Further work examining the implications of donor disease on risk of progressive CKD is required.

	LD with post implantation biopsy (n=53)	LD with no post implantation biopsy (n=125)	
Mean age (years)	53	50	
Isotope GFR (mls/min/1.73m ²)	94	95	
Female	30 (57%)	56 (45%)	
Mean BMI	25.9	25.7	
BMI >25	33 (62%)	71 (57%)	
Smoker	16 (30%)	29 (23%)	

Table 1: Clinical characteristics in LD with or without early post implantation biopsy

	BMI ≥25	BMI <25	нт*	No HT*	Smoking history	Non- smoker
			N=52			
ah ≥1	13 (25%)	9 (17%)	3 (6%)	19 (36%)	7 (13%)	15 (29%)
cv ≥1	12 (23%)	9 (17%)	3 (6%)	18 (35%)	5 (10%)	16 (31%)

Table 2: Presence of arteriolar hyalinosis (ah) or vascular fibrous intimal thickening (cv) in early post transplant renal biopsy in association with presence or absence of risk factors in LD. * History of hypertension pre-donation

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Organ donation education in schools:a comparison of outcomes in primary and secondary school children.

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Introduction: The national shortage of solid organs for transplantation is a critical issue. The need to focus on educational interventions is identified within the Taking Organ Transplantation to 2020 (NHSBT strategy) and forms part of the impending consultation on "opt out" in the UK. Although education strategies are thought to increase potential donations, there is insufficient evidence as to where this education would be most impactful. We carried out and evaluated organ donation (OD) workshops in both primary and secondary schools and compared outcomes.

Methods: A series of workshops were run in primary and secondary schools in North London involving a faculty of 2 patients, a surgeon and a nurse between 2013 and 2017. The OD workshops were evaluated by a pre- and post-workshop questionnaire. The principle outcome measure was whether the participants of the workshops discussed the topic with others following the intervention.

Results: 506 students attended primary school workshops (50% females, with ages (years) 9(8%), 10(32%), and 11(60%) and 127 students attended secondary school workshop (54% females, with ages 13 (32%) and 14 (68%)). Compared with the secondary school, a greater proportion of primary school children found the "session to be valuable" (92% vs 78%) and "a good topic to discuss" (80% vs. 68%). Following the session, 86% of primary school children discussed OD with someone compared to 71% of the secondary school group.

Conclusions: We conclude that primary school students are more likely to engage in OD workshops compared to those at secondary school. Importantly, as primary school students in our study more frequently discussed OD with others after attending a workshop, interventions targeted at this level may be more likely to have a wider impact and potentially increase organ donations.

A donor and recipient genome-wide association study of renal allograft function

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Introduction: Previous studies suggest common genetic variation influences renal transplant outcome. Our aim was to expand on this research and examine single variant effects of both donor and recipient genotypes on graft function (using estimated glomerular filtration rate (eGFR) as a proxy) taking a genome-wide association study (GWAS) approach.

Methods: We meta-analysed donor and recipient genetic variants across four cohorts screened for European ancestry. We performed both donor and recipient GWAS of eGFR at 1 year (donors, n=3,679; recipients, n=5,220) and 5 years (donors, n=2,505; recipients, n=2,851) post-kidney transplantation and examined change in eGFR between 1 and 5 years (Δ eGFR; donors, n=1,974; recipients, n=2,228). For the 1-year and 5-year analysis, where eGFR was missing due to death/graft failure the last known eGFR was used and death/failure was included as a covariate in the analysis. Samples with death/failure before 5 years were excluded in the Δ eGFR GWAS. Other covariates included the first eight principal components, donor and recipient age, donor gender and type (living/deceased). SNPs with a minor allele frequency <5% were removed.

Results: No genome-wide significant associations were found in any of the donor or recipient GWAS. We had 80% power to detect variants that explain approximately 1% or more of the outcome variation.

Discussion: It is unlikely that a single common genetic variant explains greater than 1% of the variance in 1-year, 5-year or Δ eGFR post-kidney transplant. It is possible that there are SNPs associated with eGFR post-transplant that explain less than 1% of the outcome variance but this study was underpowered to detect these. This study focused specifically on common genetic variation, therefore it is possible that rare variation in the donor and/or recipient genotype is influencing allograft function, but further work is required to answer this question.

Are there good and bad kidneys? A transcriptional approach

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Introduction: Kidney transplantation is the optimal treatment for most patients with end-stage kidney disease, but organ shortage is a major challenge. To address this, increasingly marginal donors are being considered. Histological scoring of preimplantation biopsies can be used to assist clinical decision-making, but is imprecise in its predictive value.

Aim: To study the RNA profile of donor tissue and to correlate this with patient outcome in order to develop a "Molecular Microscope" test that predicts outcome and identifies kidneys suitable for transplantation

Methods: We performed global transcriptomics using RNA sequencing on samples obtained from n=5 discarded transplant kidneys, and n=35 core biopsies obtained from the Quality in Organ Donation (QUOD) biobank.

Results: Given that core biopsies may contain varying amounts of cortical and medullary tissue, we first sought to establish the transcriptome of the different anatomical regions of the kidney. In n=5 paired samples, we found that over 5,000 genes were differentially expressed between the cortex and medulla. Using this dataset, we developed a novel method for correcting for medullary content, generating a set of specific marker genes. Using this correction method, we analysed n=35 biopsies obtained at retrieval to investigate the transcriptional state of the organ prior to any effect of cold ischemia, and correlated these data with clinical parameters – the incidence of delayed graft function (DGF) and 3 and 12 month glomerular filtration rate (GFR). We found 240 genes that were significantly associated with DGF and a smaller number with long term GFR. These gene-sets will now be tested in a validation cohort.

Discussion: These data imply that the transcriptional state of the organ at retrieval may have utility to predict outcome, increasing organ utilisation. They may also highlight potential targets for therapeutic intervention that could improve long-term graft function.

MicroRNAs predict heme oxygenase-1 upregulation in renal transplant recipients

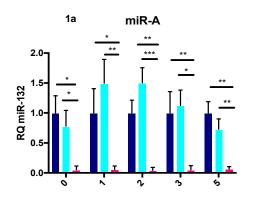
<u>Katie Connor</u>¹, Rachel Thomas², Sarah Finnie³, Lorna Marson¹, Stephen Wigmore¹, Laura Denby³

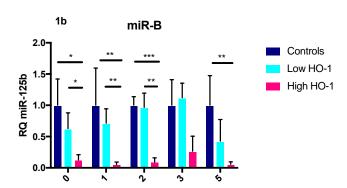
Introduction: Ischaemia reperfusion injury (IRI) remains a challenge in transplantation. Heme arginate (HA) induces the protective enzyme heme-oxygenase 1 (HO-1) in experimental models, reducing IRI and inducing an anti-inflammatory 'M2' macrophage phenotype. Preliminary studies showed HA treatment of renal transplant (RT) recipients increased HO-1 in peripheral blood mononuclear cells (PBMCs) and intra-graft macrophages. However, individual HO-1 protein production to HA significantly differed. We hypothesized that negative post-transcriptional gene regulatory 'microRNAs' (miRs) accounted for individual differences in HO-1 protein expression.

Methods: RT recipients were given HA or placebo on day 0 (D0=day of transplant) and D2. Patients were categorized as 'high' or 'low' responders based on change in D0-D1 PBMC HO-1 protein. PBMC mRNA was analysed for the CD91/CD163-Nrf2-HMOX1 pathway and those associated with M2 polarization (IL-10, MRC-1, Arg2). MicroRNAs predicted by bioinformatics to regulate the HO-1 pathway were assessed. Analysis: Δ CT = (Target gene/miR)-(Housekeeper GAPDH/RNU48). Figures: Relative Quantification (RQ) =(2^(- Δ CT)) Statistics: One-way ANOVA.

Results: Low HO-1 responders had no significant HO-1 protein upregulation vs. controls. Despite elevated HO-1 protein levels(p<0.001), high responders had no difference in *HO-1*, *Nrf2* and *CD163* (data not shown) mRNA. Heme-hemopexin receptor *CD91* (D0&D2; p<0.01) was elevated in high responders. High responders had significantly lower expression of six miRs predicted to suppress the HO-1 axis at multiple time points (anonymised examples, Fig 1a and 1b). High HO-1 response was associated with increased 'M2' markers *Arg2* (D1-5, p<0.05) and *MRC-1* (D1, <0.05), but unchanged *IL-10*.

Discussion: High HO-1 responders exhibit markedly reduced expression of microRNAs predicted to suppress HO-1 production and increased anti-inflammatory 'M2' gene expression. Differing expression of this 'miR signature' at baseline suggests that microRNAs may be novel markers that can be used to predict HA response. MicroRNAs may also be effectors of HA response, modulating post-transcriptional expression of genes that regulate the HO-1 axis or macrophage polarization.





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Notch receptor expression is significantly increased during human kidney transplant rejection

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Background: Despite significant advances in transplantation, we remain limited in our ability to appropriately modify the immune response therein. Development of therapies that promote regulation while suppressing effector immunity is imperative to improve graft survival and minimize immunosuppression. Notch receptor signaling plays a key role in T-cell development, activation and differentiation, though limited data exist on its importance in immune-regulation. In this study, we investigated the pattern of Notch receptor expression in human renal transplantation.

Methods: Transplant kidney biopsy samples obtained from patients undergoing renal transplantation & enrolled in an immune-monitoring study in our institution were evaluated. All patients had a time zero biopsy; a subset underwent further biopsy post-transplantation due to graft dysfunction, and were classified as acute rejection (n=12), or non-rejection (n=15). Immunohistochemical analysis was performed to identify intact and activated Notch receptor expression (% threshold area using ImageJ) on paraffin-embedded sections. Cellular samples isolated from another cohort of renal transplant patients during times of quiescence or acute rejection were analyzed for T-cell Notch expression.

Results: We first investigated cellular expression of Notch-1 in CD4⁺Foxp3⁻T cells (T_{conv}) and CD4⁺Foxp3⁺ (T_{regs}). during clinical quiescence, a significantly higher proportion of T_{regs} expressed Notch-1 compared to recipient T_{conv} cells and T_{regs} isolated from healthy controls. During rejection, however, the proportion of T_{conv} expressing Notch-1 significantly increased. Allograft expression of activated Notch-1, and both activated and intact Notch-2 receptors significantly increased in patients with acute rejection compared both to baseline and non-rejection post-transplant biopsies (p<0.0001, p<0.0001 and p<0.0001, respectively).

Conclusions: There is significant upregulation of both tissue and cellular expression of Notch1 during immune activation. Given the importance of Notch receptor signaling in T cell activation, treatment with Notch inhibition may provide a novel means of attenuating cellular responses in transplantation.

Pre-transplant HLA sensitisation in the absence of preformed donor specific antibodies is associated with a higher rate of alloimmune injury andrenal allograft failure

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Introduction: Broad HLA sensitisation has previously been considered a risk factor for alloimmune injury post-transplant. However, recent data suggest that with the use of highly sensitive single antigen beads, in the absence of preformed donor specific antibodies (DSA), HLA sensitisation per se does not impact on renal allograft outcomes. We aimed to determine the effect of pre-transplant non-donor specific HLA Abs on allograft outcomes.

Methods: We retrospectively analysed the clinical impact of pre-transplant HLA Abs in 745 renal transplant recipients. Patients with preformed DSA were excluded.

Results: 253/745 (34.0%) patients had pre-transplant HLA antibodies. 127 (50.2%) had class I HLA Abs, 46 (18.2%) class II and 80 (31.6%) class I+II. 107 (42.3%) had a cPRA<50%, 146 (57.7%) had a cPRA>50%. The overall HLA ABDR match was greater in the HLA+ compared with the HLA- group, p=0.012. On univariate analysis, HLA Abs were significantly associated with increased risk of rejection [HR: 1.52 (1.06-2.20), p=0.017], AMR [HR:1.98 (1.03-3.81), p=0.028] and de novo DSA development [HR:1.60 (1.00-2.57), p=0.039]. There was no significant difference in outcomes between the cPRA groups. However, patients with pre-transplant class I+II HLA Abs, were at highest risk of developing AMR, p=0.01 and DSA, p=0.002. On multivariate analysis, pre-transplant HLA Abs were an independent risk factor for allograft failure [HR: 2.21 (1.08-4.56), p=0.03] and rejection [HR:1.58 (1.07-2.34), p=0.02]. The presence of both class I+II HLA Abs were independently associated with enhanced risk of AMR [HR:3.05 (1.49-6.24), p=0.002] and DSA [HR:3.03 (1.76-5.19), p<0.001], whilst greater HLA matching significantly reduced this risk [HR:0.10 (0.01-0.74), p=0.02].

Discussion: This study shows that pre-transplant non-donor specific HLA Abs still confer an immunological risk post-transplant. Given the diverging new data emerging, wider collaborative work is now required.

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Successful ABO and HLA incompatible renal transplantation in children in the United Kingdom over the last decade

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Introduction: There is increasing evidence of good short- and medium-term outcomes for ABO incompatible (ABOi) and HLA incompatible (HLAi) with pre-transplant positive crossmatches in paediatric practice. However, there are concerns regarding the higher risks of infective complications and antibody-mediated rejections. The aim of this paper is to show that the short-term outcomes for ABOi and HLAi renal transplantation are comparable to (ABOc/HLAc) compatible renal transplants in children in the UK.

Methods: Data were obtained from the UK Transplant Registry (NHS Blood and Transplant) on all children (aged <18 years) who received a first living paediatric kidney only transplant between 1 January 2006 and 31 December 2016 from 10 paediatric transplant centres. Baseline demographic data were collected of 709 first living paediatric kidney only transplants, of which 23 were ABOi and 4 were HLAi. Estimated glomerular filtration rate (eGFR) was calculated using plasma creatinine at three months post-transplant. Comparisons of graft function following transplantation were made between ABOi, HLAi, and ABOc/HLAc compatible groups.

Results: Pre-emptive transplantation occurred in 35% and 25% of ABOi and HLAi recipients with delayed graft function in 6%, 6% and 0% of ABOc/HLAc, ABOi and HLAi respectively with no cases of primary non-function. Renal allograft survival was 100% in each group although there was one death of ABOi pRTR with a functioning graft. For ABOi transplants (n=16), the median and inter-quartile range (IQR) eGFR was 88 (63 - 150) mls/min/1.73m². The eGFR in ABOc/HLAc group had a median (IQR) of 101 (74 - 144) mls/min/1.73m². No statistically significant difference was found between these transplant groups due to the small number of patients.

Discussion: The short-term outcomes from this follow-up have shown that ABOi and HLAi renal transplantation are possible for paediatric renal transplant recipients in situations where no compatible donors are available.

New insights from the SILVER study; a 50 % reduction in calcineurin inhibitors at day 30 achieves a temporary renal-sparing effect, but does not impact on long-term renal function after liver transplantation

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Introduction: Renal dysfunction after liver transplantation (LT) is common and the long term use of calcineurin inhibitors (CNI) is associated with nephrotoxicity. The reduction in CNI at 4-6 weeks post transplantation during the SILVER study enabled evaluation of this early reduction and its impact on long term renal function.

Methods: An immunosuppressive strategy with a 50 % reduction of CNI and introduction of the mTOR inhibitor Sirolimus within 4-6 weeks after LT (group B, n=252) was compared to standard CNI-based mTOR-free immunosuppression (group A, n=255). Data was retrieved from the randomised controlled multi-centre trial of Sirolimus in Liver Transplant Recipients with HCC (SiLVER) study over a study period of 5 years.

Results: Early CNI reduction was achieved as stipulated in the protocol with median CNI reduction of 10% vs 56% and 20% vs 55% for CNI trough and dose at 3 month post-transplantation in group A vs group B in an intention-to-treat approach, respectively. A temporary renal sparing effect was observed at 3 months in the Sirolimus arm [67 (55-85) vs 76 (59-95) ml/min, p=0.003] but renal function was not significantly different at all later time points. Per protocol analysis demonstrated better eGFR at 3 month in the Sirolimus arm compared to standard CNI treatment if early CNI reduction was achieved [78 (60-95) vs 66 (55-87) ml/min, p=0.047] and this protective effect of early CNI reduction extended to 12 month [75 (59-96) vs 66 (55-82) ml/min, p=0.022] in LT recipients on concomitant mTOR immunosuppression. Using generalized estimating equations with post-transplant day 28 as baseline, no difference was found for eGFR between the groups over time for both intention-to-treat and per protocol analysis.

Discussion: This analysis suggests that a 50% reduction in CNI dose at 4-6 weeks yields better renal function early after liver transplantation; however, long-term renal function is not protected.

MODERATED POSTERS

FRIDAY 16TH MARCH

08:30

THE EXHIBITION HALL

P050- P152

The effect of baseline immunosuppression on gene transcript expression in renal transplant patients with features of antibodymediated rejection

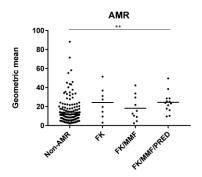
<u>Barbora Salcman</u>¹, Katherine Dominy¹, Michelle Willicombe², Terry Cook², Adam McLean², Jack Galliford², David Taube², Candice Roufosse¹

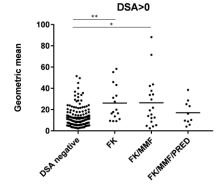
Background: Patients with antibody-mediated rejection (AMR) in their renal transplant have elevated endothelial and NK-cell related transcripts. The effect of immunosuppressive treatment on gene expression is not known. Here we investigate if the baseline immunosuppressive regimen is associated with AMR-related gene transcript levels, thereby possibly indicating more effective prevention or treatment of AMR.

Methods: 203 renal transplant biopsies with RNA available for qPCR were graded using Banff 2015 classification. From this cohort, patients with a donor specific antibody (DSA) or a diagnosis of AMR/suspicious for AMR were selected for further analysis. Gene expression analysis was carried out through qPCR for 6 AMR-related transcripts (DARC, PECAM1, KLRF1, MYBL1, FGFBP2, SH2D1b) and results were analysed using the $\Delta\Delta$ CT method and calculation of the geometric mean of the transcripts. Kruskal-Wallis test was used to assess the significance.

Results: Within all patients with a DSA (n=45), no significant difference was observed when comparing different baseline immunosuppressive regimens (FK n=16; FK/MMF n=19; FK/MMF/PRED n=10). In an analysis of patients diagnosed with AMR/suspicious for AMR (n=31) (with or without DSA), there was no statistically significant difference between the groups (FK n=8; FK/MMF n=10; FK/MMF/PRED n=13).

Conclusion: We show that baseline immunosuppressive regime has no effect on expression levels of AMR-related genes, either in a cohort of patients with DSA, or in patients with a diagnosis of AMR/suspicious for AMR in their renal transplant biopsy. This suggests that the baseline immunosuppressive regimen does not affect the pathophysiological processes related to the effect of DSA on the graft.





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Differential immunogenicity of autologous and allogeneic cholangiocyte cellular therapies derived from primary cells and induced pluripotent stem cells

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Introduction: Cellular therapies derived from primary tissue or induced pluripotent stem cells (iPSCs) are both promising alternatives to solid organ transplantation, but it is unclear if they are equally immunogenic. To address this question, we compared immunogenicity of two human cellular therapies we have developed for the treatment of cholangiopathies: Extrahepatic Cholangiocyte Organoids (ECOs) derived from primary biliary epithelium and Cholangiocyte-Like Cells (CLCs) derived from iPSCs.

Methods: ECOs and CLCs were derived using tissue from deceased organ donors with appropriable informed consent and ethical approval. *In vitro* expression of immunogenic markers by human ECOs, CLCs and control primary cholangiocytes, with or without exposure to IFN-γ, was assessed using qPCR, immunofluorescence and FACS analysis. *In vivo* immunogenicity of autologous and allogeneic ECOs and CLCs was investigated by transplantation under the kidney capsule of immunodeficient NSG mice humanised with bone-marrow obtained from the same or different deceased organ donors.

Results: Exposure to IFN-γ caused a significant upregulation of HLA I and restored expression of HLA II in ECOs, to levels equal to or greater than primary cholangiocyte controls. Conversely, CLCs showed upregulation of HLA I but little expression of HLA II. Expression of other immunogenic molecules such as CD40 and CD44 was similar between CLCs and ECOs. Allogeneic ECOs transplanted into humanised mice demonstrated structural disruption and extensive infiltration of human CD45+ cells, while autologous grafts remained structurally intact and showed little CD45+ cell infiltration.

Conclusion: Our data suggest that autologous cholangiocyte cellular therapies are non-immunogenic while their allogeneic counterparts elicit a significant immune response *in vivo*. Moreover, primary-derived and iPSC-derived cholangiocyte cellular therapies appear to have different immunogenicity profiles *in vitro* under inflammatory conditions and may require different levels of immunosuppression to prevent their rejection. The method of generation of cellular therapies in general may therefore be an important determinant of immunogenicity.

Perinephric adipose tissue contains immunocompetent lymphocyte subsets with antigen-presenting capacity

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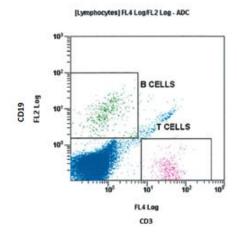
Introduction: The kidney is surrounded by a thick layer of Perinephric Adipose Tissue (PAT) between Gerota's fascia and the renal capsule. During transplantation, variable amounts of PAT are transplanted along with the kidney. Since fat contains immunocompetent cells, we postulated that PAT could also contain immunocompetent cell potentially increasing the immunogenicity of the donor organ.

Methods: We sampled PAT from 19 living donor renal allografts prior to implantation. Of these samples, 7 were weighed, homogenised, and a density gradient employed to isolate lymphocytes. The remaining 12 samples were weighed, digested using Collagenase D, filtered, washed and the cellular fraction harvested. The cellular fraction was characterised by flow cytometric analysis using antibodies directed against CD3, CD4, CD11c, CD14, CD15, CD19, CD25, CD45RA, CD45RO, FOXP3 and HLA-DR.

Results: Our preliminary data confirms the presence of lymphocytes in PAT, namely B and T cells (Figure 1). Additional work has been conducted to further characterise the cellular fraction using the Collagenase D digested samples, examining for the presence of naïve T cells, Tregs, memory T cells, T helper cells, neutrophils, Natural Killer cells, APCs, monocytes and dendritic cells. An artefact was present in all samples (highlighted in blue in Figure 1) has making accurate characterisation of the cellular fraction difficult. Further work is required to remove this artefact and thus accurately identify all populations present in the cellular fraction.

Discussion: This study identifies the presence of T and B lymphocytes within human PAT. Concurrent transplantation of PAT with the kidney may by harmful by increasing the immunogenicity of the organ, or beneficial through transplantation of Tregs. The practice of removal or retention of PAT before transplantation requires additional investigation.

Figure 1: Flow diagram demonstrating the presence of T cells (in pink), B cells (in green) and an unidentified cell line (in blue).



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Feasibility of delivering cell therapy during kidney ex vivo normothermic perfusion

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Introduction: The advent of warm perfusion technologies has brought about exciting new opportunities for the pre-transplant delivery of novel treatments direct to organs. This includes cell therapies that may facilitate immunomodulation or reconditioning of marginal organs to minimise ischaemia reperfusion injury. Multipotent Adult Progenitor Cells(MAPC®) are a well characterised, adult bone marrow-derived cell population with similar anti-inflammatory properties to mesenchymal stromal cells. They possess an increased capacity for expansion and are minimally immunogenic making them the ideal 'off-the-shelf' therapy candidate. The purpose of this pilot series was to investigate the feasibility of MAPC cell delivery during kidney ex vivo normothermic perfusion (EVNP).

Methods: Ten declined human kidneys were included in this study; 8 were treated with MAPC cells and 4 vehicle-treated controls. EVNP was performed as per the Hosgood/Nicholson protocol for 7hours. Following 1hour of stable perfusion $50x10^6$ MAPC cells were delivered to the kidney via arterial cannula bolus. Physiological output was recorded at 30minute time-points. Contrast enhanced ultrasound (CEUS) was performed before cell treatment, 15 minutes after infusion and at 5 hours. Fluorescent microscopy was used to evaluate engraftment and tracking of fluorescently labelled MAPC cells.

Results: There was no impairment to physiology during EVNP. Renal blood flow (ml/min/100g), vascular resistance, oxygen consumption, acid/base balance, urine production and serum electrolytes were matched in controls and cell treated kidneys. CEUS demonstrated no significant impairment of global perfusion following cell administration. Fluorescent microscopy demonstrated engraftment of MAPC cells, often localising to the glomerulus.

Discussion: We have described the first reported series of cell therapy successfully delivered directly to a kidney in an isolated ex vivo perfusion platform. We conclude, MAPC therapy is feasible during EVNP and does not impair kidney physiology providing us with exciting novel opportunities to recondition marginal organs prior to transplantation.

Adipose-derived regenerative cells: therapeutic potential

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Introduction: A novel rodent model of renal ischaemia- reperfusion injury (IRI) has shown significant improvement in renal function and histology after administration of adipose-derived regenerative cells (ADRC)s. It is thought that the pleomorphic ADRC suspension exert their ameliorative actions through a number of mechanisms but overall they remain poorly understood. Our research aims to build on the basic science behind ADRCs and their role in renal IRI repair.

Methods: Male adult Fisher 344 rats underwent a 2/3 nephrectomy and 2.5 weeks later a severe ischaemia of 120 minutes was induced in the intact kidney. ADRCs extracted from syngeneic rat inguinal fat was then injected via the renal artery prior to reperfusion of the kidney. Rats were terminated at 4 different time points and organs were harvested for mRNA studies, protein analysis and histology.

Results: Messenger RNA extracted from the injected kidneys of ADRC treated rats compared to vehicle control demonstrated a greater than 2.5 fold expression in factors related to angiogenesis: VEGFa, Ang2, immune function: Csf2, CXCL1, CXCL2, Ifn-γ, IL-18, IL-6 and anti-oxidant: heme oxygenase-1. Protein extracted from the injected kidneys indicate increased levels in ADRC treated rats compared to vehicle control for proliferation marker: PCNA and for proteins in immune function: L-selectin, ICAM-1 and MIP3α.

Discussion: Subcutaneous fat provides an accessible and robust supply of ADRCs that do not require culturing and have shown to reduce the damaging effects of IRI in our rat model. ADRCs seem to exert their ameliorative effect via encouraging cell proliferation and through proangiogenic and antioxidant properties. The notable changes in RNA and in protein levels of leukocyte trafficking and activation-related factors suggest a major role for leukocyte infiltration in early IRI repair. Continuing research focuses onto downstream cellular mechanisms.

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Multicentre epidemiological study on prevalence of recurrent glomerular disease post-transplantation in the United Kingdom

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on behalf of the NIHR Health Informatics Collaborative (HIC) Transplantation Theme, London, United Kingdom.

Introduction: Primary glomerulonephritis (GN) can recur in the renal allograft and are possibly associated with poorer allograft outcome. The prevalence of recurrence varies widely and large-scale studies on a UK population have never been performed. The NIHR Health Informatics Collaborative (HIC) was set up to collect and standardise patient data across the Comprehensive Biomedical Research Centres for the purposes of enabling translational research. Proof of concept was by delivery of an exemplar project. The exemplar project for the Transplantation theme is focusing on recurrent disease within renal allografts and epidemiological factors influencing recurrence.

Methods: Data is being collected on renal transplant recipients transplanted between 2005-16 at four UK transplant centres, namely Cambridge, Guy's, Imperial and Oxford. A total of 6001 recipients have been identified. Episodes of recurrent disease are being identified from histology reports using the development of text-mining software. The software output is being validated against manual clinical interpretation of 10% of reports. We have calculated the prevalence of disease for each GN and are analysing demographic influences focusing on age, gender, ethnicity, type of transplant and immunosuppression. We also studied the time to recurrence in each GN and the incidence of allograft failure.

Results: Preliminary results have demonstrated that FSGS and IgA nephropathy are the two most common recurrent diseases post-transplantation. We are now in the process of analysing the influence of various demographics on recurrence.

Discussion: This exemplar study demonstrates the ability of four large UK renal transplant centres to collaborate and produce large-scale data to support translational research in the future. Standardisation of data, especially unstructured data such as biopsy reports provides a major challenge for automated collection but can be overcome using modern computing. Such collaboration allows research into areas such as recurrent disease where numbers in individual centres are too small for meaningful analysis.

Diagnostic utility of anti-hepatitis E virus antigen-specific ELISA compared to PCR in a cohort of liver transplant patients in a large university hospital

Sonya Hessey¹, Germander Soothill¹, Michael Ankcorn², Marios Erotocritou³, Samreen Ijaz², Douglas Thorburn¹, Dianne Irish¹

Background: Hepatitis E virus (HEV) is increasingly recognised as an important infectious hepatitis that causes both acute and chronic disease. Chronic hepatitis E predominantly affects people who are immunosuppressed and recent evidence suggests that liver transplant patients are at a particularly increased risk (personal communication). HEV serology is unreliable in immunosuppressed patients, so HEV polymerase chain reaction (PCR) is the current diagnostic gold standard. In this study, we compared a commercially available anti-HEV antigen-specific ELISA to HEV PCR. Our aim was to assess the utility of a low cost assay in detecting HEV in a large liver transplant patient cohort at risk of developing chronic infection.

Method: The serum samples of liver transplant patients visiting the outpatient clinic at the Royal Free Hospital over an 8-month period were tested with the Fortress anti-HEV-Antigen IgM ELISA assay kit (Fortress Diagnostics, Antrim, United Kingdom, BXE0903A). HEV-antigen (HEV-Ag) was captured in microwells pre-coated with antibodies directed against the it (anti-HEV-Ag). The presence of HEV-Ag was detected by adding a second anti-HEV-Ag antibody conjugated to the horseradish peroxidase (HRP), an enzyme that hydrolyses chromogens to produce a colour change. The intensity of colour change (or absorbance) measured by a fluorescence detector is proportional to the amount of antibody captured in the wells. Samples were reported as positive or negative for HEV-Ag based on manufacturer's thresholds. All samples were then tested for HEV RNA using the MGB-modified TaqMan probe RT-qPCR assay (Applied Biosystems, Foster City, CA, USA). The primers targeted the OFR3 of the viral nucleic acid.

Results: A total of 490 patient serum samples were tested. The prevalence of hepatitis E virus infection was 0.20% (n=10). Table 1 summarises the performance of the ELISA compared to PCR in our cohort. The sensitivity of the ELISA was 100% with a specificity of 98.2%. The PPV of the antigen specific ELISA was 10% with a NPV of 100%.

Discussion/conclusion: The anti-HEV antigen-specific ELISA could have a role in diagnosing HEV infection in this patient cohort. There were no false negative results, which supports the utility of the antigen-specific ELISA as a screening tool. Further investigation including cost analysis is indicated to determine the efficacy of anti-HEV antigen-specific ELISA testing in a screening context and clinical investigation of hepatitis E infection.

	HEV PCR positive	HEV PCR negative	Total
HEV Ag test positive	1 (True positives)	9 (False positives)	10 (Total positives)
HEV Ag test negative	0 (False negatives)	480 (True negatives)	480 (Total negatives)
Total	1	489	490

 Table 1: Comparison of the anti-HEV antigen-specific ELISA test versus the reference real time PCR test for diagnosis of HEV.

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Stoma formation after early graft pancreatectomy: are the risks underestimated?

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Introduction: Early graft pancreatectomy (EGP) may be required for many indications after SPK transplantation, including graft failure or leakage of enteric or enzyme-rich contents. With enterically drained grafts, management of the recipient's abdomen after EGP can be challenging, and a small bowel stoma may be required. A retrospective analysis of our programme was undertaken in order to better define the risks of EGP and stoma formation.

Methods: All primary SPK transplants performed in our unit between 1.1.13 and 17.5.17 were included. Graft drainage was exocrine-enteric to the jejunum or ileum, and portal-systemic, in all cases. Electronic records were searched to identify all returns to theatre (RTT) within 6 months of transplantation (excluding transplant ureteric stent removal). If a stoma was formed after EGP, the patient was followed-up for the date of stoma reversal.

Results: 122 SPKs were carried out within the study period (81 DBD, 41 DCD), with median (IQR) donor age 33 (22-47) years, donor BMI 24 (21-26) kg/m^2 , recipient age 43 (36-49) years, and pancreas CIT 11h17m (9h40m-13h00m). 46 recipients had a RTT (37.7%); of those with RTT, median (range) number of RTTs was 1 (1-19). Sixteen recipients had EGP (13.5%) due to enteric/enzyme leaks (9), graft ischaemia (6) and severe pancreatitis (1). Of these 16 patients, 4 required small bowel stoma formation to deal with hostile abdomens (overall rate 3.3%). The median (IQR) number of days until stoma reversal was 175 (131 – 500). Recipients with a RTT had longer index admission inpatient stays than those without (20 (12-30) vs 11 (9-14); p<0.01).

Conclusions: EGP is not uncommon in our programme, and a quarter of patients required stoma formation if EGP occurred (overall rate 3.3%). These data provide additional information for the appropriate counseling and consenting of potential SPK recipients.

Deaths following combined kidney and pancreas transplantation: a single centre experience

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Introduction: Kidney and pancreas (SPK) transplantation is reported to be associated with higher short term mortality but better long term survival than a deceased donor kidney alone. We reviewed post-operative mortality in our programme.

Methods: The records of all recipient SPK transplants since the programme commenced in January 2001 were reviewed up until 3rd November 2017.

Results: 267 pancreas transplants were studied. The mean age of recipients was 42 years (range 24 to 63), and the mean duration of diabetes before transplantation was 28 years (range 11 to 53 years). 28% were not on dialysis when transplanted while the rest had a median 14 months dialysis exposure (range 1 month to 7 years). 22 patients died following transplantation. Pancreas graft failure preceded death in 8 cases by a median of 423 days (range 59 days to 10 years), while kidney graft failure preceded death in 8 cases by a median 680 days (range 193 days to 6.5 years). The actuarial 1, 5 and 10 year patient survivals were 98.8%, 94.0%, and 85.3% respectively, with the actual 10 year survival for the 50 patients transplanted before 20 November 2007 being 84%. The commonest causes of death were cardiovascular, cerebrovascular, cancer and sepsis. There were two deaths related to surgery, both ruptured mycotic aneurysms following graft pancreatectomy.

Cause of death	Number	Time since transplant (months)
Cardiovascular	3	23, 50, 100
Cancer	3	14, 40, 70
CVA	3	19, 100, 122
Sepsis	4	27, 47, 105, 123
Haemorrhage-mycotic aneurysm	2	7, 24
EPS	1	7
Intestinal infarction	1	8
Autoimmune haemolytic anaemia	1	51
Withdrawal from dialysis	1	111
Unknown	3	45, 70, 80

Discussion: Good long term survival can be achieved with combined kidney and pancreas transplantation. The common causes of death are as might be expected in this patient population; cardiovascular, cerebrovascular, infections and cancer.

Pre-emptive renal transplantation versus tranplantation after a period of dialysis in paediatrics: a meta-analysis of outcomes

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Introduction: The benefits of pre-emptive renal transplantation (PKT) as compared with transplantation after a period of dialysis (non-PKT) are well reported in adults but less clear in children.

Methods: A comprehensive search was performed of 6 databases including Embase, Medline, Web-of-science, Cochrane, Pubmed publisher and Google Scholar. All studies including the terms pre-emptive renal transplantation were screened. The methodology was in accordance with the Cochrane Handbook of Systematic Reviews of Intervention and written based on the PRISMA statement.

Results: The initial search yielded 3528 results; 222 were selected for examination of the full text; 17 studies were identified as paediatric and data extraction attempted; 11 yielded outcomes that were used for the meta-analysis. In total the analysis included 7278 patients of which 1851 (25%) received PKT. On comparing PKT with non-PKT using a random effects model, there was no difference in patient survival (OR 1.011; 95% CI 0.603-1.695; p=0.9665) at a median follow-up of 5 years. There was significantly less graft loss at 5 years (OR 0.63; 95% CI 0.54-0.73; p<0.0001), and less acute rejection (OR 0.7; 95% CI 0.6-0.81; p<0.0001) in PKT as compared with non-PKT.

Discussion: Among paediatric recipients, PKT appears superior to non-PKT in terms of renal allograft survival and acute rejection, but not patient survival. There is a higher proportion of live donors and congenital disease in the PKT group and the review included low level evidence with heterogeneity between studies. Nevertheless, steps should be taken to prevent the need for dialysis before transplantation in children with ESRD. This means earlier referral for transplantation to allow more time for identification and screening of live donors and transplantation earlier in the course of disease.

Quality governance for quality outcome - extended death-censored graft survival analysis of a single centre outlier in the annual kidney centre report

Roberto Cacciola

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Introduction: Renal Transplantation (RT) is the best Renal Replacement Treatment (RRT) for eligible patients with ESRF. Transplant Units outcomes are reported by ODT annually. Early failures and patient deaths in the first 30 days post-transplant are captured by ODT with the CUSUM signal. This single centre analysis is focused on Death-Censored Graft Survival (GS) and cross referenced between the local database with ODT data.

Methods: All first transplants performed between 1/4/2012 and 31/3/2016 excluding Double Kidney Tx and Donors <18years were analysed. GS at 30 days was divided as Peri-Operative (PO) and MDT to capture graft failures occurred in the immediate PO period or after. SCr was used to evaluate functions at 1year. Failures occurred after 1year and GFR<15 were used to calculate "Provisional" and "Projected" GS at 5years. Kaplan-Mayer Survival and X2 test were performed to compare with National average.

Results: There were substantial discrepancies between ODT and local database. We identified 234 transplants and 29(12.4%) Graft Failures at 1year. Cause and timing of failure are in Fig1-2; of note there were 9 (3.8%) deaths with a functioning Tx. At 1year, suboptimal/poor functions were observed in15% of patients. After 1year from transplant with a follow-up 13-56months 50% of patients had stable or improved functions; the remaining: unknown/transferred (10%), worse functions (19%), Imminent graft loss with GFR15 or less (4.2%) or dialysis (5.5%).

Conclusion: The benefit of RT and the immense efforts to provide usable organs should be protected by rigorous governance, more efficiently coordinated between providers, regulatory bodies and commissioners. Centres significantly below expected outcomes, should undergo substantial peer review in all aspects of the service, ideally guided by Kaplan-Mayer survival. Similarly to other areas of health care, an accurate definition of the MDT should be clearly suggested by BTS and commissioners



Improved diagnosis and management of paediatric renal transplant recipients using the Banff 2013 histopathological classification

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Introduction: Since the publication of the 2013 Banff classification, adult studies have shown evidence of improved prognosis using the new histopathological criteria. Our study assesses for the first time the impact of the new classification on the diagnosis of acute antibody-mediated rejection (AMR) in paediatric renal transplant recipients (pRTR).

Methods: This single-centre study is a retrospective evaluation of 56 paediatric post-transplant de novo DSA-positive patients who had a percutaneous renal transplant biopsy due to renal allograft dysfunction from January 2006 to March 2012. Their biopsies were re-scored by a solitary specialist trained in 2013 Banff classification. The results were compared with previous classification as per 2003/2007 Banff criteria with results presented as range (median).

Results: At the time of biopsy, pRTR were aged 1.6 - 17.5 (median 14.9) years old with 412 - 2735 mean fluorescence intensity (MFI; maximal at 713 - 31,625; median 3466 and 4809). Following the 2013 Banff classification, there was a total of 5 cases of acute AMR compared to one confirmed and one suspicious AMR with the 2003/2007 Banff classification (with no change in the remaining 51 patients' classification). Consequently, 5.3% (3 of 56) patients would have been diagnosed with T-cell mediated rejection with suboptimal treatment. There was an overall 70% (48 - 112%) decrease in the renal allograft function in the 6 months follow-up period after aggressive treatment for acute AMR and 2 of 3 patients had further rejection episodes in the following year.

Conclusion: This research supports the new Banff 2013 classification as a more precise classification in pRTR in the diagnosis of AMR with 5% of patients being correctly diagnosed and managed with improvement in renal allograft function.

Pre-emptive live donor renal transplantation versus live donor tranplantation after a period of dialysis in adults: a meta-analysis of outcomes

Samuel Turner^{1,2}, Liset Pengel³, Jeff Lafranca^{2,4}, Wichor Bramer⁴, Frank Dor^{2,5}

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Introduction: The benefits of pre-emptive renal transplantation (PKT) as compared with transplantation after a period of dialysis (non-PKT) are well reported but no formal meta-analysis has been done. We restricted this analysis to adult live donor renal transplants only.

Methods: A comprehensive search was performed of 6 databases including Embase, Medline, Web-of-science, Cochrane, Pubmed publisher and Google Scholar. All studies including the terms pre-emptive renal transplantation were screened. The methodology was in accordance with the Cochrane Handbook of Systematic Reviews of Intervention and written based on the PRISMA statement.

Results: The initial search yielded 3528 results; 222 were selected for examination of the full text; after exclusions and removal of duplicates 22 yielded outcomes that were used for the meta-analysis. On comparing PKT with non-PKT using a fixed effects model, there was significantly lower 5 year patient death (OR 0.698; 95% CI 0.58-0.83; p<0.0001) and less acute rejection (OR 0.76; 95% CI 0.71-0.82; p<0.0001) in PKT. Using a random effects model, there was significantly less delayed graft function (OR 0.474; 95% CI 0.39-0.58; p<0.0001) and significantly lower graft loss at 5 years (OR 0.62; 95% CI 0.51-0.76; P<0.0001) in PKT as compared with non-PKT.

Discussion: PKT appears superior to non-PKT among live donor transplants in terms of delayed graft function and 5 year allograft survival, and to a lesser extent in terms of acute rejection and patient survival. Whilst we accept that the review included low level evidence with heterogeneity between studies, steps should be taken to prevent the need for dialysis before transplantation in adults with ESRD. This means earlier referral for transplantation to allow more time for identification and screening of live donors and transplantation earlier in the course of disease.

Recipient age is a significant factor in immunological and infective complications following kidney transplantation

<u>Rachel Hung</u>¹, Raymond Fernando^{1,2}, Sumoyee Basu¹, Gabrielle Goldet¹, Sacha De Serres^{3,4}, Mark Harber^{1,5}, Gareth Jones^{1,5}, Alan Salama^{1,5}, Ciara N. Magee^{1,5}

Introduction: Increasing numbers of older patients (>65 years) are undergoing kidney transplantation. While there is growing evidence that the ageing immune system is characterized by immunosenescence, many centres don't have age-specific protocols for immunosuppression. We examined the effect of recipient age on the development of complications of immunosuppression post-transplantation.

Methods: We investigated 90 kidney transplants performed in our centre between April 2009-March 2016 in recipients aged >65, 42 of whom were >70; comparisons were made to 214 controls matched for HLA-mismatches and divided into groups according to age at transplantation (18-34, 35-49 & 50-64). Recorded variables included rejection, development of donor-specific anti-HLA antibodies (DSA), and CMV viraemia.

Results: Rates of rejection were higher in the younger age groups (29%, 15.3% and 16.3% of patients aged 18-34, 35-49 & 50-64 vs 10.4% & 11.9% in those aged 65-69 & >70; p=0.068). Development of de novo Class I DSA was significantly higher in younger patients (13.3%, 1.4% & 15% in patients aged 18-34, 35-49 & 50-64 vs 4.2% & 7.1% in those aged 65-69 & >70; p=0.018); development of de novo Class II DSA followed a similar trend. Conversely, rates of CMV viraemia were significantly elevated in older recipients (77.1% and 73.8% in patients aged 65-69 and >70 years vs 38.7%, 27% and 54.3% in those aged <35, 35-49 & 50-64; p<0.001). CMV viraemia increased across all D/R serostatus pairings, but was most striking in the D-/R+ and D+/R+ groups: 22/51 (43%) vs 20/28 (71%), and 52/100 (52%) vs 36/45 (80%) in patients aged <65 and >65; p=0.0195, p=0.0017).

Conclusion: These data show that older recipient age is associated with reduced rates of rejection and *de novo* DSA but significantly increased risk of infection, suggesting increased vulnerability to immunosuppression and providing support for development of age-specific protocols.

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Development of a classification of immunosuppressant medication nonadherence tool to enable the objective measurement of immunosuppressant medication nonadherence in kidney transplant patients

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Introduction: KDIGO define nonadherence to immunosuppression as a 'deviation from the prescribed medication regimen sufficient to adversely influence the regimen's intended effect'. There is however, no agreed standard by which to measure nonadherence post-transplant and no agreed taxonomy in order to define adherence in terms of the number of missed doses, the early/late administration of doses, the measurement of subtherapeutic or highly variable tacrolimus levels or other criteria by which we may assess the patient as being nonadherent in clinical practice. The absence of a taxonomy has led to confusion in the literature with different authors using arbitrary cut-offs or percentages to classify patients as adherent or nonadherent. The aim of this study was to develop a classification for immunosuppressant medication nonadherence to enable its objective and consistent measurement in transplant patients.

Methods: A stakeholder group was set up consisting of transplant nephrologists, surgeons, nurses, pharmacists and patients. The project lead reviewed the current immunosuppressant medication adherence literature which was summarised and used to develop a list of the criteria which had been used most commonly to define nonadherence. Each of these criteria were discussed and a classification agreed for each to enable the objective and consistent measurement of nonadherence which also takes account of the associated risk to the patient and to their graft.

Results: A tool [below] was developed which lists each criterion identified in the classification of immunosuppressant medication nonadherence, how that criterion will be objectively measured, the adherence rating and an overall adherence score.

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Conclusion: The classification of immunosuppression medication nonadherence is complex and lacks formal agreement in the literature. This classification tool will enable the objective and consistent measurement of immunosuppressant medication nonadherence in kidney transplant patients. The tool will be piloted prospectively in a group of transplant patients.

Utilisation of kidneys from increased infectious risk donors: local outcomes and national practice

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Introduction: Use of kidneys from increased infectious risk (IIR) donors is an increasingly employed strategy to expand the donor pool. We investigated the outcome of transplants from these donors in our centre, with reference to the stringency of post-transplant virological testing, and also examined national practice.

Methods: Data were collected on all transplants performed in our centre from 2012-16 from donors meeting the Canadian Standards Association 2012 criteria for IIR. End-points included graft function, the proportion of patients who underwent antibody or nucleic acid testing (NAT) for HIV, HBV and HCV in months 0-2 (early) or 3-12 (late) post-transplant, and seroconversion. All UK renal transplant centres were also contacted to determine their practice.

Results: We performed 30 transplants from 22 IIR donors (15 DBD, 7 DCD) with a median age of 33 years during this 5-year period. Donor NAT results were not available prior to the implantation of any of these organs. 24/30 (80%) of grafts experienced primary function and median eGFR was 60mls/min 3 months post-transplant. Only 50% and 60% of patients underwent early and late viral screening, respectively. Overall, 67% of recipients were tested for viral transmission within 12 months post-transplant; no seroconversions were detected. 18/23 (78%) of UK units responded to our questionnaire: 14/18 (78%) utilise organs from IIR donors, but only 2/18 (11%) have a formal protocol for post-transplant testing.

Discussion: Kidneys from IIR donors provide excellent graft function and can be safely implanted into appropriately-counselled recipients. Only a minority of UK units have a formal protocol for post-transplant recipient testing, and this study highlights the need to implement such a protocol in our centre.

Use of immunosuppression in older kidney transplant recipients: UK practice

Rachel Hung¹, Gareth Jones^{1,2}, Alan Salama^{1,2}, Ciara N. Magee^{1,2}

Introduction: Increasing numbers of older patients (>65 years) undergo kidney transplantation. There is growing evidence that patients develop age-related changes to their immune system, termed immunosenescence, placing them at increased risk of infective complications. Yet, there are no recommendations for age-specific immunosuppression protocols. We sought to understand the use of immunosuppression in older kidney transplant recipients (oKTRs) across UK transplant units.

Methods: An online survey was sent out via email to consultant transplant nephrologists and transplant surgeons in 22 transplant units. The survey was split into three sections: standard induction and maintenance immunosuppression; determination of modification of immunosuppression in oKTRs; and assessment of interest in/need for investigation of agespecific protocols.

Results: 17/22 (77%) transplant units responded to the survey. All units reported use of basiliximab as an induction agent, while 5/17 (29%) also used anti-thymocyte globulin, and 7/17 (41%) also used alemtuzumab. Tacrolimus was universally used, but with significant variability in target trough levels across units, ranging from 5-14 in months 0-3, and 4-9 thereafter. Mycophenolate mofetil (MMF) was administered at a dose of 1.5 g/day by 3/17 units (17%), while 14/17 units (82%) used 2 g/day. Immunosuppression was modified for oKTRs by 8/17 units (47%); adjustments included avoidance or reduction in dose of an induction agent, avoidance of maintenance steroids, and reduced dosing of maintenance mycophenolate or tacrolimus. Transplant clinicians from 10/17 (59%) responding centres agreed that the use of reduced immunosuppression in oKTRs merits investigation in the form of a trial.

Conclusion: Our data shows that widely different immunosuppression regimens are used across the UK and most units do not modify their immunosuppression regimen for oKTRs. Increasing awareness of age-specific changes in immune responsiveness, however, underscores the importance of robustly investigating this issue in efforts to reduce significant infection-related morbidity in older recipients.

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Culture-positive ureteric stents in renal transplantation, who should be treated?

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Introduction: Ureteric stents were used in renal transplantation in cases of uerteric injury. However, it was shown that routine double J stent placement at the time of transplantation reduce uerteric complications. This is a reterospective review of renal transplant patients in whom positive culture from the ureteric stent was encountered at the time of removal, whether this group needed antimicrobial therapy and lastly, if these infections had impact on the transplant graft outcome. In this study we tried to identify cases with culture positive ureteric stents warranted treatment.

Methods: We performed a retrospective review of 86 patients who underwent renal transplantation between April 2016 and February 2017. Our protocol is to remove the transplant ureteric stents at 6th week post-transplant with a single dose of broad spectrum antibiotic peri-procedure. All JJ stents are sent for culture and sensitivity as a routine.

Results: In total, 20 patients (23%) had positive ureteric stent culture. Eight (40%) patients of the twenty were symptomatic for urinary tract infection and had positive urine culture versus 12 (60%) asymptomatic cases and had negative urine culture. Four (20%) patients of the symptomatic group were admitted and treated for urosepsis and the other four (20%) treated for urinary tract infection on an out-patient bases. None of the asymptomatic group with positive stent culture and negative urine culture received any treatment. The average tacrolimus level for the positive ureteric stent culture group and negative ureteric stent culture group were 8.8 ng/L and 8.0 ng/L respectively. Serum creatinine level among the positive stent culture and negative stent culture was 178umol/L and 159 umol/L respectively.

Discussion: The incidence of culture positive ureteric stents was 23%. Only 40% of positive ureteric stent culture developed urosepsis proven by urine culture. Treatment was only indicated if the positive stent culture was associated with symptomatic UTI.

ABO-incompatible renal transplantation at a UK university teaching hospital: 3-year outcome

Adham El-Bakry, Abdul Wahab Elmghrbee, Hemant Sharma, Jessica Overton, Sanjay Mehra, Daniel Ridgway, Ajay Sharma, Abdul Qader Hammad

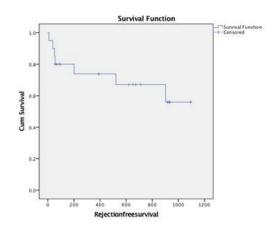
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Introduction: The primary cause of graft loss in ABO-incompatible kidney transplant is antibody-mediated rejection (AMR). Recent studies have reported 17.9% up to 30% incidence of AMR in ABO-incompatible kidney transplants. The objective of the study is to measure the rate of acute antibody mediated rejection (AMR), patient and graft survival.

Methods: This is a single centre retrospective analysis of consecutive renal transplant from November 2008, when the first ABOi renal transplant was performed at our centre, till June 2017. A total of 20 ABO-I transplants were followed up. Our Antibody removal protocol included administration of Rituximab (375mg/m2), maintenance immunosuppression as, tacrolimus, mycophenolate and steroid avoidance, Immunoadsorption (IA) aiming antibody titre of 1: 8 or less, IV immunoglobulin infusion and up to three sessions of IA post-transplant with the freedom of less sessions if antibody titre is 1 in 8 or less associated with favourable allograft function.

Results: The Overall graft and patient survival was 93.4% and 100 % respectively. One graft loss (5%) secondary to sepsis and immunosuppression non-adherence. Biopsy proven rejection was 20%. All cases were acute cellular rejection. All cases of ACR occurred within the first 3 month post-transplant and responded well to pulse steroid therapy, none required ATG or plasma exchange.

On cox proportional regression model 6 month creatinine was significant for rejection free survival (HR, 95% CI HR p=0.0.). On linear regression analysis, serum Creatinine at 6 &12 months, CMV infection P values were statistically significant for rejection free survival.



							95.0% (Ratio	CI for Hazard
	В	SE	Wald	df	Sig.	Hazard Ratio	Lower	Upper
CMV	14.260	217.365	.004	1	.948	1560324.989	.000	1.639E+191
BK	4.575	2.440	3.516	1	.061	97.064	.813	11592.229
@612creat	026	.018	2.001	1	.015	.975	.941	.982
creat1212	.065	.038	2.969	1	.085	1.067	.991	1.148
creat2yrs	.027	.037	.552	1	.457	1.028	.956	1.104

Conclusion: The 3-years follow-up results showed that, there was no graft loss due to neither acute antibody mediated rejection nor acute cellular rejection. The graft loss was secondary to non-immunological reasons. Our ABO incompatible living donor Renal Transplant program has maintained high standard and is of excellent outcome comparable to the national U.K results.

Enhanced recovery after surgery and the renal transplant recipient – useful or a waste of time? The University of Adelaide experience

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Introduction: Despie significant interest in enhanced recovery after surgery (ERAS) pathways in renal transplant recipients, the published results are variable and a clear consensus doesn't exist in the utility of these pathways. The renal transplant unit at the Royal Adelaide Hospital introduced an ERAS protocol for the management of the renal transplant recipients from June 2017. We present the outcomes of 27 consecutive renal transplant recipients.

Methods: All renal transplant recipients from June 2016 till the time of writing this abstract were enrolled in the ERAS protocol. Briefly the protocol included pre-op weight optimization on dialysis prior to transplant for those on haemodialysis; pre and post operative carbohydrate loading; goal directed fluid therapy and opiate avoidance and use of transversus abdominis plane wound infusers. In this period 3 recipients received kidneys from a live donor, 24 from deceased donors of which 19 were donation after brainstem death (DBD) and 5 donations after circulatory death (DCD).

Results: 92.7% patients were discharged from hospital by post-operative day 4. 2 patients had longer in-patient stay. None of the live recipients had delayed graft function requiring dialysis; 2 of 5 recipients from DCD donors had delayed graft function (40%) and 6 of the 19 recipients from DBD donors had delayed graft function (31.5%). The mean weight gain on post-operative day 1 was 1.26Kg. The cost of 1 bed stay in Adelaide is \$1000.00 and institution of this protocol so far has resulted in a \$25,000 cost saving.

Conclusion: Our experience challenges the widespread practice of fluid loading post renal transplant. We haven't witnessed an increased rate of delayed graft function across various recipient groups in this period. Our re-admission rate has not increased and early results suggest that there are significant cost savings that can be made.

The impact of patient expectations on quality of life after kidney and pancreas transplantation

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Introduction: Transplantation offers numerous benefits to those with end-stage organ failure. The aim of this study was to quantify the impact of the reported patient experience on quality of life outcomes.

Methods: A questionnaire was sent to simultaneous pancreas-kidney (SPK) and deceased and live donor kidney recipients (DDR and LDR, respectively). Validated psychosocial outcome measures (capturing life satisfaction, mood, distress and health-related quality of life (HRQoL)) were included alongside questions on benefit, expectations, regret and perceived life change after transplantation.

Results: 115 responses were received (18 SPK, 34 DDR, 63 LDR). The majority of recipients reported benefit (96.5%) and no regret (97.3%). 10% of recipients' expectations were not met and 14.5% felt their life had remained unchanged or had worsened. Unmet expectations and belief that life had not changed for the better was associated with significantly lower life satisfaction and HRQoL, and higher distress and depression (Tables 1 and 2).

Discussion: A significant proportion of recipients report unmet expectations and a belief that life has not changed for the better since transplantation. This is associated with psychological distress. It is therefore imperative that recipients' expectations are managed and those who feel disappointment are identified and supported.

Table 1:

	Expectations	N	Mean	Std Deviation	Р
Life Satisfaction	Met	88	25.38	6.314	<0.001
	Unmet	10	14.20	4.158	
Distress	Met	96	9.76	5.662	<0.001
	Unmet	11	19.09	8.654	
Depression	Met	99	0.88	1.357	<0.001
	Unmet	11	2.73	2.240	
HRQoL	Met	98	44.47	8.795	<0.001
	Unmet	11	31.09	8.093	

Table 2:

	Life change	N	Mean	Std Deviation	Р
Life satisfaction	Better	82	25.46	6.256	<0.001
	Worse/unchanged	13	17.08	7.805	
Distress	Better	89	9.85	5.898	0.006
	Worse/unchanged	15	14.80	8.629	
Depression	Better	93	0.87	1.385	0.002
	Worse/unchanged	15	2.20	2.077	
HRQoL	Better	92	44.54	8.835	0.002
	Worse/unchanged	14	36.36	10.551	

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Exploring immunosuppressant medication adherence in kidney transplant recipients

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Introduction: Nonadherence to immunosuppressive medication (IM) is associated with poor outcomes following kidney transplantation. The aim of this study was to describe the beliefs, understanding and experience of IM adherence in kidney transplant recipients (KTR) in order to inform clinical practice in improving IM adherence in KTRs.

Methods: Five focus groups, each including up to 6 KTRs were video recorded, transcribed and the content coded. Codes from each focus group were categorised and themes identified.

Results: Participants had a good understanding of the allogenicity of the transplanted organ and the resultant need for lifelong IM. Missing doses, irregular timing, not taking tacrolimus on an empty stomach and nonattendance at clinic appointments were all defined as nonadherence by the participants. Concern was expressed regarding the risk of adverse effects from IM, especially when taken in the long-term but tended to be balanced against the risk of not taking IM. Common barriers to adherence identified were forgetfulness, distractions, establishing and maintaining a routine around medicine taking and pill burden. Self-filled compliance aids, alarms, smart-phone apps, establishing a routine and placing IM in an obvious place were all popular tools used to improve adherence. Participants felt they had benefitted from support provided by the clinical team in the early post-transplant period but that more medicines adherence support should be provided before and after the transplant and that adherence should be reviewed formally and at regular intervals during clinic appointments.

Conclusion: Although participants understood the need to take IM a number of barriers were identified that impaired their ability to fully adhere. Barriers to adherence can change over time and participants felt that more formal and regular review of their IM adherence during clinic appointments would allow the identification of problems at an early stage and facilitate the identification of interventions to help patients maximise their IM adherence.

Using the Japanese KJ Ho method as a qualitative creative problem solving technique to address clinicians' and young kidney transplant patients' needs concerning treatment.

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Introduction: Treatment adherence in kidney transplant patients is particularly challenging during adolescence and young adulthood. This produces adverse consequences such as higher transplant failure, decreased quality of life and increased mortality. A novel qualitative creative problem-solving method (KJ Ho), widely used in Japan, has been applied in the United Kingdom (UK) to disentangle clinicians' and young kidney transplant patients' perspectives on this problem area. The study forms the first stage in the development of a user-driven digital intervention to improve long-term treatment adherence. KJ-Ho has contributed widely to clinical practice and knowledge in multiple contexts in Japan; our first application of this method in the UK should similarly contribute to improving post-transplant practice and knowledge.

Methods: KJ Ho is a Japanese creative problem solving method to organize qualitative research data. Clinicians were invited to take part in a two hour creative workshop. Data were analysed in a step-wise approach from which several overarching themes emerged. Similar workshops for patients (aged from 13 - 30 years) and their family members are being conducted. KJ Ho findings will be synthesized with two systematic literature reviews being undertaken in parallel.

Results: Six overarching themes were identified during the clinicians' workshop: (1) non-adherence; (2) communication; (3) continuity in care; (4) values; (5) family; (6) patient-centred. Similar data concerning young kidney transplant patients' needs is currently being collected and analysed. Triangulation of the KJ Ho data with standard systematic review outputs will provide a robust evidence base for intervention development.

Discussion: Integration of this original KJ Ho problem-solving method with standard Western systematic literature review methods can better identify factors currently influencing treatment adherence. This co-creation phase will be followed by a codesign stage to produce a digital intervention able to improve treatment adherence among young kidney transplant patients, which will be tested in a future large-scale trial.

Over the limit? Renal transplantation in patients above the age of 70 years. A retrospective single centre study

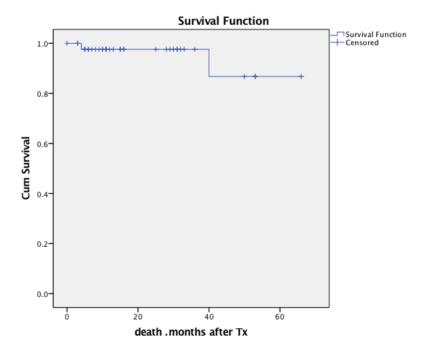
Jessica Overton, <u>Helen Bermingham</u>, Hemant Sharma, Daniel Ridgway, Ajay Sharma, Sanjay Mehra, Abdul Hammad, Adham El-Bakry

The Royal Liverpool and Broadgreen University Hospital, Liverpool, United Kingdom.

Introduction:_Transplantation is the renal replacement modality of choice for end stage renal failure (ESRF) patients deemed medically suitable. However for patients over 65 years of age, transplantation is carried out primarily to improve their quality of life.

Method: We included 45 patients who underwent renal transplant at the Royal Liverpool University Hospital between February 2010 and September 2016 and were aged 70 years or older on the day of transplant. The primary outcomes were patient and graft survival. Secondary outcomes included biopsy proven rejection, complications and graft function.

Results: 45 patients were identified with a median age of 73 years (range 70- 84); 29 were males. 52 kidneys were transplanted; 7 dual and 38 single graft transplants. The organ donor pool included 5 living donor renal transplants, 40 deceased donors, of which 28 were DCDs and 12 were DBDs. Patient survival was 80% at 1 year (36), 64.5% at 3 years (20/31 accounting for loss to follow up). Death censored graft survival (DCGS) was 97.6% at 1 year and 86.8% at 3 years. Causes of death (18 patients) were Malignancy = 4, Infection =1, Miscellaneous =3, and 10 unknown (following repatriation to referring units). Eleven patients underwent transplant graft biopsies, 2 showed acute cellular rejection both received campath induction and 9 were reported as ATN. 12 patients developed cytomegalovirus (26.7%), of those 11 were Alemtuzumab induction and 1 was Basiliximab induction. 3 patients developed BK viraemia (6.7%). 4 patients developed post-transplant diabetes (9.3%). 4 patients sustained cerebral vascular event (CVA) (9.3%) and 2 patients suffered myocardial infarction (MI) (4.6%). 9 cases of Malignancy (20%). Median creatinine at 1 year was 137umol/L, 112umol/L at 3 years.



Discussion: Renal transplantation in the over 70-year-old age group can have favourable outcomes with uncompromised survival rates and non-inferior death censored graft survival.

A pathway for young person's transition to adult services for kidney transplant

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Introduction: End-stage kidney disease (ESKD) is the commonest cause of end stage organ disease in children and adolescents. Our service currently manages 250 young patients (YP, 18-26 years). Transition from paediatric to adult services is challenging with a high reported incidence of allograft loss and non-adherence (Watson 2012). Whilst a transition pathway to adult services implementing "Ready Steady Go" and "Hello" already existed in our services, no pathway specifically targeting YP transitioning around the time of renal transplantation was in place.

Methods: Close discussions between the paediatric multidisciplinary team (MDT), adult transition nephrologist, renal youth worker (RYW) and the adult transplant team established a pathway for YP transitioning with imminent transplantation/listing. Paediatric patients approaching 18 years old were identified. Consideration was given to how their needs could best be met through the transplant process.

Results/Pathway: All YP were first seen in the paediatric clinic supported by the RYW and adult transition nephrologist for preliminary discussion about transplantation. They then attended adult services for transplant education and assessment, supported by the paediatric MDT. The RYW introduced the patient and family to outpatient and renal ward staff, allowing them to familiarise themselves with the new environment. Paediatric MDT, adult transition lead and adult transplant team discussed the patient and their investigations in the adult transplant MDT prior to wait list activation. Early post-transplant follow-up was determined by a combination of the patients' preference and their needs as assessed by the paediatric and adult teams. Our aim is to empower the young patient with a view to improving their adherence and long term allograft function.

Discussion: The importance of the relationship between the YP and family, the paediatric, adult transition and adult transplant teams is fundamental in delivering this service.

Follow-up and outcomes of Epstein-Barr virus negative recipients after a kidney transplant from an Epstein-Barr virus positive donor

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is one of the most serious complications of chronic immunosuppression after an organ transplant. One of the major risk factors for early PTLD (within a year after transplantation) is Epstein - Barr virus (EBV) seronegative status at the time of transplantation.

Methods: Our objective was to evaluate the management of EBV negative patients who received an EBV positive kidney transplant in our department one year after the implementation of an EBV viral load surveillance guideline in 2016.

Results: During the first year following the implementation of our guideline (EBV viral load checked immediately after the transplant, then monthly for 6 months then every 3 months up to one year), 16 EBV seronegative patients received a kidney transplant from an EBV seropositive donor. The median length of follow-up after transplantation was 8 ±4.5 months and 62.5% of our patients (10/16) developed detectable EBV viraemia during this time. In seven out of ten cases (70%) immunosuppression was decreased, and in four patients mycophenolate was discontinued. This was followed in one case by a rejection episode, but in four cases there was a reduction in EBV viral load. Two patients developed symptomatic viraemia but had a negative PET-CT scan and were referred to haematology for further advice. EBV seroconversion was assessed in only five patients but was present in four of them (80%). At completion of follow-up, no patient developed early PTLD and all had a functioning kidney transplant.

Discussion: EBV viral load surveillance in EBV seronegative patients after receipt of a kidney transplant from an EBV seropositive donor assists in tailoring immunosuppression to prevent early PTLD.

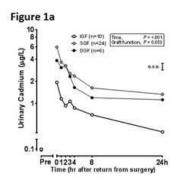
Urinary cadmium and copper as biomarkers of acute tubular injury in renal transplantation

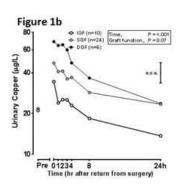
<u>Jennifer Allen</u>^{1,2}, David Gardner², Catherine Byrne¹, Richard Greenhow¹, Zsolt Hodi³, Tom McCulloch³, Keith Rigg¹, Mark Devonald^{1,2}

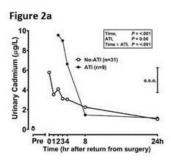
Introduction: Ischaemia reperfusion injury (IRI) during renal transplantation can result in acute tubular injury (ATI) which may lead to slow/delayed graft function (SGF/DGF). Serum creatinine (SCr) is the gold standard measure of renal function after transplantation but is a poor marker of ATI. From a porcine model of IRI (Gardner et al AJP-Renal 2014) we demonstrated that urinary copper (Cu) and cadmium (Cd) are potential early biomarkers of ATI.

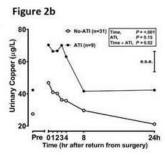
Methods: In adults undergoing renal transplantation urine was sampled at baseline, 0, 1, 2, 3, 4, 8 and 24hr following surgery. Urinary elements were measured using ICP-MS and analysed corrected for urinary Cr. SCr was measured as part of standard care. Graft function was defined as immediate (IGF) (no SGF or DGF), SGF (SCr > 265μmol/L on day 5 or <30% reduction in SCr by day 3) or DGF (need for dialysis within 7 days, excluding single session for hyperkalaemia). Biopsies within 30 days were examined for ATI. Outcome measures were presence of SGF/DGF or ATI on renal biopsy. Data are presented as means (SD or SEM).

Results: We recruited 40 patients; 73% male; median age 49yr. Transplants were 88% deceased donor, 23% pre-emptive. 25% had IGF, 60% SGF and 15% DGF. 15 underwent biopsy, 60% biopsies showed ATI. Urinary Cd and Cu rose after transplantation with levels higher in SGF and DGF relative to IGF (Fig.1a,b). In biopsied participants with ATI vs no-ATI, pre-transplant levels of Cd and Cu were similar but increased post-transplant (Fig.2a,b).









Discussion: IRI in renal transplantation causes significant rise in urinary Cd and Cu with levels higher in histologically proven ATI, SGF or DGF. Further work will identify if each can predict graft function (SGF/DGF). We suggest that after renal transplant, urinary Cd and Cu are promising biomarkers of ATI.

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Comparison of sleep quality in hemodialysis vs kidney transplant recipients using Pittsburgh sleep quality index (PSQI).

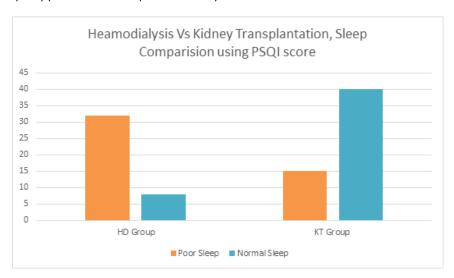
Shafiq Ahmad Chughtai, Benish Afzal, Jean Scott, Shakeeb Khan, Mayor Ghazal Aswad, James Yates, John Black, Anna Rizello, Tahir Doughman, Ahmed Ali, Atul Bagul

Leicester General Hospital, Leicester, United Kingdom.

Background: Disturbed sleep causes depression and poor health related quality of life (HRQoL). Poor sleep quality is an independent predictor of mortality in patients with end stage renal disease (ESRD). To compare the effect of kidney transplantation (KT) on sleep quality, we did a prospective study comparing patients on haemodialysis (HD) with kidney transplant recipients.

Material/methods: Pittsburgh sleep quality index (PSQI) was used to assess 40 patients each following KT and those undergoing HD. A PSQI score of 5 or more was considered indicative of poor sleep quality. All patients were requested to fill the questionnaire (self-assessment) while attending for HD sessions or follow up clinics. All transplant recipients were within 6 months of kidney transplantation and were not dependent on HD at the time of filling the questionnaire.

Results: There were 40 respondents in each group. Mean age in KT group was 50.7 years (21-75, 62% M, 38% F). Mean age in HD group was 62.3 years (26-90, 64% M, 36% F. Those with previous psychiatric history were excluded. In KT group, 15 out of 40 (37.5%) had PSQI score of more than 5. In HD group, 32 out of 40 (80%) had PSQI score of more than 5 (p< 0.5). The highest PSQI score was 17 in renal transplant patients and 16 in haemodialysis patients. Most of the respondents reported better sleep quality prior to the development of kidney disease.



Reasons for poor sleep are multifactorial however pain was the most coomon reason reported in bith groups.

Conclusion: Incidence of poor sleep was much higher in patients on HD when compared with KT recipients. Even after transplantation, the proportion of respondents reporting sleep disturbances were higher than general population. Poor sleep quality continues to adversely affect HRQoL. Further research and clinical attention for sleep disturbances in these patients is warranted.

Treatment outcomes of recurrent primary focal segmental glomerulosclerosis (FSGS) after kidney transplantation

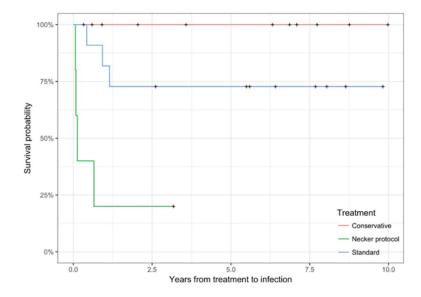
Rute Aguiar¹, Alessandro Gasparini², Fernando Pereira³, Paramit Chowdhury⁴, David Game⁴, Dimitrios Moutzouris⁴

Introduction: Primary FSGS can recur in the renal allograft and is associated with poor graft outcomes. There is no established therapeutic intervention to prevent or treat recurrent primary FSGS. We studied the outcomes and the complications of the different treatments used in our renal department for recurrent FSGS post-transplantation.

Methods: We retrospectively collected data on renal transplant recipients transplanted in our hospital from 2005 to 2016 who were diagnosed with primary FSGS and transplant biopsy proven recurrent primary FSGS. We compared the graft and patient survival along with complications of the different treatment options.

Results: 27 patients were diagnosed with recurrent FSGS. 10 (37%) received conservative treatment (steroids \pm RAS blockade), 12 (44%) received standard treatment (steroids \pm RAS blockade \pm Plasma exchange (PEX)) and 5 (19%) received the Necker Protocol (steroids, PEX and intravenous ciclosporin). After 1-year of follow up, there was no difference regarding the graft survival among the groups. There were two deaths in the Necker group and one death in the other groups. However, this did not reach statistical significance and the patient survival was comparable among treatments. Compared with the other treatments, patients treated with the Necker protocol were at a higher risk of infection (p< 0.01).

Discussion: Renal transplant patients diagnosed with recurrent FSGS and treated with the Necker protocol were at a higher risk for infection compared to other therapeutic options. There was no difference in terms of allograft survival and patient survival among the treatment groups.



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Recurrent FSGS post-transplantation: prevalence and risk factors

Rute Aguiar¹, Alessandro Gasparini², Paramit Chowdhury¹, David Game¹, Dimitrios Moutzouris¹

Introduction: Primary focal and segmental glomerulosclerosis (FSGS) can recur in the renal allograft and is associated with poor graft outcomes. The prevalence of recurrence varies widely. The aim of this study was to assess the prevalence of recurrent FSGS and to evaluate if clinical criteria can identify patients at high risk for recurrent disease.

Methods: We retrospectively studied our renal transplant recipients (2005-2016) with primary FSGS, who were diagnosed with biopsy proven recurrent primary FSGS post-transplantation. We calculated the prevalence of recurrent FSGS post-transplantation. In addition, we compared the demographics (age, gender, ethnicity and type of transplant) between the group of patients with recurrent FSGS and the group who did not recur. Subsequently, we focused on identifying risk factors for FSGS recurrence in this population.

Results: The prevalence of recurrent FSGS post-transplantation in our population was 22.3%. Patients with recurrent FSGS were younger at transplant date in comparison to patients that did not recur (p=0.05). No statistically significant differences were found for the other covariates included in the study. Most of the patients with recurrent FSGS were Caucasians (77.8%) and had living donor transplantation (62.9%). For patients who recurred post transplantation, the median time to ESRD was 3.1 years (IQI 0.92-5.70) and for the patients with a previous transplant, the median allograft survival was 1.5 years (IQI 0.92-2.18). The median time from transplantation to recurrent FSGS diagnosis was 3.96 months (IQI 0.90-18.5). There was no correlation between the histological type of FSGS in the native biopsy and in the allograft biopsy.

Discussion: The prevalence of recurrent FSGS post-transplantation in our population was lower than the reported in the literature. Renal transplant patients with recurrent FSGS were more likely to be Caucasians, younger at transplant date, with rapid progression to ESRD and rapid loss of previous allografts.

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Alkaline-encrusted pyelitis in a renal allograft: a case report

Paul Devine, Aisling Courtney

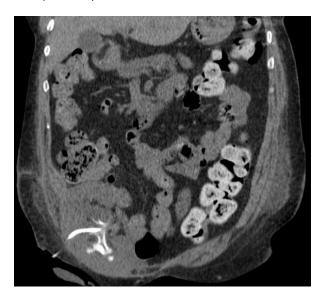
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Case history: A 55-year-old woman was admitted with visible haematuria 18 months after a kidney transplant. The patient had a history of neurogenic bladder with ileal conduit formation in childhood.

Investigations: Blood tests revealed graft dysfunction and elevated inflammatory markers (creatinine 362 μ mol/L, C-reactive protein 85 mg/L). Graft ultrasound showed extensive calcification of the collecting system with associated hydronephrosis. The working diagnosis was of an obstructing calculus and pyelonephritis. Similar appearances were noted on CT imaging (Figure).

Management: A nephrostomy tube was inserted and treatment with piperacillin/tazobactam commenced. Urine cultures were sterile. Despite antibiotic therapy there was no improvement. Creatinine rose to 514 μmol/L. Further review of imaging suggested alkaline-encrusted pyelitis as a diagnosis. Urinary pH was >9.0. Prolonged culture of the initial urine sample identified *Corynebacterium urealyticum*, confirming the diagnosis. Vancomycin therapy was initiated and acidification of urine was undertaken with Suby G solution administration via nephrostomy tube. Additional interventional radiology intervention allowed mechanical removal of some of the renal pelvis debris. Haematuria resolved, creatinine and CRP improved. To facilitate discharge the patient was trained to self-administer Suby G solution and switched to oral doxycycline. Treatment was discontinued after six weeks when the calcification had resolved. Five months later the patient remained well with serum creatinine of 97 μmol/L.

Learning points: Alkaline-encrusted pyelitis is a rare disease characterised by deposition of struvite within the renal pelvis. The causative organism, *Corynebacterium urealyticum*, is difficult to culture. Thus the diagnosis may be overlooked. Renal transplant recipients are at particular risk due to immunosuppression use and increased prevalence of urological abnormalities. The diagnosis must be considered in any recipient displaying urinary symptoms associated with culture-negative, alkaline urine and calcified urothelium on unenhanced CT. Graft loss may be prevented by intravenous vancomycin and urinary acidification via nephrostomy tube.



The positive clinical impact of a BK virus screening programme

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Introduction: BK virus infection after kidney transplantation can cause graft dysfunction and failure. An effective prophylaxis strategy is lacking, but early detection of the virus allows immunosuppression reduction and minimisation of complications. Our transplant centre introduced a BK screening programme, in accordance with national guidance, recommending monthly blood samples in all recipients for 6 months post-transplantation, with further samples at months 9 and 12. The aim of this study was to evaluate the clinical impact of this quality improvement project.

Methods: Patients who received a kidney transplant between 1st Oct. 2015 and 30th Sep. 2016 were eligible for inclusion. The regional Renal Transplant Database and an electronic laboratory results system were interrogated. Samples until 1st Nov. 2017 were included.

Results: There were 106 eligible recipients. Baseline demographics are outlined in Table 1.

Table 1: n= 106*	
Age, years (median, range)	52 (17-78)
Male	58 (55%)
Pre-emptive	36 (34%)
Living donor	70 (66%)
Use of induction agent	30 (28%)
Antibody incompatible	7 (7%)
*Patients excluded if they e	xperienced graft loss, death
or transferred to another	region within 12 months

All patients had at least 2 samples and overall sampling rate at each time point was 75-90%. 28 patients (26%) demonstrated BK positivity on at least one blood sample. The median time from transplant to first positive BK sample was 87 days (range 32-587). In 57% the initial BK viral load was <15000 copies per ml. Three (11%) BK positive patients had a mild, transient creatinine rise associated with viraemia, that did not provoke biopsy. There were no biopsy-proven episodes of BK virus nephropathy in other 'for cause' biopsies in this cohort.

Discussion: Introduction of a screening programme promotes early detection of BK when the viral count is low and not clinically apparent. This allows appropriate immunosuppression reduction and prevention of overt BK virus nephropathy.

Comparison of incidence of BK viraemia and BK virus associated nephropathy between renal transplant recipients on standard immunosuppression and augmented immunosuppression

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Introduction: BK viraemia (BKV) can progress to BK virus associated nephropathy (BKVAN) which can cause graft loss. Augmented immunosuppression involves agents such as Anti-thymocyte globulin (ATG), Campath and Rituximab for treating acute rejection in renal allografts. They may cause a state of over-immunosuppression and possible viral reactivation

Aims: To compare incidence of BKV and BKVAN in patients who received standard versus augmented immunosuppression

Method: This is a retrospective study on patients that received kidney transplants in our unit from 1st Jan 2006 until 31st Dec 2015 and were followed up until Dec 31st 2016. Standard immunosupresion included Basiliximab (induction) and triple maintenance therapy including CNI/Prednisolone/MMF or Azathioprine and high dose steroids to treat acute rejection episodes. Augmented immunosuppression involved use of ATG/Campath/Rituximab to treat acute rejection episodes in addition to standard immunosuppression. BK viraemia was diagnosed on BK PCR results and BKVAN was diagnosed on renal biopsy. Data was collected from electronic data base. Fisher's exact T test was applied using graphpad software for statistical analysis.

Results: As shown in the table, augmented immunosuppression group had statistically significant increased incidence of BKV (p=0.007) when compared to standard immunosuppression group. However, there was no statistically significant difference in incidence of BKVAN in the two groups (p=0.344). At 1 and 5 years, mean eGFR was 40 ml/min and 38 ml/min; mean creatinine was 144 and 210 respectively in standard immunosuppression group. At 1 and 5 years, mean eGFR was 34 ml/min and 30 ml/min; mean creatinine was 191 and 285 respectively in augmented immunosuppression group. None of the patients that received Rituximab (n=8) developed BKV or BKVAN.

	Standard IS	Augmented IS	p-value
BKV	36	12	0.007
Negative for BKV	427	49	
BKVAN	4	3	0.34
Negative for BKVAN	32	9	

Conclusions: Patients receiving augmented immunosuppression in the form of ATG and Campath need to be monitored more frequently as there is a statistically higher incidence of BK viraemia in this population.

Survival, cancer and PTLD diagnoses after late EBV infection in adult kidney transplantation

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Introduction: While EBV seronegative recipients have a high risk of early PTLD knowledge is lacking regarding the implications of EBV DNAemia in stable patients in the late post-transplant period. We aimed to investigate the relevance of EBV DNAemia on subsequent long term clinical outcomes.

Methods: In this single centre observational study stable adult kidney transplant recipients were screened at recruitment and 4 monthly for EBV DNA in blood (copies/ml) and classified after 1 year as undetectable (UVL), low level (LVL), and high level viral load (HVL) carriers. Long term follow up of participants was performed with analysis made of patient and graft survival and cancer diagnosis including non-melanoma skin cancer (NMSC) and PTLD.

Results: We recruited 499 patients, 62% male, 93% white, 6% ATG use, with median (years (IQR)) age: 52 (42-61), time from transplant: 7 (2.5-12.3) and follow up after recruitment: 6.8 (5.2-7.0). During follow up 19% patients died and 9% experienced graft failure. While EBV DNA status at recruitment (31% positive) did not significantly affect patient or graft survival, persistently UVL patients had lowest inter-group mortality at 13% (31/234) OR=0.58, p=0.036, and HVL greatest (5/31 (16%)). NMSC was diagnosed in 102 (20%) patients including 9/31 (29%) HVL and 44/234 (18.8%) UVL. Death occurred in 25% NMSC patients with detection of EBV DNA at recruitment associated with worse survival following diagnosis (p=0.002) including death in 37.5% EBV DNA + Squamous Cell cases v 13.6% DNA. PTLD was diagnosed in 14 patients (57% cases EBV positive) including 3/31 (9.7%) HVL, OR: 3.94 (p=0.044) and 4/234 (1.7%) UVL. Other cancers were diagnosed in 6% patients with no EBV association.

Conclusions: While single timepoint assessments of EBV DNAemia do not significantly associate with overall patient survival, DNAemia, in particular chronic HVL carriage, may predict NMSC and PTLD development and poorer outcomes after skin cancer diagnosis.

Polyomavirus (BK) monitoring and early reduction of immunosuppression reduce graft loss secondary to BK virus nephropathy

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Introduction: The BK viremia related renal graft loss is up to 60% before screening. We report the effects of BK monitoring, and modification of immunosuppression on the 5-year allograft survival in patients who developed BK viremia after kidney transplant.

Methods: This was a retrospective study of 101 renal transplant patients in a period of 12 months from April 2011 with a five years follow up. Twenty patients were excluded due to lack of follow-up data. All patients underwent BK PCR screening protocol monthly for the first 6 months, and 3 monthly up to 2 years after transplant.

Immunosuppression: Forty two patients recieved Alemtuzumab and 39 patients recieved basiliximab as induction therapy. Maintenance therapy for all patients was Tacrolimus and Mycophenolate Mofetil (MMF). Our protocol is based on steroid avoidance.

Results: Twenty two percent of patients (n=18) had BK viremia. The first peak appearance of BK viremia was seen in 83% (n=15) within the first 18 months of transplant and latent viremia occurred in 17% (n=3) after 36 months of renal transplant. Thirty three percent (n=6) had significant viremia (BK viral load >10,000 copies) and 67% (n=12) had non-significant viremia. Our strategy is to stop MMF, start prednisolone for significant viremia and maintaining Tacrolimus level at 4 -5ug/L, while for non-significant viremia close monitoring and reduce MMF on clinical need. The average time to clear significant and non-significant viremia was 16 months vs 7 months respectively. Clearance achieved in all except for 3 cases of significant viremia in which 2 cases didn't clear the virus over study period and 1 case died before clearance. Five-year graft survival for those with and without BK viremia was 89% vs 92% and graft loss 2.4% (n=2) secondary to BK virus nephropathy.

Conclusion: Our BK viremia related renal graft failure after screening was only 11%.

Tuberculosis infection post renal transplantation and its implications for prophylaxis guidelines

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Introduction: Renal transplant patients have a high risk for developing Tuberculosis (TB) with poorer outcomes. Currently, TB prophylaxis is given to renal transplant patients from countries of high TB incidence but there is no national consensus for assigning prophylaxis. The incidence of TB in certain London boroughs is up to 75/100 000 which is defined as high incidence by the UK Health Protection Agency. NICE recommends offering an interferon-gamma release assay (IGRA) after a solid organ transplant to detect latent TB infection. The aims of this study were to (1) assess the prevalence of TB after transplantation, (2) verify whether traditional risk factors are useful to identify patients needing prophylaxis and (3) discuss findings in view of prophylaxis allocation.

Methods: Retrospective study of patients who developed TB post renal transplant from 2009 - 2017. Patient demographics, clinical features of disease, use of TB prophylaxis and treatment outcomes were examined.

Results: 4 patients developed TB post transplantation. 3 were male. The median age at infection was 54 years. 3 cases occurred in the year 2016. Of note, 1 patient was White-British and born in the UK. 2 originated from high prevalence countries and received TB prophylaxis. Median time from transplant to TB infection was 22.8 (IQR 7.5 - 75.1) months with time from symptom onset to diagnosis being 36.4 (IQR 23.5 - 66.7) days. 50% of patients had hepatotoxicity from TB treatment requiring drug regimen changes but all completed treatment.

Discussion: The majority of cases of TB post renal transplantation were diagnosed in recent years, coinciding with London becoming a more high-risk area for developing TB. This makes prophylaxis in these patients of the utmost importance. IGRA testing should be suggested and if positive, patients could receive treatment for latent infection prior to transplantation to reduce drug toxicity and interactions.

Leflunomide use in BK nephropathy – a single centre UK experience

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Introduction: BK virus nephropathy remains a threat to long-term graft survival. The current standard of care consists of reduction in immunosuppressants but introduces the risk of rejection. Leflunomide is a prodrug with antiviral and immunosuppressant properties that has been used as an adjunct in the management of BK nephropathy. However, results to date in small studies have been disappointing and its role remains questionable.

Methods: In our unit Leflunomide forms part of our protocol for the management of severe cases of BK infection alongside immunosuppressant reduction. This is a retrospective review of leflunomide use in our unit between August 2014 and October 2017 focusing on drug tolerance and graft outcomes.

Results: During the review period 17 patients were administered Leflunomide at a dose of 40mg per day. Mean age was 55 years with a male to female ratio of 15:2. 15 were kidney alone transplants and 2 had received simultaneous pancreas and kidney transplants. The mean time to BK detection following transplant was 175 days. Leflunomide was introduced following withdrawal of MMF in all cases. 2 patients had biopsy proven rejection prior to the introduction of leflunomide. In all patients there was a gradual fall in BK viral load over time but only 1 patient cleared the virus during a mean follow up period of 19 months. Graft function has been preserved or improved in all patients with no further rejection episodes. Leflunomide was withdrawn in one patient because of diarrhoea and in two because of neutropenia. Liver dysfunction was observed in one patient but this was later found to be due to an unrelated cause.

Discussion: In our experience Leflunomide appears to be generally well tolerated, even with prolonged use, with excellent graft survival. However, its precise role in the outcomes observed remain unclear. An adequately powered randomised controlled trial is needed.

Are we compliant with cancer screening during pre-transplant workup assessment as per United Kingdom national guidelines? - a single centre experience

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Introduction: Cancer screening during the pre-transplant assessment allows detection of early-stage diseases for which curative treatment can be implemented, this can improve reducing cancer-related mortality and morbidity post-transplantation.

Methods: Retrospective data were collected on patients active on the renal transplant list in our center (n=110). Age appropriate national guidelines (NHS.gov.uk) for cancer screening were used to identify the patients who were eligible (Table 1). Medical database and electronic case notes were used to collect demographics and cancer screening uptake.

Malignancy Screening Guidelines for Pre -Transplant recipients:

Screening tests	National guidelines (U.K)
Colonoscopy/FOBT (Colorectal cancer screening)	60-74yr (every 2 yr); >75yr (self referral)
Mammography	50-70yr
Cervical smear	25-49yr (every 3 yr); 50-64yr (every 5 yr)

Results: Among the cohort of n=110 patients (m = 57, f = 53), the mean age of patients was 54.75 ± 14.14 years. The majority of the patients (68%) were from the 4th to 6th decade. The number of patients eligible for bowel cancer screening was **n=38 (60-74yrs) none (0%)** of these had recent FOBT/colonoscopy. In females, n=27 (50-70yrs) were eligible for a mammography, of which **78%(n=21/27) patients**, the remaining 22 %(6/27) were not screened. Similarly, n=32 patients {(25-49yrs & 50-64yrs)} were offered cervical smear, **65.6% (n=21/32)** of patients had a test with 1 patient being diagnosed with pre-cancerous cervical cells, whereas in 34.4% (n=11/32), the test was not done.

Discussion: As per the national screening statistics (2012 -2015, U.K), uptake of colorectal screening is 52-58%, 70 – 73% for cervical and 74 % for breast cancer. In conclusion, in comparison to the national standards screening for colorectal and cervical cancer in patients awaiting renal transplants is below the national uptake whereas breast cancer screening is similar to the general population. Involvement of primary care provider in pre-transplant workup assessment may improve the **uptake of** the screening process.

Travel associated Talaromyces marneffei infection after kidney transplantation: the first UK case

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Introduction: *Talaromyces* marneffei is a thermally dimorphic fungus endemic in Southeast Asia. This organism mainly affects individuals with human immunodeficiency virus infection but has infrequently been reported in solid organ transplant recipients. We report the first UK case, to our knowledge, of *Talaromyces* marneffei infection in a renal transplant recipient.

Presentation of the case: A 53-year-old patient with polycystic kidney disease post living donor transplantation on maintenance immunosuppression with tacrolimus and mycophenolate mofetil travelled to southern China in October 2016 for a period of 5 weeks. In July 2017 she developed persistent respiratory symptoms which persisted despite antibiotic treatment which prompted a chest X-ray which showed a left upper lobe mass. Computerised tomography followed by positron emission tomography scan (Image 1) in October 2017 confirmed a large apical mass with mediastinal lymphadenopathy concerning for cancer. The graft function had remained stable throughout this period. Endobronchial ultrasound (EBUS) with Rapid on-site evaluation (ROSE) was performed. Necrosis and focal granulomas were noted. Rapid-Diff slide image showed histiocytes containing fungal organism (Image 2), confirmed on Grocott stain. The organism grew as a mould on Sabouraud agar at 30 degrees with the production of a characteristic red pigment, and a yeast at 37 degrees. Identification was confirmed as *Talaromyces. marneffei* by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). The patient was treated with liposomal amphotericin B induction followed by long-term oral itraconazole.

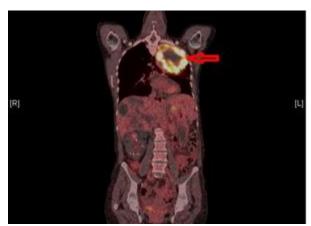


Image 1: Positron emission tomography scan (coronal view)

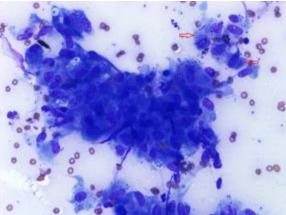


Image 2: Rapid-Diff slide showing histiocytes containing fungal organisms

Conclusion: Timely diagnosis and treatment are vital as *Talaromyces. marneffei* has shown to be a significant cause of morbidity and mortality in solid organ transplant recipients. Patients should also be advised of these rare geographical opportunistic infections. Travel history is also crucial in assessing the transplant recipient with infection.

Post-transplant lymphoproliferative diseases (PTLD) in paediatric kidney transplant recipients: prevalence and outcomes in a large dual-centre cohort

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Introduction: Post-transplant lymphoproliferative diseases (PTLD) are a heterogeneous group of diseases that are best described as uncontrolled proliferations of lymphocytes within the context of post-transplant immunosuppression. In this study, we aimed to highlight prevalence and outcomes for PTLD within a paediatric cohort.

Methods: All paediatric recipients and their respective donors who underwent kidney transplantation at two UK paediatric transplant centres between January 2011 and December 2015 (inclusive) were included in this study, provided follow-up records were immediately available. Donor information was compiled from NHS Blood and Transplant Data and recipient information was collected retrospectively using electronic patient records. Outcomes evaluated included: age at PTLD development, time for PTLD to develop post-transplant, graft function and graft outcome.

Results: 203 children were included in this study. A total of 4 children (2 Male, 2 Female) developed PTLD (mean age at diagnosis = 13.7 years, SD = 5.1) and one patient had previously had PTLD after another transplant. On average, PTLD developed in recipients 375 days post-transplantation (SD = 231.1). 1/4 patients had also developed new-onset diabetes after transplantation. Mean GFR at latest clinic follow-up was 75mL/min (SD = 11.4), with all grafts still functioning. In comparison, mean GFR at last clinic follow-up for non-PTLD recipients was 59.8mL/min (SD = 23.4).

Discussion: Monitoring for EBV infection is essential in PTLD surveillance, allowing appropriate and timely modification of immunosuppression. These results demonstrate that children with PTLD can be managed effectively, with graft function being comparable to patients without PTLD.

Effect of ethnicity on tacrolimus (adoport) trough concentrations in renal transplant recipients. A single centre retrospective study

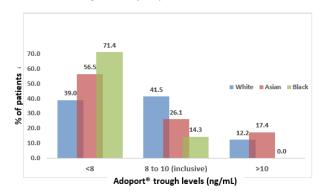
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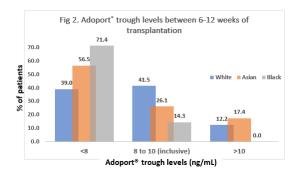
Introduction: Calcineurin-inhibitors (CNI) have a narrow therapeutic window and warrant close therapeutic dose monitoring (TDM). CNI metabolism and consequently its serum trough concentrations (C0) depend on multiple factors, one of which is ethnicity. This prompted us to study the Tacrolimus trough levels in our patients from different ethnic background using a standard dosing regimen.

Materials and methods: Renal transplant done between 01 January 2016 and 31 December 2016 were retrospectively studied. All patients were given tacrolimus as adaport using of 0.05mg/kg twice a day. Data was collected from the hospital electronic database and included ethnicity, adaport trough level and serum creatinine. A mean value for C0 was recorded for first 6 weeks and 6 to 12 weeks post transplantation. C0 was then compared with serum creatinine and ethnic backgrounds.

Results: There were 116 recipients, 71% (n=82) were White, 20% (n=23) were Asian, 6% (n=7) were Black. 3% (n=4) were of other ethnicities. In the first 6 weeks, 42.7% of White, 26.1% Asian and 28.6% Black patients achieved therapeutic levels of tacrolimus (8-10 ng/ml). Majority of the Asian (60.9%) and Black (57.1%) patients had sub-therapeutic trough levels.



Between 6 to 12 weeks of transplantation, 41.5% of Whites, 26.1% of Asian and 14.3% of Black patients achieved therapeutic levels of tacrolimus. Majority of the Asian (56.5%) and Black (71.4%) patients had sub-therapeutic Tacrolimus levels.



No association was seen between CO, serum creatinine and ethnic background.

Conclusion: Majority of the patients of Asian and Black ethnicity achieved sub-therapeutic CO levels (below 8ng/dl).with in the first 3 months of renal transplantation; however serum creatinine remained the same irrespective of CO concentration. We conclude that studies are needed to assess validity of tacrolimus dosing and target trough concentration amongst recipients from different ethnic backgrounds.

Correlation between mycophenolate dosage and occurrence of adverse effects in renal transplant patients

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Background: Mycophenolate mofetil (MMF) is effective in improvement of graft survival and prevention of acute rejection after kidney transplantation. It has been shown in a study that decreasing MMF dose due to infection does not increase the incidence of rejection or graft failure. However, another study showed dose reduction of MMF had increased acute rejection and poorer long-term graft survival. As there is contradictory evidence regarding the optimal dose of MMF, we studied the correlation between MMF dose and occurrence of adverse effects (infection/rejection) in renal transplant patients.

Method: This is a retrospective, single centre study on patients who received a renal transplant from 1st January 2011 to 31st December 2013, in our unit. All transplant recipients who was commenced on MMF as part of triple immunosuppression on the first day post-transplant were included and followed up for three years. Information was obtained from hospital electronic records. MMF dosage immediately following transplant, at three, six, 12 and 36 months post transplant were recorded and average dose was calculated. Infection was determined if positive cultures, high inflammatory markers or positive viral loads. Rejection was analysed if biopsy proven.

Results: There were 165 renal transplants. 74 patients had completed 3-year follow up. Table 1 shows the results.

Conclusion: A link between dosage of MMF and infection/rejection rates has not been observed in this study. Further data will need to be analysed for a conclusive result.

Table 1: Mycophenolate dose and Incidence of Infection or Rejection

	Low (= 1g/day)<br (%)	High (>1g/day) (%)	P Value Fisher's exact test
Infection	23 (31)	4 (5)	0.17
No Infection	32 (43)	15 (20)	
Rejection	6 (8)	1 (1)	0.70
No Rejection	49 (66)	18 (24)	

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Outcomes following 233 paediatric kidney transplants

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Introduction: In paediatric renal transplant recipients, early diagnosis and active therapy before and after transplantation enables most children to live relatively normal lives. However, long-term graft survival rates, disease recurrence and growth rates are among the few facets of post-operative outcomes that invite room for improvement. The aim of this study was to investigate outcomes following paediatric kidney transplantation in two UK transplantation centres.

Methods: All recipients who underwent kidney transplantation at two large UK paediatric transplant centres between 2011-2015 were included. 40 recipient peri-operative care parameters were compiled retrospectively using electronic patient records. Donor information was compiled from NHS Blood and Transplant Data. Data was then analysed for general and comparative trends using statistical analysis software.

Results: 233 children (140M, 93F) were transplanted in the 5-year period (66 DBD, 10 DCD, 157 living). Mean follow-up length was 1.6 years (±0.06). 18/202 (8.9%) of patients developed new-onset diabetes after transplantation (NODAT), 13/209 (6.2%) had transplant renal artery stenosis (TRAS), 8/198 (4%) had disease recurrence and 4/203 (2%) developed post-transplant lymphoproliferative disease (PTLD). Polyoma, CMV and EBV viraemia rates were 28/180 (16%), 52/181 (29%) and 122/179 (68%) respectively. Higher-grade post-operative complications were found to significantly increase the risk of graft failure (P<0.05). The rate of acute rejection did not differ between Azathioprine-based and mycophenolate mofetil-based immunosuppression groups (P>0.05), although patients receiving azathioprine-based immunosuppression were more likely to suffer EBV viraemia post-transplantation (P<0.05).

Table 1: Type of rejection episodes in 1st year post-transplantation

Type and frequency of rejection episodes in 1st year post-transplantation (n=54)			
		Frequency	Percent
ABMR	1	4	
	2	1	
	Total	6	11.1
TCMR	1	17	
	2	2	
	3	2	
	Total	27	50
Vascular	1	2	3.7
Borderline	1	19	35.2
Total	-		100

Table 2: Highest Clavien-Dindo classification score of surgical complications in 1st year post transplantation (n=207)

Clavien-Dindo classification grade	Frequency	Percent	Cumulative Percent
0	82	35.2	39.6
1	14	6.0	46.4
2	51	21.9	71.0
3	57	24.5	98.6
4	2	.9	99.5
5	1	.4	100.0
Missing	26	11.2	
Total	233	100.0	

Discussion: Multi-centre prospective studies are required to investigate these findings further. Renal transplantation remains the gold standard renal replacement therapy in children albeit the burdens of NODAT, TRAS, recurrent disease, PTLD and infections.

A novel 3D-printed hybrid simulation model for robotic-assisted kidney transplantation (RAKT)

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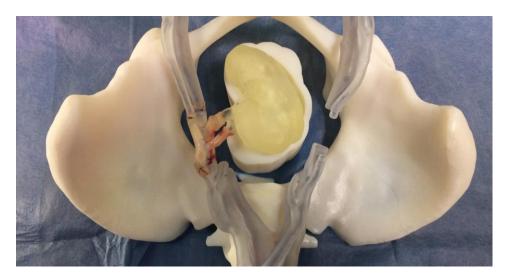
Introduction: Robotic assisted kidney transplantation (RAKT) offers key benefits for patients that have been demonstrated in several studies. A barrier to the wider uptake of RAKT is surgical skill acquisition. This is exacerbated by the challenges of modern surgery with reduced surgical training time, patient safety concerns and financial pressures. Simulation is a well-established method of developing surgical skill in a safe and controlled environment away from the patient.

Methods: We have developed a 3D printed simulation model for the key step of the kidney transplant operation which is the vascular anastomosis. The hybrid model consists of two components, one biological and one prosthetic.

Results: We demonstrated the feasibility of the model by performing two vascular anastomoses using the model in the operating theatre. Two surgeons successfully performed the anastomoses in 20 minutes. The anastomoses were demonstrated to be watertight.

Discussion: The model is anatomically accurate, based on the CT scans of patients and it incorporates deceased donor vascular tissue. Crucially, it was developed to be used in the robotic operating theatre with the operating robot to enhance its fidelity. It is portable and relatively inexpensive when compared with other forms of simulation such as virtual reality or animal lab training. It thus has the potential of being more accessible as a training tool for the safe acquisition of RAKT specific skills. We demonstrate this model here.

Image: completed model showing the anastomoses in the cradle.



Laterality or complex donor vascular anatomy should not preclude successful living donor kidney transplantation

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Introduction: Living donor (LD) kidney transplantation is the optimum form of renal replacement therapy for suitable patients. Decline of otherwise suitable potential donors on the basis of anatomical complexity may not be justified in terms of graft outcome, and potentially compromises equity of access to transplantation.

Methods: The records of all potential LDs evaluated in one UK region between 01 Apr. 2012 and 31 Mar. 2017 were reviewed. They were categorized into three groups based on the complexity of donor anatomy, and outcomes evaluated.

Results: Of the 464 potential LDs evaluated in the 1-day assessment pathway, 117 (25%) exited (43 medically unsuitable, 31 incompatible received an alternative donor, 17 recipient reasons, 26 miscellaneous issues). Of the remaining 347, 46 are yet to donate, 7 pairs had surgery elsewhere, and 21 altruistic donor kidneys were exported. The remaining 273 pairs all proceeded with transplantation irrespective of donor laterality or vascular anatomy. Results reported in Table 1. Backbench reconstructive techniques comprised of bifid and trifid trousering (10), internal iliac artery interposition grafting (2) cadaver donor vessel interposition grafting (2) and end to side anastomosis (1). There were no technical failures in any of the groups. There were no statistically significant differences between mean creatinine values in each category at 12 month follow-up.

Discussion: Laterality or complex vascular anatomy even necessitating back-bench reconstruction provides recipients with good quality grafts and should not preclude organ donation.

Table 1:

		Latera	lity (n)	Grafts failed	Creatinine (µmol/l) at 12	Analysis of	
Group	Anatomy	Left Right		≤12 months	months* (mean, SD)	variance	
I	single vessels	173	23	4 (2%)	118 (40)		
II	>1 artery or vein, no backbench reconstruction	46	16	1 (2%)	127 (34)	p=0.2	
III	complex anatomy, backbench reconstruction	14	1	0 (0%)	133 (31)		
*6 move	ed to another region for follow-up	, for 38 la	atest crea	itinine value is betv	veen 6-12 month		

Informed consent in paediatric renal transplantation; the development of a national consent form

Jane Tizard¹, Jan Dudley¹, Anusha Edwards²

Introduction: With the change in legal requirements following the Montgomery v Lanarkshire ruling the process of taking informed consent for surgery has to be improved. A previously presented review of consent forms in our adult practise highlighted that surgeons are good at consenting for "surgical risks" such as bleeding but are less likely to mention more "medical risks" such as the complications of immunosuppression. This led to the idea that we should develop a procedure specific consent form to be used in paediatric transplantation.

Method: A new form was developed with collaboration between nephrologists, surgeons and Trust legal teams. Based on the results of previous audits it was split three sections: 1. Medical risks, to be discussed at the time of listing, 2. Surgical risks to be discussed at the time of listing and to be completed at the time of transplantation3. A final section confirming understanding of previous discussions and "on the day" organ specific issues. It was written in patient/parent friendly language.

Results: This was then trialled locally in joint paediatric nephrology/surgeon clinics and the views of clinicians and families taken on board when revising the form. The form has now been approved by paediatric KAG and will be introduced nationally shortly.

Discussion: The process of taking informed consent is becoming increasingly more important in clinical practice. A procedure – specific form has been developed locally, trialled and introduced nationally to improve the process and documentation of this for parents and their children.

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Use of superior mesenteric vein for renal transplantation in extensive inferior vena cava thrombosis; a case report

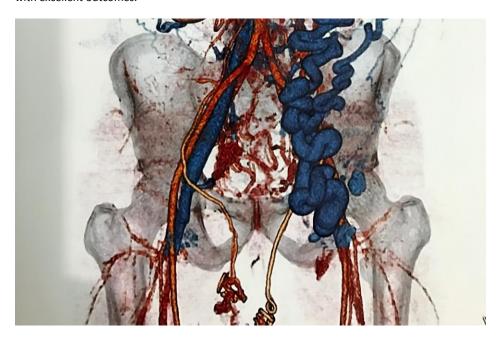
Nalaka Gunawansa^{1,2}, Ahmed Halawa¹, Ajay Sharma¹

Introduction: In renal transplantation, allograft venous outflow is routinely constructed to the recipient external or common iliac vein (CIV). In paediatric recipients and certain re-transplants, it may be done to the inferior vena cava (IVC). In systemic thrombotic disease that occludes the CIV and IVC, alternate outflow routes need to be explored. The portal-mesenteric system is often spared in such disease and offers hope.

Methods: A 28-year-old female with systemic lupus erythematosus and end stage renal failure was referred for transplantation. She was on long-term warfarin for recurrent lower limb deep vein thrombosis. Her mother (47-years), came forward for live donation. Duplex and magnetic resonance angiography were done to visualize her venous anatomy. The iliac veins and infrahepatic IVC showed extensive thrombosis with multiple collaterals along left epigastric veins. The superior mesenteric vein (SMV) and portal vein appeared pristine and were chosen as the potential outflow. A midline laparotomy with a medial rotation of the right colon was done exposing the IVC and aorta. Donor renal artery was elongated with an extension graft (recipient great saphenous vein). Allograft vein was anastomosed to proximal SMV in an end-to-side configuration. Renal artery was anastomosed end-to-side to the aorta. The ureter was anastomosed to the native right ureter (end-to-side).

Results: The allograft showed immediate function with good diuresis. Normal serum creatinine levels were achieved by day-03. Duplex imaging (day-04) showed excellent graft perfusion and venous drainage. Overall allograft as well as liver function has been excellent and she remains well (9 months post-op). A single episode of acute rejection (day-28) was successfully treated with steroid pulses.

Discussion: Thrombosis of IVC and CIV should not be considered contra-indications to renal transplantation. Alternate venous drainage via portal-mesenteric system should be considered where possible and allows successful transplantation to proceed with excellent outcomes.



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Renal transplant in recipients with complete IVC thrombosis

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Introduction: Thrombosis of the inferior vena cava (IVC) poses a unique challenge for renal transplant. Absence of adequate venous outflow for the transplant kidney makes transplant technically challenging and in most cases, impossible. In this abstract we present four cases of renal transplant with complete IVC thrombosis.

Methods: Retrospective review of all transplants between 2010 and 2016, where the recipients were known to have complete IVC thrombosis. All recipients were investigated extensively with mapping of possible venous drainage of potential transplant. Possible strategies for transplant were discussed and agreed in a multidisciplinary meeting.

Results: Four renal transplants were carried out in the study period. Mean recipient age was 30.5 years, all of whom were established on haemodialysis. Three of these recipients had positive thrombophilia screen (Table 1). A deceased donor transplant was planned in view of uncertainty in establishing a venous drainage and avoiding an 'orphan' living donor kidney. Three transplants were successful, whereas one failed to establish adequate venous drainage and was removed soon after transplant. All recipients were placed on long term anticoagulation.

Table 1: Details of transplant procedures

Recipient Age	Sex	Cause of CKD	Thrombophilia Screen	Donor	Venous Drainage	Outcome
37	F	Diabetic Nephropathy	Factor V Leiden - Heterozygous	44/F/ DBD	Left ovarian vein	Successful
38	M	Renal Dysplasia	Factor V Leiden - Heterozygous + Antiphospholipid	30/M/DBD	Suprarenal IVC	Failed on table
30	М	Interstitial Nephritis	Lupus anticoagulant	48/M/ DBD	Right external iliac vein	Successful
17	М	Congenital Nephrotic Syndrome	None	46/M/ DBD	Left native renal vein	Successful

Conclusions: Renal transplant is possible where the recipient has complete IVC thrombosis. A thorough investigation and venous mapping is critical to planning. A multidisciplinary discussion and agreed plan for transplant will help achieve a favourable outcome. Role of life long anticoagulation seems justifiable, although evidence is lacking in this area.

A patient perspective survey on their length of stay following laparoscopic donor nephrectomy : do patients get what they want?

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Introduction: Enhanced recovery protocols and minimally invasive techniques for donor nephrectomy aim to deliver shorter length of stay (LOS). However there is little in the literature as to whether a short LOS is really what patients 'want'. Living a long distance from the transplant centre and complex social problems related with transplantation may be factors. This retrospective pilot study aims to survey patient's perceptions on their LOS following donor nephrectomy.

Methods: Patients undergoing pure transperitoneal laparoscopic nephrectomy in a tertiary transplant centre between March 2017 and September 2017 were included. Telephone survey was conducted, asking (1)complications which required medical attention after discharge to 4-weeks post-operatively, (2)perceived adequacy of their LOS on a Likert scale of 1-5 (1=too short, 3=just right, 5=too long), and (3)reasons for the score if it is not 3.

Results: 25 out of the 39 patients included in the study responded (response-rate 64%). Median LOS in the responders was 3 days (range 1-13). Average distance between hospital and home address was 26 miles (range 3-106). 7 patients reported complications post-discharge, with one requiring re-admission (Clavien-Dindo grade I-II). 18 patients had a perceived adequacy of LOS scores of 3 (72%), 6 had score 2 (24%) and 1 patient score 1 (4%). Reasons for scores of 1/2 included: long distance from home, pain inadequately controlled, relative (recipient) still in hospital, and ability to address complications earlier if longer LOS. Sub-group comparison showed patients with score 1/2 had a longer distance to home compared to those with score 3 (mean 21vs37.7miles).

Discussion: Over a quarter of patients undergoing donor nephrectomy perceived their LOS as too short with none complaining it was too long. Financial pressures to provide a short LOS should be carefully weighed against patient wishes. Further prospective work is clearly needed to build on this pilot study.

How should we teach live donor nephrectomy?

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Introduction: Live Donor Nephrectomy (LDN) presents a challenge for both trainers and trainees. The sensitive nature of performing major organ-preserving surgery on a healthy person, with no benefit to them as an individual, means that opportunities for trainees are often minimal and limited to the same low-risk part of the procedure, for instance mobilization of the lateral border of the kidney. Further, the variety of techniques available means that many will complete training with an amalgam of experience in several techniques. The options available to attain independence are either a fellowship or mentorship as a Consultant. We present one solution.

Methods: A newly appointed Consultant, with mixed experience of hand-assisted and laparoscopic LDN, received a period of mentorship with direct supervision under a Consultant colleague in totally laparoscopic LDN. The operation was divided into 14 defined stages. Before each LDN, an agreement would be made as to which stages of the procedure would be performed and which would be observed, varying the pattern each time. Formal verbal feedback was given in the operating theatre immediately after each procedure. Gradually the stages were combined until the mentee was performing the whole procedure with the mentor scrubbed as first assistant. Cases were then selected for the mentee to perform with the mentor unscrubbed. The next stage was to perform cases with the mentor completely outside the theatre complex.

Results: The training period ran for 6 months. The mentee observed 2 totally laparoscopic LDNs before beginning to take on stages. Stages of the next ten LDNs were then completed before the mentee performed the entire procedure with the mentor scrubbed. After a further 2 cases, the mentee then performed an LDN with the mentor unscrubbed. Following this, on some occasions the mentee continued to observe the mentor performing the entire case. At the end of the training period, the mentee was competent in performing laparoscopic LDN independently in straightforward cases.

Discussion: LDN is a challenging operation, and a challenge to teach and learn. We have presented one effective solution involving a staged approach with direct supervision and regular feedback at the appropriate level of experience. The outcome has been safe and effective mentorship enabling independence of the mentee in laparoscopic LDN.

Transplant renal artery stenosis – can we improve recognition?

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Introduction: Transplant artery stenosis is a recognised complication of renal transplant surgery and can lead to graft dysfunction and loss. Early recognition and intervention can mitigate against this. This study aimed to identify risk factors in our population that would allow quality improvement in early detection and management of this condition.

Methods: The records of all renal transplant recipients in one UK region between 01 October 2012 and 30 September 2017 were included. The prospectively recorded Renal Transplant Database and electronic radiology system were interrogated.

Results: Of 542 renal transplants, 19 (3.5%) developed functionally significant renal artery stenosis. Donor details are in Table 1. Mean recipient age was 53.9. It was the first transplant in 15 (6 pre-emptive), second transplant for 4 patients; 5 patients already had >9 years of renal replacement therapy. Average waiting time for those on dialysis was 91 months.

Table 1:

	Donor Type				
Live Donor	Donation after Brain stem Death	Donation after Circulatory Death	Average Age	Median Ischaemic Time (minutes)	Extended Criteria Donor
8	7	4	53.6	708	47%

The majority of patients presented with hypertension +/- oedema. 2 patients presented with early graft dysfunction; both had a background of extensive vascular calcification and smoking. Interventional radiology demonstrated ostial stenosis in 16%, proximal in 32% and anastomotic in 47%. Patients underwent angioplasty or stenting, some required >1 intervention. There were 3 major complications: 1 dissection requiring emergency intervention, 1 haematoma and 1 pseudoaneurysm necessitating surgical repair. At a follow-up of 2-60 months, 1 patient died of vascular disease, the others all have functioning grafts with a mean creatinine of 137umol/L.

Discussion: Early recognition of, and intervention, in transplant artery stenosis facilitates successful outcomes. With increasing willingness to transplant extended criteria recipients, many of whom have established vascular disease, incidence is likely to increase and vigilance is required.

Interventional radiology provides a graft preserving option for juxta-anastamotic transplant renal artery pseudoaneurysm

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Aim: Juxta Anastamotic Renal artery pseudoaneurysms (rPA) although uncommon are a potentially catastrophic complication in renal transplants. Surgery is high risk and often unsuccessful leading to graft loss. The significant advances in interventional radiology in the last decade has paved the way for an alternative approach to rPA.

Materials and methods: This single centre case series presents the outcomes of management of juxta anastamotic rPA in five transplant recipients.

Results: Ratio of patients 4male:1female with a mean age of 55.1. All donor kidneys were cadaveric; mean donor age was 42. All transplants were done in a standard fashion with single artery to external iliac artery. All five patients were investigated for an elevated serum creatinine and or resistant hypertension. Abnormal ultrasound findings were followed up with magnetic resonance imaging. 3 out of 5 patients had co-existing renal artery stenosis (RAS), 2 patients had positive blood cultures and no RAS suggesting a mycotic aneurysm. The three patients with co-existing RAS had angioplasty of the stenotic segments followed by ebolization using coils, onyx and PVA. All three patients are currently well with serum creatinine <150. The two patients with suspected mycotic aneurysms were surgically explored due to clinical state. Both had nephrectomies, one had EIA stent inserted radiologically intra-op. The second patient was initially treated with radiologically thrombin injection followed by stents into RA and EIA but subsequently required a delayed nephroctomy due to sepsis.

Conclusion: Radiological treatment is feasible and effective for treating juxta-anastamotic pseudoaneurysms in renal transplants with graft preserving outcomes in non-septic patients.

Intra-operative crisis management – models from mass casualty incidents

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Introduction: Intra-operative crises are prevalent in transplant surgery. Nevertheless, formal crisis training and multidisciplinary team simulation are not routinely practiced. In contrast, emergency medical and law-enforcement organisations have standardised and well-rehearsed methods of responding to mass casualty incidents. The study aimed to review existing literature on crisis management and derive surgical crisis response models.

Methods: A literature review was performed over a 20-year period, addressing urban terrorism, natural disasters and other civilian mass casualty events requiring emergency intervention. "Management", "control", "mitigation", "resolution" and "recovery" were used as search criteria defining event response. Military scenarios were excluded. Thematic analysis (NVivo 11.4) of the data was undertaken using the framework method to derive surgically applicable models.

Results: 32 articles matched in the study criteria, of which 29 were included. Data indexing and sorting identified 333 thematic codes. Following refinement and thematic consolidation, the codes were clustered into three super-themes: "crisis resolution", (212 codes/13 sources/11 subthemes), "crisis planning" (105 codes/10 sources/5 subthemes) and "crisis culture" (16 codes/10 sources/3 subthemes). "Crisis planning" identified 2 strategies: 1) pre-emptive creation of resilient, integrated and adaptive systems and 2) crisis plan rehearsal. "Crisis resolution" identified mutually exclusive 'tactical' and 'strategic' command structures (the 'dual control' model in surgery), as well as rapid resource mobilisation. Crisis resolution methods consisted of source, damage and definitive control, resulting in the "triple strike" surgical response theory ('stabilise, neutralise and finalise'). The final super-theme identified the need for a 'culture' of crisis expectation, normalisation of adversity and active engagement from responders.

Discussion: The study suggests a need to change surgical attitudes to crisis training and management, but also provided a new control and response model for intra-operative emergencies. These have direct practical applications for the resolution of surgical crises. Validation of the model in a simulated environment is needed.

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Upper limb early cannulation arteriovenous grafts (ecAVG) for complex vascular access –a healthy alternative to central venous catheters (CVC)

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Introduction: Patients with few transplant options and failing dialysis access are challenging to manage. Transitioning away from a CVC to fistula / graft is often difficult. We describe the use of upper limb ecAVGs for dialysis access in an attempt to avoid CVCs.

Methods: Analysis of prospectively collected data of patients with upper limb ecAVG (Gore Acuseal) between April 2014 to April 2017 from a single centre.

Results: 41 patients (21 males) with a mean follow up of 458 days (85-814days). Mean age 61.5 years (24-79). Primary cause of ESRF: Diabetes 29% (12), hypertension 15% (6), glomerulonephritis 15% (6) and idiopathic 15% (6) and miscellaneous causes 26% (11). Past access History: 95% (39) patients had previous dialysis access (CVCs, AVF or AVG); 56% (22) had 3 or more prior accesses. 9.7% (4) patients were active on transplant waiting list.

Type of ecAVG	Brachioaxiallary graft	Forearm loop graft			lpsilateral brachiosubclavian graft
			loop graft	Bruit	2. ac 2. a. c.
Numbers (%)	(49%) 20	(14%) 6	(12%) 5	(21%) 9	(2%) 1

Complications: Haematoma(1), steal (1) and infection (1). Dialysis adequacy: Median time to needle the graft was 2 days (0-67). Mean urea reduction rate was 72.5% at 6 months. Patency: Functional patency rates were 73% (31 grafts) and 52% (22 grafts) at 6 and 12 months. Radiological interventions: On average, there were 1.1 radiological interventions per patient during the study follow up.

Discussion: Upper limb ecAVG can provide an alternative to CVCs in complex dialysis patients with few options. Excellent adequacy with few complications are possible. Durability is comparable to other graft series.

Perioperative systemic lactate levels may be used as a biomarker for delayed graft function and patient outcome following renal transplantation

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Intrtoduction: Delayed graft function (DGF) post renal transplantation is associated with inferior allograft outcomes. Ischaemic reperfusion injury is thought to be the pathological mechanism behind DGF. Serum lactate may be used as a biomarker of systemic hypoperfusion and oxygenation. We hypothesised that transplant patients who are hyperlactaemic (HL) in the perioperative period may be at higher risk of DGF.

Methods: Perioperative lactate levels and clinical data on 450 renal transplant recipients were collected and analysed.

Results: HL was associated with DGF. 69/103 (67.0%) patients with DGF were HL compared with 188/347 (54.8%) patients without DGF, p=0.02. Compared with living donors, recipients of DCD transplants were more likely to have HL at 69/138 (50.0%) and 64/95 (67.4%) respectively, p=0.009. There was no difference between DBD and DCD donors, p=0.09. There was also no difference in cold ischaemic times between the HL+ and HL- groups, p=0.15. Other variables found to be associated with HL included: diabetes [85/257 (33.1%), p=0.002], non-caucasoid ethnicities [182/257 (54.0%), p<0.001] and not receiving a preemptive transplant [30/257 (11.75), p<0.001]. On univariate analysis, HL was not associated with death censored allograft failure [HR:1.66 (0.94-2.96), p=0.10] but it was associated with inferior patient survival [HR:2.87 (1.26-6.53), p=0.029]. The impact of serum lactate levels on patient survival was maintained on multivariate analysis, with older age [HR 1.06 (1.01-1.12), p=0.015] and DGF [HR 3.00 (1.22-7.37), p=0.017] being associated with reduced patient survival, whilst a normal lactate level was associated with a favourable patient prognosis [HR: 0.25 (0.07-0.85), p=0.026]

Conclusions: Perioperative systemic HL is associated with both DGF and inferior patient survival post renal transplantation. The reason for this requires further study to clarify whether HL is a de novo contributing factor or reflects pre-transplant donor and recipent factors associated with these unfavourable outcomes.

Laparoscopic versus finger assisted open donor nephrectomy technique: where do they stand?

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Introduction: Widespread use of laparoscopic technique is a standard of care for donor nephrectomy. However, progress has also occurred with open techniques. The aim of the study was to compare an innovative finger assisted open donor nephrectomy (FAODN) technique versus standard laparoscopic living donor nephrectomy (LDN).

Materials and methods: Laparoscopic hand assisted technique was used for comparison. Retrospective data was collected for donor age, gender, race, surgical parameter, hospital length of stay, and 1 year donor renal function (serum creatinine and GFR) using two different institution's electronic databases (UVA and ICL), The analyses included 95 donors in each group during a similar period of time.

Results: The FAODN group had more males donors (48.4% vs. 51.6% p=0.03), while the LDN group had a statistically significantly larger number of females donors (70.5% vs. 29.5%, p=0.003). Median body mass index (BMI) was similar between groups (28 vs. 26, p=0.032). Left nephrectomy was overall preferred in both groups. Overall frequency of minor postoperative complications was significantly lower in the FAODN group as compared to the LDN group (14.7% vs. 31.6%, p=0.0094). LDN group demonstrated a significantly higher creatinine (1.1 vs. 0.9 mg/dl, p<0.001), and a significantly lower donor GRF at 1 year (60 vs. 89 ml/min/1.73m2, p-value<0.001) post donation. Surgical parameters demonstrated a significant longer surgery time (3.5 vs 1.2 hrs, p<0.001), a longer combined length of incision (6 vs.5 cm.,p=0.001)and higher cost in LDN group , while demonstrating a statistically significantly shorter median hospital length of stay (3 vs. 4 days, p<0.001).

Discussion and conclusion: Our study demonstrates that FAODN is a successful alternative to laparoscopic techniques. It appears to provide renal donors a favorable outcome in terms of complication, surgery duration, and renal function at 1 year post donation.

Comparison of clinical outcomes post-parathyroidectomy: subtotal vs total

Roshni Rathore^{1,2}, Mark Lambie², Kerry Tomlinson², Ajay Sharma¹, Ahmed Halawa¹

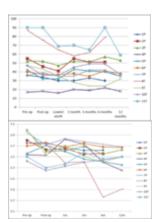
Introduction: Best practice in management of persistent hyperparathyroidism in renal transplant recipients has been debated and there is no consensus on whether medical or surgical management is better. Subtotal parathyroidectomy(PP) is considered superior than total parathyroidectomy(TP) and we have conducted this study with the following objectives:

- 1. To compare outcomes of PP (after adenoma identified on MIBI imaging) with TP in terms of calcium, PTH levels and graft function over 12 months
- 2. To determine if there was sustained deterioration in graft function post parathyroidectomy

Methods: In this single centre retrospective study, we identified patients that had parathyroidectomy between 1/01/2007 and 1/01/2017 (n=22). Graft survival and bone biochemistry were evaluated over 12 months. Patients with failed transplants and multiple transplants were excluded. Remaining 11 patients were divided into 2 groups –total parathyroidectomy (TP) vs. subtotal parathyroidectomy (PP).

Results

- In TP group, 100% achieved normocalcaemia and in PP group 57% achieved normocalcaemia. Calcium levels were marginally elevated in remaining 43%
- 2. In 75% of TP group, there was sustained decline in eGFR at 1 year.
- 3. Only minor complications occurred post-op: 2 patients had cyst formation in PP group and 1 patient in TP group.
- 4. IV Calcium post-operatively was required in 1 patient in TP group and in none of PP group.



Conclusions:

- 1. Subtotal parathyroidectomy can safely lower calcium and PTH levels in renal transplant recipients with persistent hyperparathyroidism.
- 2. No requirement for IV Calcium makes it more favourable.
- 3. Graft function is largely unaffected by either of the 2 types of procedures and for those that have decline in graft function post-op- in the majority, eGFR stabilises by 1 year.
- 4. Longer term study is needed to determine best practice to improve long term outcomes in terms of bone biochemistry and associated morbidity.

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Effect of pneumoperitoneum on renal resistive index in patients underwent laparoscopic living donor nephrectomy (LLDN):a pilot study

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Introduction: Laparoscopic donor nephrectomy (LDN) in kidney transplantation has been widely used as a treatment modality for end-stage renal disease. However, though this method has a better outcome than open nephrectomy, several studies showed many complications, including reduction of blood flow to the kidney due to pneumoperitoneum, shown by resistive index (RI). This study aims to find the use of RI measurement during LDN for monitoring organ function and donor's quality of life.

Methods: This is a pilot study conducted at Cipto Mangunkusumo National Hospital, Indonesia. Patients were divided into two groups (pneumoperitoneum with 8-10 mmHg and 12-14 mmHg), then demographic and RI value was recorded. Measurement of RI was done in five different stages; before

pneumoperitoneum insufflation, 1 hour post insufflation, 3 hours post insulation, after surgery and 24 hours post surgery. Statistical analysis was performed to know the comparison between variables.

Results: There was 45 samples in this study, predominantly male (62.2%), age 31 (21-58) years old. In comparison between 8-10 and 12-14 mmHg

pneumoperitoneum, significant changes were observed only on 24-hours post operation (8-10 mmHg vs 12-14mmHg: $0.65 \pm 0.04 \text{ vs } 0.70 \pm 0.04$; p<0.001). Moreover, in 12-14 mmHg pneumoperitoneum, there was a significant difference between 1 hour post insuflation and 24 hours post surgery with baseline RI value (p=0.011 and 0.002, respectively). Overall, the proportion of patients with RI >0.67 were higher in 12-14 mmHg group compared to 8-10 mmHg (p=0.012).

Conclusion: There was an association between pneumoperitoneum pressure and RI value, particularly at 24 hours post-surgery. However, further research is needed to know the fluid administration, hemodynamic outcome, post surgery follow-up time and clinical condition of the patients.

Role of body mass index in determining outcomes after renal transplantation: a retrospective single-centre observational study

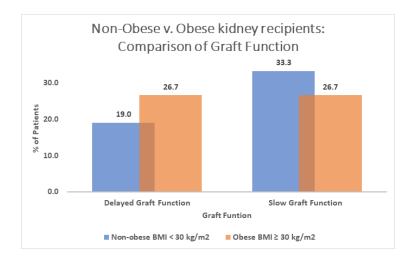
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Introduction: The impact of obesity on graft function in renal transplant recipients (RTR) is still controversial. Many centres set an upper limit on recipient body mass index (BMI) when considering patients suitable for transplantation, however the optimal cut-off BMI is yet to be established. The aim of this study was to compare the outcomes between obese and non-obese RTRs based on their pre-transplantation BMI.

Methods: RTRs at the Leicester Renal Transplant Unit between 01 January 2016 and 31 December 2016 were retrospectively studied. Data was collected from the electronic renal database The World Health Organisation International Classification of adult weight was used to categorise patient's BMI (Obese BMI \geq 30 kg/m², Non-Obese < 30 kg/m²). BMI was then compared with serum creatinine at 3 months post transplantation.

Results: A total of 93 recipients were studied of which, 32.2% (n=30) were obese and 67.8% (n=63) were non-obese. 26.7% of obese recipients had delayed graft function compared to 19% non-obese recipients.33.3% of non-obese recipients had slow graft function compared to 26.7% of obese recipients. Majority of the patients irrespective of BMI had serum creatinine levels between 101 to 200 μmol/L.



Rejections rates were 13.3% (n=4) in Obese vs 7.9% in Non-Obese recipients (n=5).

Conclusion: Obesity appears to be associated with higher risk of delayed graft function and rejection episodes when compared with Non-Obese recipients. Clinicians should try to incorporate adequate nutrition resuscitation and weight reduction strategies when preparing recipients towards kidney transplantation. Studies are needed to assess long term effect of recipient's BMI on transplant outcome.

Hand assisted retroperitoneoscopic nephrectomy for second malignancy in a patient 27 years after liver transplantation following neuroendocrine neoplasia

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Introduction: There is an ongoing debate about how to train future transplant surgeons in nephrectomy, particularly regarding the "patient tailor made" approach versus the "surgeon preferred technique". Hereby we present a case where retroperitoneoscopic hand assisted nephrectomy was considered as the best surgical approach in a patient with a complex abdominal situation following numerous laparotomies.

Case: A 62-years old male who underwent liver transplantation for a neuroendocrine neoplasia and numerous consecutive surgeries including pancreatico-duodenectomy (Whipple's procedure), laparotomies for small bowel obstruction and incisional hernia repairs presented with a 2.7 cm enhancing mass at the superior pole of the left kidney at a regular follow-up. Since the lesion was not DOTATATE avid on Ga68 DOTATATE PET/CT, a suspicion of a second malignancy was brought into discussion. The patient was morbidly obese and on haemodialysis for the last four years. Due to previous transperitoneal operations, decision was opted for retroperitoneoscopic hand assisted (HARP) left radical nephrectomy. The surgeon's hand entered the patient's retroperitoneum via a suprapubic incision and facilitated the mobilisation of the left upper pole stuck to the enlarged spleen (21 cm diameter). A complete mobilisation of the kidney was then possible, followed by the stapling of the vessels and of the ureter with the retrieval through the Pfannestiel incision. Histology demonstrated a multifocal clear cell renal carcinoma. The postoperative course was uneventful. The patient was discharged on the 4th postoperative day. At the last follow-up five months after nephrectomy there was no evidence for disease recurrence.

Conclusion: We believe that the minimal invasive approach selected for this patient played a major role for his intra- and postoperative course free of morbidity and his enhanced recovery. Retroperitoneoscopic procedures should become an integral part of surgical training not only for transplant surgeons but also for surgeons dealing with retroperitoneal tumours.

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Managing external iliac artery stenosis due to iatrogenic injury after kidney transplant (KTX)

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Introduction: The renal transplant stenosis after KTX is a rare complication with an incidence around 2%. Rarer is an arterial injury proximally to the anastomosis due to clamp damage during the KTX.

Methods: 47 year old female patient on haemodialysis for small kidneys underwent a deceased donor kidney transplant from a 60 year-old male DCD with MM: 2-1-0, cold ischemic time 11 h and 29 minutes and warm ischemic time 42 minutes. Dardik vascular clamps were used for clamping the external iliac artery during implantation. The patient had a long history of extensive lymphadenopathy and had completed antituberculous therapy prior to transplantation. The patient had delayed graft function following transplantation. Graft ultrasonography for 3 days showed "dampened flow" within the renal transplant artery with resistive indices between 0.37 to 0.6. The patient had a slightly weaker right femoral pulse but no other signs or symptoms of claudication or critical limb ischemia. MR angiogram performed showed a short high grade stenosis of the external iliac artery just proximal to the renal transplant anastomosis. This was confirmed to be hemodynamically significant by intra-vascular manometry during angiography and successfully treated by percutaneous transluminal angioplasty (PTA) using 6mm conventional balloon with prolonged inflation. Post procedure recovery was uneventful, and patient was discharged after 3 weeks with creatinine of 117 umol/L.

Discussion: Latrogenic external iliac artery injury is a rare complication after KTX. Angioplasty versus stenting is debatable with no clear consensus. We decided against stenting in our case due to the age of the patient and risk of KTX arterial occlusion by the stent. Such endovascular procedures should be considered in managing vascular complications of KTX.

"Children of a lesser God". Mortality of patients suspended from the national kidney transplant waiting list (NKTWL)

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Introduction: A significant and increasing proportion of patients initially activated on the NKTWL end up being suspended. The scale and cause of mortality of this large cohort of patients remains poorly described. We aim to identify the mortality and cause of death (COD) of patients suspended on the NKTWL.

Methods: We linked the UK Transplant Registry to ONS mortality data and identified all patients activated on the NTKWL between 1/1/2000 and 31/12/2010. We categorised patients by whether they had been suspended for a period of 30 days or more (excluding the first 90 days of registration) and classified COD into 10 categories according NHSBT criteria. We stratified the databases into 4 cohorts; a) suspended, not transplanted b) suspended, transplanted c) not suspended, not transplanted d) not suspended, transplanted and used the X² test to compare the proportion and COD across the 4 cohorts and Kaplan-Meier curves to assess the relationship between suspension and survival from listing. Cox regression models investigated the association between suspension and survival following case-mix adjustment.

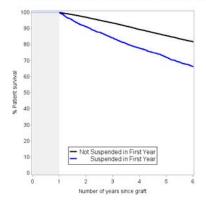
Results: A total of 18,618 patients were included in the analysis. 40% of all patients experienced a period of suspension and 28% did not receive a kidney transplant. Two thirds of patients suspended and never transplanted died, significantly more from cardiovascular related causes (p<0.05). Suspension from the waiting list was associated with worse survival outcomes in both unadjusted (log-rank test p<0.05) and adjusted (HR 1.90 95% CI 1.75-2.07) analysis.

Discussion: Patients activated on the NKTWL are at a high risk of a suspension. Suspended patients have a significantly increased risk of mortality from potentially preventable COD including cardiovascular causes. Improved monitoring of patients waiting for transplantation and increased organ utilisation would help reduce mortality on the NKTWL. New allocation policies should consider clinically relevant mortality risk factors, including a suspension event.

Table 1: Number and proportion of patients included in the study cohort stratified by status of suspension transplantation and mortality (N=18618)

	Not susp N=11,139		Suspended N=7479 (40.0%)			
	Not- transplanted N=1275 (7%)	Transplanted N=9864 (53%)	Not-transplanted N=3888 (21%)	Transplanted N=3591 (19%)		
Total number deceased	1020	2269	2481	728		
Total proportion deceased	80%	23%	64%	20%		

Graph 1: 6-year patient survival from listing in patients stratified by suspension status (n= 16,576).



^{*}Conditional on patients surviving to one year from registration on the NKTWL

Effect of the surgical intervention of laparoscopic donor nephrectomy on proteomic changes in living kidney donors using either propofol or sevoflurane anaesthesia

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Introduction: Surgical trauma induces perioperative stress impacting on systemic inflammatory and humoral responses that are associated with postoperative comorbidity. Different types of anaesthesia and anaesthetic agents are known to selectively depress normal physiological processes including T-cell and B-cell responses. In this study the biological effect of the surgical intervention combined with propofol or sevoflurane anaesthesia in living kidney donors undergoing laparoscopic surgery was assessed by proteome profiling of blood plasma samples.

Methods: Plasma samples of patients participating in the VAPOR-1 trial were used. Sample points were: before surgery (T0), immediately after surgery (T1), and 24 hours after surgery (T2). Patients were anaesthetised with either propofol (n=19) or sevoflurane (n=17) and matched by age, gender, BMI, comorbidity and medication. Samples were subjected to proteome profiling by mass spectrometry followed by data analysis with MaxQuant software and relevant statistical methods.

Results: Quantitative protein identification resulted in detection of 633 plasma proteins. A subset of 28 proteins showed statistically significant (P<0.05) expression level changes between time points. Proteins with over two-fold change comprised a smaller group of 9 upregulated targets that are known to be involved in acute phase inflammatory response (CRP, SAA1, SAA2, LBP, SERPINA1, SERPINA3) and tissue regeneration (FGL1, LRG1, MAN1A1). These targets were common in all patients, except MAN1A1 that was upregulated only in propofol anaesthesia.

Discussion: The highest detected changes in protein levels were found to be independent of anaesthesia type, while proteome profiles also displayed a number of moderate level anaesthesia-specific changes. More proteins with statistically significant level changes were detected one day after surgery (T2) as compared to immediately after surgery (T1), in both anaesthesia groups. In the majority of cases the direction of protein level change was upregulation, with affected proteins involved in a delicate balance between acute phase inflammatory response and tissue regenerative processes.

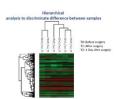


Table 1: Differentially expressed proteins between time point in PROP and SEVO anaesthetic type

			A	NALYS	IS:	А	NALYSI	S:	А	NALYSI	S:	A	NALYSI	S:	А	NALYS	S:	A	NALYS	IS:
Protein-	Gene name	Function	PRO	P_T2_\	rs_T0	PRO	P_T1_v	s_TO	PRO	P_T2_v	s_T1	SEV	D_T2_v	s_TO	SEV	0_T1_v	s_TO	SEV	O_T2_v	rs_T1
ID				FOLD	FOLD-		FOLD-	FOLD-		FOLD-	FOLD-		FOLD-	FOLD-		FOLD-	FOLD-		FOLD-	FOLD-
			T-MTC	MAG	DIR	T-MTC	MAG	DIR	T-MTC	MAG	DIR	T-MTC	MAG	DIR	T-MTC	MAG	DIR	T-MTC	MAG	DIR
P02741	CRP	Host defense	P<0.01	35.8	U				P<0.01	64.4	U	P<0.01	70.1	U	-			P<0.01	12.6	U
P0DJI8	SAA1	Major acute phase protein	P<0.01	9.1	U	-	-	-	P<0.01	55.3	U	P<0.01	110.7	U	-	-	-	P<0.05	23.4	U
PODJI9	SAA2	Major acute phase protein	-	-	-	-	-	-	P<0.05	28.2	U	P<0.01	48.7	U	-	-	-	P<0.05	11.9	U
		Promotes the release of cytokines in response to																		
P18428	LBP	bacterial lipopolysaccharide	P<0.01	4.0	U	-	-	-	P<0.01	5.0	U	P<0.01	4.0	U	-	-	-	-	-	-
P01009	SERPINA1 (Alpha-	Inhibitor of serine proteases	P<0.01	1.5	U	-	-	-	P<0.01	2.0	U	P<0.01	1.8	U	-	-	-	P<0.01	2.2	U
G3V3A0	SERPINA3	Alpha-1-antichymotrypsin	P<0.05	3.1	U	-		-	-	-	-		-	-	-		-		-	-
		Leucine-rich alpha-2-glycoprotein. Positive regulation of																		
		angiogenesis. positive regulation of transforming																		
P02750	LRG1	growth factor beta receptor signaling pathway	P<0.01	2.5	U				P<0.01	3.1	U	P<0.01	3.0	U	-			P<0.01	2.3	U
		Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA.																		
		Involved in the maturation of Asn-linked																		
P33908	MAN1A1	oligosaccharides	P<0.01	2.1	U	-	-	-	P<0.05	2.1	U	-	-	-	-		-	-	-	-
		Fibrinogen-like protein 1. Has hepatocyte mitogenic																		
Q08830	FGL1	activity	P<0.01	11.7	U	-	-	-	P<0.01	15.9	U	P<0.01	10.7	U	-	-	-	P<0.05	5.7	U

U: Up regulation; T-MTC: Test-Multi Test Correction

Living donor, cadaveric whole and split liver transplantation: a cost-descriptive matched pair study at a single liver transplant centre

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Introduction: Despite liver transplantation (LT) being amongst the costliest interventions provided by the NHS, little is known about the cost structure of the different types of grafts transplanted. This study aimed to provide cost-utility data of the resources utilised by living donor liver transplantation (LDLT), cadaveric split liver transplantation (CSLT) and cadaveric whole liver transplantation (CWLT).

Methods: We conducted a cost-descriptive study. Demographic, clinical and economic patient data were retrospectively collected at a single centre liver transplant unit from 1st January 2016 to 31st September 2017. Five adult recipients of LDLT were matched to CSLT and CWLT according to age, gender, BMI and UK model for end-stage liver disease (UKELD) score. Nine markers of resource utilisation were identified through micro-costing analysis of the patient pathway from admission for transplant to discharge. The Patient Level Information Costing Service (PLICS) was used to calculate total monetary costs of each resource.

Results: LT recipients had a mean age of 47 years and UKELD score of 56. The costliest procedure, LDLT (£34,303), was 10.6% and 22.9% higher than CSLT (£31,023) and CWLT (£27.916) respectively. Theatres (29-32%), overhead services (16-34%) and bed utility (11-22%) formed the highest proportion of total costs, followed by pharmacy costs (7-13%). Radiology, pathology, junior doctor and consultant costs (excluding theatre) each utilised less than 5% of total costs. Mean total bed stay of LDLT (13.8 days) was longer than CSLT (9.0 days) and CWLT (9.4 days).

Conclusion: We present an analysis of economic data and resource utilisation associated with LDLT, CSLT and CWLT in the UK. Focusing on the main cost drivers provides hospitals with the means to reduce costs whilst maintaining satisfactory surgical and patient outcomes.

Accepting young donors: do gender and type of donation play a role?

Sarah Atkinson¹, Jen Lumsdaine², Gabriel Oniscu², John Terrace²

Introduction: The lower legal age limit for living kidney donors in the UK is 18 years (16 years in Scotland). The long-term risks for donors may dissuade clinicians from accepting young candidates. This study evaluated professionals' views on young age as a factor in the decision to proceed.

Methods: An anonymised online survey about personal views and units' clinical practice was distributed to transplant professionals (surgeons, nephrologists, coordinators) in transplant centres and referring units in the UK.

Results: There were 54 responses. 43 worked in a transplant centre and 11 in a renal unit, with a dedicated living donor MDT present in 46 responses. The median minimum acceptable age for a living donor based on the personal views of the respondents was 22 years. In clinical practice, there were differences between the median age of the youngest donor according to the type of donation [21 years (range 18-35) for directed compared to 26 years (range 21-45) for non-directed donation (NDAD)]. The nature of the directed donor-recipient relationship played a significant role in the decision to accept a young donor for 36 (67%) respondents. There were significant gender differences in the interpretation of young age for living donors. For an 18-year-old male NDAD, 12 respondents were happy to proceed, 29 would postpone until an older age and 8 would refer to another centre. In contrast, for a female, 7 would proceed, 36 would postpone and 6 would refer. Five respondents would not proceed with donation from an 18-year-old NDAD. If the donation was directed, 24 respondents would consider changing their decision, 6 stating this would be for male donors only.

Discussion: Variation is seen among the views and actual practice of professionals in the decision to accept a young living donor. This may be influenced by age, gender and the type of donation.

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Improving living donor kidney transplantation in south Asian community: living donor transplant initiative

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Introduction: Living donor kidney transplantation (LDKT) is superior to deceased donor transplantation; it offers greater patient and graft survival of t in addition to offering savings to the tax payer and NHS. Despite LDKT 2020 strategy, the number of LDKT is declining over past three years and this is especially true in the Asian community where numbers are static at 7.6% for last five years. The aim of this project was to explore barriers.

Methods: Focus group exercise was conducted in three different groups; non-renal health care professionals (n = 6), kidney donors (n = 6) and kidney recipients (N = 8). Focus group exercise was facilitated with prompt questions around personal, cultural religious aspects of donation; and also around information received and processes at transplanting centre. This project focused on Hindu community members only.

Results: The salient features and themes that emerged from focus groups were to receive information on LDKT early on in their native language in a culturally sensitive manner. They would like to see the negative aspects of dialysis covered at the information day and reasons for long wait experienced by Asian patients on waiting list. There were cultural dilemmas around daughters donating kidney to parents and religious dilemma around karma and re-incarnation. The major emphasis on information should be on improvement of Quality of Life (QoL) following LDKT.

Discussion: The focus group exercise in Hindu community at Leicester has highlighted cultural and religious barriers pertaining to their faith but also concluded that the emphasis should be on QoL improvement following LDKT on both patient and family. Information if delivered in a culturally sensitive method in a native language has the potential to improve understanding on LDKT and its take up. Following this focus group, we are developing a targeted video and peer educator network to address the barriers.

Impact of ethnicity on long-term blood pressure and CKD outcome in Asian living kidney donors

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Introduction: Long-term outcome following kidney donation is one of the important consideration whilst counselling potential donors. Asian ethnicity is associated with higher risk of CKD and hypertension compared to Caucasian population in UK. There remains an ethical and clinical dilemma, especially when assessing younger Asian donors as no data is available regards to impact of Asian ethnicity on outcome following kidney donation as compared to Caucasian donors.

Methods: A single centre analysis was performed comparing outcome of donors from Asian and Caucasian ethnicity. Outcomes considered included systolic Blood Pressure, proportion of donors with eGFR (EPI) below 45 ml/min, random glucose >11 and if any requiring renal replacement therapy. Cases with less than three months follow-up, missing data and another ethnicity were excluded. Data for ethnicity were collected from various electronic sources. Statistical analysis was done using QuickCal (Graphpad) using Fisher exact test.

Results: Ethnicity data were available in 84% (536 cases out of 639) kidney donors. 389 (353 - Caucasian and 36 - Asian) donors were further analysed. Summary of outcome measures are presented in table 1 (below).

	White	Asian	p value
No	353	36	na
Age (Median)	47	36	nd
Follow-up (Median years)	6.2	5.5	nd
eGFR (Median, ml/min)	61	66	ns
eGFR < 45 ml/min (%)	5.40%	0%	0.39
SBP > 140 mm Hg (%)	59%	12.50%	0.0014

Table 1 (nd – not done, na – not applicable, ns – not significant)

Discussion: There is no difference in severity of CKD in donors of Asian and Caucasian ethnicity during a follow-up of 6-7 years. Donors from Caucasian ethnicity has significantly higher systolic blood pressure (> 140 mm Hg) compared to Asian community. There was no case with kidney failure during this follow-up period. Further analysis is required using national data to confirm this finding in UK.

Incidental findings amongst potential living related kidney donors: another barrier to living organ donation

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Introduction: Living Related Donor (LRD) Kidney transplantation is the optimum treatment for suitable patients with End Stage Renal Disease. National data has shown low live donor and pre-emptive kidney transplant rate in the West Midlands. "Transplant First" project was introduced in 2015 to improve access to kidney transplantation. In our non- transplanting centre, we conducted this study to evaluate the LRD program particularly looking at the number of incidental findings amongst live donors and the impact on recipient's outcomes.

Methods: The records of all live donors work up between 2012 and 2016 were reviewed. Those with incidental findings were identified and categorised into radiological, laboratory and other abnormalities (outlined below).

Results: In the five years period there were a total of 68 live donors who had their transplant work up, out of which 17 (25%) were found to have incidental findings. The majority were abnormal radiological scans (58.8%) followed by abnormal blood results (29.4%) and other issues (11.7%). Most of these live donors required further investigations and referral to other specialist. Only 2 were suitable to donate after further work up with an average time delay of 7 months. 8 live donors (47%) were excluded from donation, the outcome of their potential recipients were alternative LRD (N=3), cadaveric transplant (N=2), on-going dialysis (N=2), and one waiting on the deceased list. The rest of live donors were put on hold or their recipients were no longer deemed suitable for transplant.

Discussion: A quarter of presumed healthy live donors had incidental findings identified during the transplant work up. Almost half of them were completely excluded from donation. This highlights an obstacle to the growth of the LRD program. There is a need for a transplant lead in non-transplanting centres in line with the UK strategy for Living Donor Kidney Transplantation 2020

	of Incidental Finding(N								
Abnormal Radiological Results (N=10)	Abnormal Laboratory Results	Others (N=2)							
	(N=5)								
Abnormal CT Abdomen (N=6)	Biochemistry (N=3)	Psychological issues							
	-Low e GFR								
-Renal Stones									
	-Abnormal LFTs								
-Renal tumour									
-Vascular abnormality	-Raised cholesterol								
-Gastric cancer									
-Liver lesions and small renal stone									
-Accessory renal artery									
Unequal split function on DMSA (N=2)	Microbiology (N=2)	Anaphylaxis at anaesthetic induction							
	-Malaria Antigen								
	-HCV PCR								
Low ejection fraction on ECHO (N=1)									
Nodular shadows on CXR? Sarcoidosis (N=1)									

Profile of people in the organ donor register in relation to health literacy

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Introduction: Health literacy about Deceased Organ Donation (DOD) is an area which has been scarcely researched. Even though there are numerous awareness campaigns the gap between the supply and demand in transplantation is a persistent worldwide challenge. Numerous studies show that although there is a generalised positive attitude towards organ donation, there is lack of knowledge about specific issues related to DOD. The aim of this project is to explore differences among people who are or not registered as organ donors regarding knowledge on health issues and DOD.

Methods: We distributed a survey, which was completed by 359 participants, of whom 41% were medical students of a London-based University, 42% renal patients, and 18% administrative staff at a hospital in London. We used Kruskal-Wallis test, Generalised Linear Model (GLM), and Correspondence Analysis (CA) to assess any difference on knowledge regarding health issues and DOD between registered and non-registered participants.

Results: The Kruskal-Wallis test showed that knowledge about health issues and DOD had a significant effect on distinguishing between registered and non-registered participants (p-value 1.11e-05). GLM also showed that awareness on health issues was a statistically significant variable (p-value 0.04687) which mattered in the classification of registered donors. CA confirmed that participants with knowledge on health issues had high odd-ratio of being registered donors.

Discussion: This study suggests that knowledge about general health issues as well as knowledge about specific issues regarding DOD can be an element distinguishing registered organ donors from non-registered individuals. These findings can certainly support the design of meaningful health literacy campaigns to promote DOD.

How long does it take a recipient to write their first message to their donor's family?

Hannah Tolley

NHS Blood and Transplant, Cambridge, United Kingdom.

Introduction: Recipients of deceased organ donations are able to write a message of thanks to their donor's family. We know that these letters are often a great source of comfort to the family and help to promote organ donation. NHSBT's Donor Records Department (DRD) acts as an intermediary in this message-writing process: they receive letters from recipients via recipient coordinators, match their details to their donor's, and forward the messages to the donor's family via the SN-OD. The DRD collects data on the incoming letters, such as the recipient's transplant centre and whether it is first contact. These data were analysed to determine the average length of time it takes a recipient to write their first message.

Method: The length of time taken to write a letter was calculated by: *Time taken to write = date letter received at DRD – date of organ donation.*

Results: As of 22/11/2017, the average (median) time taken for a recipient to write their first message was:

Lung recipients: 0.82 years [9.9 months] (n=10) Heart recipients: 0.82 years [9.9 months] (n=11) Liver recipients: 0.52 years [6.2 months] (n=55)

Pancreas recipients: 1.37 years (n=1) SPK recipients: 1.16 years (n=4)

Kidney recipients: 0.34 years [4.1 months] (n=84) Other recipients: 0.34 years [4.0 months] (n=2)

These median times were also broken down further by recipient centre. There is variation in time taken to write between recipient centres but the sample sizes are still small.

Discussion: These median times are recalculated every week with more data from the DRD. The differences between transplant types perhaps reflect differing recovery processes and needs, and the level of support that is available for writing at different centres. However, the results do not take into account what is likely a large proportion of recipients who have not yet written a letter or do not ever intend to.

CT cortical volumetry for assessment of live donor differential kidney function

Rose Johns¹, Natasha Sawyer², Richard O'Neill², Sam Dutta², Amanda Knight², Keith Rigg², Alun Williams²

Introduction: Living kidney donors undergo extensive investigation pre operatively to confirm their suitability as donors and also to ensure that risk of long term damage to their own health and renal function is minimised. We use computed tomography (CT) to assess vascular anatomy. Split renal function (SRF) is assessed by static cortical renography, using Tc-99m dimercaptosuccinic acid (DMSA). Using a pixel-based algorithm we estimated renal cortical volume based on the CT, rather than using geometric algorithms based on whole kidney size which can differ despite equal SRF. We compared the diagnostic accuracy and correlation of SRF assessments using CT cortical volumetric and DMSA.

Methods: Percentage cortical CT volumes and SRF from DSMA scans from 17 potential live kidney donors were analysed.

Results: The mean SRF of right kidneys was 49.73% (range 47 - 57) and left was 50.27% (range 43 - 55). The mean cortical volume as assessed by CT was 49% (range 44.53 - 56.67) on the right and 51% (range 43.33 - 55.47) on the left. There was no functional left:right difference despite some observed variation in geometric volume of whole kidneys. There was a significant correlation between CT volume derived split renal volume and DSMA derived SRF r = 0.68, p = 0.003.

Discussion: Calculation of SFR from CT correlated with SRF from DSMA scanning. In the future CT volumetry may become the only test of SRF required prior to live kidney donation thus avoiding two separate investigations.

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Living donor transplantation starts and stops with the recipient: time to go back to the start

Jen Lumsdaine¹, Julie Glen², Pamela Niven³, Gabriel Oniscu¹

Introduction: Improving equity of access to education about living donor kidney transplantation should increase actual numbers of transplants. Most information is targeted at potential donors, but it is often the recipient who is left making the initial approach. Advice on how to do this may be varied or scarce. We explored perceived barriers and difficulties encountered by the recipient.

Methods: All recipients active on the transplant list in Scotland received a written invitation to a living donor information event in 2016. Recipients in the East of Scotland (n=120) were subsequently contacted by letter then telephone with a follow up survey questionnaire.

Results: Telephone responses were obtained from 112 recipients. Fourteen recipients active on the list had attended an information event, 98 had not. Fifteen would not accept a kidney from any directed living donor (6 of these had potential donors), with 57 willing to accept but had no potential donors. Difficulty in raising the subject of living donation was cited by 22 recipients and 17 had decided they would not accept a kidney from an identified donor due to concern about their age/medical issues/family circumstances, with no approach to the clinical team. Nine recipients preferred to wait on deceased donor transplant but may now consider living donation.

Discussion: Information events are usually targeted at those approaching end stage renal failure, but for those on the list there may be preconceived barriers and lack of information on changes in clinical practice. Following this survey we introduced a leaflet for recipients with advice on how to raise awareness within family and friend groups, and 'myth busting' perceptions about donor risk and who may be suitable to donate. We would like to explore cautious use of social media for raising awareness for individuals in the future.

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Analysis of the living kidney donor assessment pathway

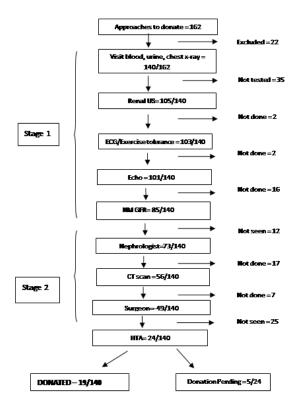
Lilibeth Piso, Carmelo Puliatti, Cinzia Sammartino

Royal London Hospital, London, United Kingdom.

Introduction: Living kidney donation (LKD) is an eminent option for bridging the gap between organ supply and demand. This is an audit of LKD assessment pathway at our institution looking at the number of visits and the numbers of donor that proceed towards donation. The outcome will be used to develop changes in practice in order to improve living kidney donors' pathway for the assessment process.

Methods: The design of this study was a retrospective single-centre analysis. Participants were all potential consecutive 162 kidney donors from 1st September 2015 to 31st August 2016. The data collected was via our renal electronic database

Results: Results are in the following flowchart.



Discussion: Several areas have been identified for further investigation within this project. Fifty percent of the delays or incomplete pathways were due to donor factors such as: donor withdrawal, donor unsuitable, donor unavailability leading to delaying of the donor assessment and donor being undecided about proceeding with the assessment. A more in depth analysis can be undertaken in determining the reasons for potential living kidney donor withdrawal after coming forward for assessment. Results also indicated that the potential LKD assessment could be done quicker if we reduce the number of visit and this can lead to an increase number of potential donor to become effective donor.

Social media guidance for organ and tissue recipients

Hannah Tolley

NHS Blood and Transplant, Cambridge, United Kingdom.

Introduction: Organ and tissue recipients are often identified by the families of their donors using social media. At best, this can lead to a meaningful new relationship that provides solace and closure to both parties. At worst, it can lead to stalking, harassment and disappointment through mismatched expectations. Whilst we want to encourage and increase rates of letterwriting between donor families and recipients, we also have a responsibility as transplant professionals to protect their anonymity as much as possible, something that is a unique challenge in the age of pervasive social media.

Method: Through Internet-based research, discussions with recipient coordinators, Marketing & Communications employees at NHS Blood and Transplant and international colleagues, it became apparent that there is little guidance for transplant recipients on the topic of safe social media use. Whilst transplantation is a relatively recent phenomenon, social media is even newer and most donation and transplantation organisations around the world are having to quickly decide what their policies on it are. A comprehensive social media guide for recipients is currently in draft, including advice on how to review current social media privacy settings, the reasons why they should not reveal too much information about their transplant, advice for parents/carers of children who have had transplants and some guidance on writing a thank you message to the donor family.

Results: As of 22/11/2017 this guidance is still in draft, but we hope that by the time of the congress it will be ready to circulate to the British transplant community.

Donation comic - an image says more than a thousand words

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Introduction: The project was initiated by a local donor family member through the University of Dundee, with support from NHS Blood and Transplant, to create an illustrated comic for use as a resource for education in schools. The aim being to portray the donation process from the perspective of the donor family member, Specialist Nurse Organ Donation and organ recipient. Williams (2012) describes comics as being able to 'effectively relate the patient experience and indeed that of the carer or healthcare provider, and that they might have a particular role to play in the discussion of difficult, complex or ambiguous subject matter'. The hope is to produce an alternative resource which is educational, promotional and supportive, with the potential to reach a wide audience.

Methods: A three strand narrative, describing the donation process as a whole. Each stake holder was interviewed, the conversation recorded and transcribed. This provided the script for the story board prior to the finished art work. Currently only first draft of SN-OD narrative and illustration available. Initial feedback and validation regarding SN-OD narrative, sought from senior management team regarding script content. Planned to be extended to a wider professional group at regional collaborative.

Results: Awaiting feedback and further data from regional collaborative. Planned presentation to medical students at University of Dundee for assessment of content.

Discussion: Very early awareness of potential scope for resource – not only for school education, waiting rooms and information displays in GP practices and hospitals, as well as medical and nursing training. Is this a means of providing information to families in times of heightened stress and emotion in critical care waiting areas? Initiative driven by family experiences, who feel strongly about the positive impact of organ donation on society. Resource supported but not influenced by NHSBT.

The age of altruism - nursing perceptions and ethical dilemmas

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Introduction: Since the advent of altruistic donation in 2007, numbers have continued to grow in the UK. In Scotland, we provided 19% of all the altruistic donors in the UK from the 1st of April 2016 - 31st March 2017. The age of consent in Scotland is 16 and although the youngest altruistic donor to date has been 24, we do receive enquiries from potential donors under the age of 18. Ethical dilemmas can be difficult for nurses providing care at the ward level, therefore, with this increased altruistic donor activity, are we putting our nurses under pressure to provide quality care when their ethical judgement is being called in to question?

Method: A simple questionnaire has been used to survey the nurses and health care support workers, working in the West of Scotland trnansplant ward to determine what age they feel is appropriate for altruistic donation.

Results: Out of the 16 nurses surveyed so far, 14 were trained and 2 were Health care support workers. All 16 were female. 62.5 % had children. 25% were aged between 20-29, 37.5% between 30 - 39, 25% between 40 - 50 and 12.5% > 50 yr. Results so far would indicate that nurses are more comfortable with male altruistic donors being aged 25 - 70 and female altruistic donors being between 30 - 70 years old. The data set will be completed by mid December.

Discussion: Living donation in both the young and the old provides a backdrop for debate. By excluding young adults, who are legally able to consent, are we removing their autonomy? However, with more long term data available regarding long term risks of living kidney donation are we prepared to conflict our own principles of beneficence and non-maleficence?

Deceased directed kidney donation: a recent case study from the London organ donation services team

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Introduction: Donation from a deceased organ donor is unconditional. A donor family raised directed donation during the approach for Donation after Brain Stem death. In this instance the requested organ was a kidney and the intended recipient was a close family friend. Evidence suggests that directed donation is a rare request and seldom proceeds to transplant. Anecdotally directed donation to a family friend is not known to have occurred.

Case presentation: Contact with the SNOD was only initiated post BSDT at the request of the ITU consultant. Donation had been raised with NOK –children of the deceased by the ITU consultant. Patient was registered to be a donor. SNOD met with the donor family to ascertain the decision and they asked if there was a possibility of directed donation. SNOD asked them to ascertain renal unit intended recipient was under the care of; transplant centre they were listed and their blood group. Informtion obtained -blood groups matched; recipient listed at local centre. The Regional Manager (RM) was informed of request and NHSBT policy reviewed. Contact made with the renal centre and the Transplant surgeon on call confirmed recipient ID. Agreement for directed donation to proceed was given and TT confirmed a match. Donation and transplant proceeded.

Discussion: A request such as this is not uncommon but usually falls at the first hurdle —ie the intended recipient is not listed for tx/blood group is incompatable. Ethical concerns were raised by the transplant surgeon on intial discussion as not familiar with the policy and had never had a similar request. The staff on the ITU were also concerned. For the SNODs involved in this case it was relatively straight forward. Although none had been involved in a similar case the NHSBT Policy was clear and RM support meant the request was able to be facillitated.

Consent and information for living donor nephrectomy: Are we saying enough?

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Introduction: Following the Montgomery ruling in 2015, there is increased scrutiny on how patients are informed about the risks of medical and surgical interventions and also possible alternative procedures. This process is particularly relevant in living donor nephrectomies (LDN), as these patients uniquely undergo a relatively high-risk operation with no physical benefit to the donor. We aimed to assess variation and adequacy of counselling of potential donors.

Methods: A retrospective analysis of clinical assessment and risk discussion of all 231 patients who underwent living donor nephrectomy at Manchester Royal Infirmary from January 2015 to August 2017 was performed. The information discussed was compared to the national standard of documented risks in the UK guidelines for living donor kidney transplantation (British Transplant Society/Renal Association)

Results: Mortality and future renal failure were the most commonly discussed risk factors, with chronic pain being the least frequent. Of the 231 patients, no single patient had documented discussion of all the risks, and no one risk was discussed with every patient.

Risks associated with LDN	Number of patients	%
Mortality	171	74%
Future renal failure / dialysis requirement	166	72%
Bleeding	164	71%
Risk of injury to adjacent structures	149	64%
Infection / sepsis	132	57%
Incisional hernia	123	53%
Bowel injury	114	49%
Conversion to open	99	43%
DVT / PE	92	40%
Chronic pain	84	36%

Discussion: There is great variation in the discussion regarding donation in practice, despite clear consensus provided by guidelines and recent changes in legislation regarding consent. Previous studies have concurred that this practice is prevalent throughout Europe. We would recommend that a standardised list of mandatory risks to be discussed when consenting LDN patients is instituted nationally. Further work could then clarify its potential utility on a national basis.

Living related renal transplantation from grandparental donors to paediatric recipients

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Introduction: Pre-emptive living donor renal transplantation is the gold standard therapy for children with end-stage kidney disease. Sometimes parental donation is not feasible and donation from other family members and friends may be considered.

Methods: Retrospective analysis of our paediatric renal transplant database looking at pre and post-transplant data of paediatric renal transplant recipients (pRTR) who received living related renal transplants from grandparental donors. One grandparental donor was excluded as donation was part of the National Living Donor Kidney Sharing Scheme so her grandson was not the recipient from her living donation.

Results: 7 pRTR (57% (4) male) aged 2.1 - 11.7 (median 6.9) years of whom 57% (4) has ESKD due to CAKUT underwent living related renal transplantation from grandparental donors aged 48 - 61 (median 56) years. The recipient's weight at time of transplantation was 10.8 - 46.9 (median 16.8) kg with 2 - 6 (median 3) mismatches at HLA-A,B and DR (without two mismatches at HLA-A, B and DR, apart from one fully mismatched kidney for a recipient with mitochondrial cytopathy). 43% (3) were preemptive transplants and 29% (2) re-transplantation rate after previous failed parental living donor transplantation with subsequent negative crossmatches. The outcomes were 100% patient survival rate and 86% (6) renal allograft survival rate with estimated glomerular filtration rates of 6.8 - 80.0 (median 65.2) mls/min/1.73m² at follow-up of 0.4 - 8.8 (median 2.6) years. Patients underwent 0 - 8 (median 2) percutaneous renal transplant biopsies with 57% (4) with chronic changes and one with retroviral disease.

Conclusion: Living related renal transplantation from grandparental donors should be considered for prospective pRTR and discussed with patients and families. Families may consider this option more favourable as this may extend the donor pool for recipients who may require parental living donation for their subsequent transplants.

A work in progress: Careplans developed to facilitate the smooth delivery of NHS kidney transplant care for patients with mental health and learning disabilities.

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Introduction: Facilitating the smooth and effective NHS care for adult patients with either mental health and/or learning disabilities in kidney transplantation is a challenge. Risks associated listing patients with these challenges include poor compliance, risk of graft loss, extended inpatient admissions and confusion around the best way staff can care for such patients.

Method: A careplan approach has been adapted for patients identified by the transplant team as complex with mental health and/or learning disabilities. For these patients and their carers/families a document is developed to share with relevant NHS team members. This aims to highlight relevant issues for each patient, outline mental capacity issues, guide staff about the best ways of working with the patient to facilitate a smooth journey through treatment as usual for kidney transplantation. This method has been trialed for N = 5 patients with no current evaluation in place. Careplan development involves 2-3 additional meetings with a Psychologist and/or Transplant Co-Ordinator to develop a careplan for each patient. Specifics of what the careplan outlines will be described.

Results: N=3 patients have been transplanted to date. Feedback from the teams has been positive noting that the complex capacity issues are outlined leading to less liaison/confusion about what is required, patients seem prepared and more confident about the process of being called for a transplant making them less likely to turn down kidney offers.

Discussion: This careplan approach is currently not formally evaluated, and initial feedback from Consultant Nephrologists is that the careplans reduce workload once patients are called for a kidney transplantation. Careplans also clarify issues involved in complex cases by using a multi-disciplinary approach.

Organ donation week in parliament - working together to increase organ donation awareness

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Introduction: Kidney Care UK and NHS Blood and Transplant decided to produce an organ donation week event in the UK Parliament, with a goal to increase awareness of donation in government and to encourage our MPs to reach out to their constituents on the subject. 2017 was the 3rd time over the past 5 years that we have done this and we used previous experience to target attendees.

Methods: Through a joint working group which had regular calls and one face to face meeting we linked communications, policy and government affairs. Kidney Care UK asked patients and other attendees to invite their MP to meet them at a reception, and supported patients by paying for their travel and helping them to contact their MP if needed. Using NHSBT's smart mailing system we wrote a joint letter of invitation to all MPs from the CEOs of both organizations, offering fax as well as email and written responses as options. To increase response rates, NHSBT suggested sending letters in the post during the summer which produced an increased response. We invited the Donor Family Network, a kidney recipient who is our NI patient advocacy officer, and the mother of a kidney patient who became on organ donor herself to speak. No-one moved during their mesmerizing, extraordinary speeches.

Results: A record 67 MPs attended, with Health Minister Jackie Doyle-Price giving a keynote speech and Rehman Chisti MP kindly hosting. The national interest in improving or changing consent rules may well have helped. About half the MPs used social or local media with photos and messaging from the event.

Discussion: Enabling patients and donors to tell their stories and challenging our policy makers to speak up about organ donation gives both short and long term benefits. By joining together in this way we can do so much more.

Attitudes and factors affecting donation in family members of successful kidney transplant recipients. Single-centre survey

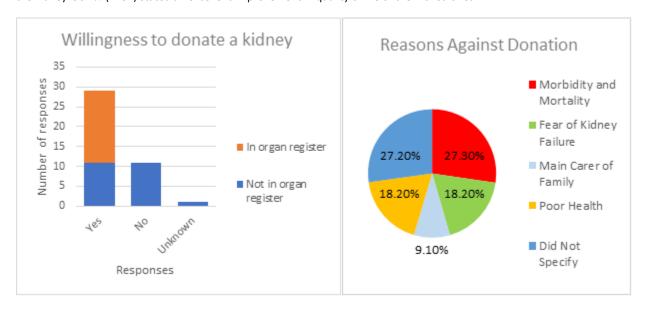
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Introduction: According to NHS Blood and Transplant, UK has the lowest rate of transplant consent in Europe. "Taking Organ Transplantation to 2020" states that UK will never have a world class donation and transplantation service if more than 4 out of every 10 families decline donation. At present, 43% families decline donation. This prompted us to conduct a survey in our transplant department amongst family members of renal transplant recipients.

Methods: A questionnaire was developed and distributed to the family members accompanying renaltransplant recipients in follow-up clinics. The questionnaire aimed to capture demographics, financial and educational status, transplantation experience and willingness to donate organs. Reasons for declining donation were specifically asked and recorded.

Results: There were 41 respondents (27 F, 14 M). 80.5% (n=33) of the respondents were of White and 19.5% (n=8) of Asian origin. The majority, 63.4% (n=26), were Christian. 34.1% (n=14) had live-donor and 58.5% (n=24) deceased-donor kidney transplantations. The majority of the study population, 92.7% (n= 38), had a first degree relative or spouse who received the kidney. 90.2% (n=37) stated an excellent improvement in quality of life of their loved ones.



Discussion: Studies revealed multiple, increasingly complex factors affecting consent to donate amongst donors. A systematic review by Irving et al has highlighted factors such as religion, culture, family influence, medical mistrust and fear of early retrieval as the most important factors negatively affecting donation. The desire to donate in family members of the study population was higher than the national average. Despite the majority of family members, 70.7% (n=29), willing to donate, 37.9% (n=11) were not in the organ donor register. Low financial status, increasing number of dependent children and main caring roles negatively affected the desire to donate. National studies are required to further explore these factors and reduce the mismatch between organ donation and supply.

A nursing focus on the psychosocial impact of solid organ donation and disease on the individual

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Introduction: To gain a deeper understanding of the available literature and evidence surrounding the impact of disease and subsequent organ transplantation on the individual with consideration to three key themes: Quality of Life, the importance of support networks in a personal, social and professional context and the role of anxiety and depression and its prevalence in the chosen patient group. The final objective aims to identify key areas in which healthcare professionals can deliver high quality, supportive and effective care from the point of transplantation to help improve mortality and morbidity.

Method: A systematic literature review of several well known clinical databases and clinical journals using advanced search options and relevant Boolean operators for clarity. CINAHL plus, The Cochrane Library, Medline and the BNI were used cohesively to obtain an extensive range of applicable literature.

Results: A deeper understanding of the role of psychosocial health in relation to physiological well being and recommendations for future practice and dissemination of information discovered to clinical members of the multi-disciplinary team. A range of factors were found to be influential, including that the non-clinical needs of patients are not always addressed in practice and are not always included in the decision making process in regards to their treatment.

Conclusions: From the three chosen themes, it is clear that affectations in either category can have a detrimental effect on long term health, mortality and morbidity, in both the disease process and transplant recipients. Careful consideration must be given in practice to the psychosocial aspect of patient care delivery to ensure holistic and therapeutic care. Living with a long term health problem can generate long standing psychosocial issues surrounding functionable sufficiency and it is essential that qualified staff working alongside this patient population in a clinical setting understand the impact upon the individual.

Use of paired healthcare professional and patient testimonial videos on increased risk donors achieves resonance and offers an opportunity to contribute to longitudinal consent

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Introduction: The average waiting time for a kidney transplant in the UK is 2.5 years. A significant amount of educational information is disseminated in transplant work-up, but patient knowledge fades with time. Meanwhile, consent processes around transplantation have become more complex with increasing use of increased risk donors. It is also now recognised that consent should be an ongoing process rather than limited to a single interaction in an emotionally stressful time. We endeavoured to assess whether videos were an effective means of patient education for such complex issues.

Method: 61 kidney transplant candidates completed an online questionnaire with embedded videos while receiving haemodialysis. Two videos relating to issues surrounding an organ offer, with particular focus on use of an organ from an increased risk donor (history of primary cerebral malignancy), were shown, one featuring a healthcare professional, the other a patient with personal experience thereof.

Results: The proportion of correct answers to knowledge-based questions on the healthcare video content significantly improvement following the video (p<0.001), with the greatest improvement seen for a question on increased-risk donors, 'I might be offered a kidney from a donor that had a brain cancer'. 95% patients reported synergy between the healthcare professional and patient videos, while 87% reported that the patient video made the healthcare professional video more of a reality for them.

Discussion: It is increasingly recognised that peer testimonials have the greatest resonance with patients. Pairing short digital videos featuring a healthcare professional and an experienced patient enhances delivery of information in an engaging and effective format. Furthermore, delivery of information in this format facilitates repeated access to the content, which can contribute to longitudinal education and the consent processes surrounding complex issues in transplantation.

UK living kidney sharing schemes (UKLKSS): achieving maximum patient benefit

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The UK Living Kidney Sharing Schemes (UKLKSS) offer an effective pathway to optimise both access to and the outcome of living donor transplantation.

In our centre we take a multidisciplinary team (MDT) approach to maximise the potential for living donor kidney transplantation. Patients presenting with ABO and /or HLA incompatible (HLAi) donors are considered by the MDT and in the first instance entered into the UKLKSS for the opportunity of an antibody compatible transplant. From July 2013 if a patient is unsuccessful in obtaining a HLA compatible donor, their chances are maximised by delisting unacceptable specificities resulting from lower antibody levels to permit an HLAi transplant. From October 2014 patient and donor pairs having a poor HLA match are offered the option of entering the UKLKSS.

We have audited the activity in the programme to assess the patient benefit from the strategies to amend antibody profiles and improve HLA matching. In the 4 year period from July 2013 to July 2017, 87 patients from our centre have been registered on the scheme achieving 71 matches and 44 subsequent transplants.

In 36/87 (30%) patients the list of unacceptable specificities was amended for the matching run and this strategy resulted in 13 successful transplants. 10/13 (77%) transplants were HLA antibody incompatible, but represented a lower risk HLAi transplant than would have been possible through direct donation.

Twelve patients were registered to obtain a better HLA matched transplant. 11/12 (92%) were transplanted with an improved HLA-A, B,DR mismatch grade and for 10/11 (91%) patients this was achieved in the first matching run.

24/44 (55%) of the UKLKSS enabled transplants at our centre have resulted from the above strategies, benefitting patients both locally and nationally. Local patients are transplanted with lower risk HLAi or better HLA matched kidneys and more transplants are enabled nationally.

IgG de novo donor-specific antibody subclass analysis in patients undergoing allograft nephrectomy after transplant failure

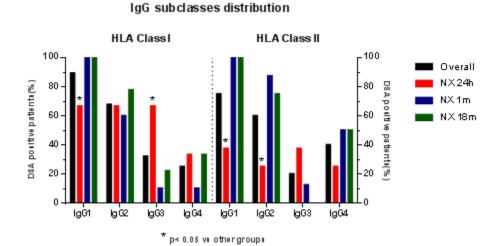
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Introduction: different immunising events can stimulate the production of disparate antibody subclass profiles, reflecting a diverse extent of T-cell activation. Transplant nephrectomy (NX) is a known cause of donor-specific antibody (DSA) production after graft failure, and its effect on the generation of IgG subclasses has never been investigated.

Methods: 35 unsensitized patients who underwent first-graft NX were included and divided according to the timing of NX: group 1 (within 24h from implantation, n=11), group 2 (1-30 days after transplant, n=13), group 3 (1-18 months after transplant, n=11). Sera obtained 24 months after NX were assessed for IgG subclasses for HLA-A/B/Cw/DR/DQ using the single antigen Luminex assay.

Results: 9/11 patients in group 1, 10/13 in group 2 and 9/11 in group 3 were DSA positive at 24 months (p=n.s.). All four IgG subclasses were produced for both DSA classes (Figure 1). Compared with the other groups, group 1 showed lower proportion of IgG1 and higher proportion of IgG3 positive patients for class I, and lower proportion of IgG1 and IgG2 positive patients for class II (Figure 1). Group 1 was also characterised by lower prevalence of patients generating DSAs with subclass profile 1-2-- and 1--- for class I (p=0.049 and 0.034), lower prevalence of the profile 1-2-- for class II (p=0.019), and a tendency to lower prevalence of profile 1--- for class II (p=0.097) compared to the other groups.

Discussion: our findings suggest that NX results in a continuous immunological stimulus leading to the production of all IgG subclasses up to 24 months later and regardless of the timing of the NX. The different distribution of the subclasses prevalence and profiles across the study groups may indicate that the early, within 24 hours NX is characterized by a different pattern of T-cell activation compared to NX performed later after the transplant.



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Immunological risk stratification pre-transplantation and risk of early AMR – analysis of UK AiT registry data

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Introduction: Risk stratification based on antibody assays is currently performed to improve opportunity for transplantation; with CDC positive antibody level considered as highest risk and Single antigen bead alone antibody level as lower risk (but higher than standard risk). We analysed multi-centre data from antibody incompatible kidney transplantation in UK.

Methods: A total of 663 cases transplanted between 2001 and 2015 were considered and 136 cases were excluded if data was missing. The cases were stratified in to five groups based on their antibody levels (strata 1- CDCpos, Flowpos and SABpos; strata 2 – CDCnot done, Flowpos and SABpos; Strata 3 – CDCneg, Flowpos and SABpos; Strata 4 – CDCneg, Flowneg and SABpos and Strata 5 – CDCneg, Flowneg and SABpos).

Results: Overall Pre-treatment antibody level and at transplantation antibody level was significantly associated with AMR (p-values were 0.000026 and 0.00065 respectively). There was no significantly higher AMR in strata 1 and 2 compared to strata 4 based on pre-treatment antibody levels (Table 1). However, based on at transplant antibody level only strata 2 had higher risk of AMR compared to strata 5 (Table 1).

Table 1: AMR based on antibody level (* - comparison of strata against strata 4 and ** - comparison of given strata with strata 5)

Pre-Treatment antibody level					
	Strata	No	AMR	% AMR	p value*
	1	69	33	48	0.002919
	2	44	28	64	1.50E-05
	3	223	81	36	0.073276
	4	191	53	28	
At Transplantation antibody level					
	Strata	No	AMR	% AMR	p value* *
	1	19	8	42	0.424289
	2	17	14	82	0.0002
	3	161	66	41	0.202528
	4	251	82	33	0.891388
	5	79	25	32	

Conclusion: SAB alone positive and complete antibody negative at time of transplantation has similar AMR risk. Strata 2 (CDCnot done, Flow pos and SAB pos) has higher risk of AMR within three months post-transplantation. Interestingly,

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HLA-DP antibody incompatible kidney transplantation: a single centre review

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Introduction: HLA donor-specific antibodies (DSA) are associated with acute rejection and decreased graft survival. The national deceased donor allocation algorithm does not take HLA-DP sensitisation into account when allocating kidneys. We present our centre's experience of HLA-DP incompatible offers and outcomes.

Methods: Patients were included in the study if HLA-DP DSA alone (MFI>1000) was identified in, or within six months of, the time of offer (TOO) serum sample. Cross-matching and clinical outcomes were compared to a control group, which included recipients with a TOO sample containing non-donor-relevant HLA-DP antibodies.

Results: Between 2013 and 2017, 31 recipients were identified and followed for a median of 654 days. The majority (84%) of patients received a deceased donor graft, and 52% were re-transplants. In addition to possessing HLA-DP antibodies, 45% were highly sensitised with a cRF≥85%. Flow cytometric (FCXM) and CDC T-cell crossmatch results were negative in all cases. Five patients in the DP-DSA cohort generated B-cell positive FCXM results, but no association with HLA-DP MFI levels was observed (10381 B-FCXM negative, vs 12141 B-FCXM positive, p=0.672). Within the DP-DSA cohort, transplants proceeded with a plan for augmented immunosuppression (n=10) and plasma exchange (n=4). The estimated 1-year rejection free survival was reduced in the DP-DSA cohort compared with the control cohort (See Table 1). The 1-year graft survival was 86%. The median g+ptc score was 2 (IQR 3) in the biopsies obtained from the DP-DSA group, and 1 (IQR 4.5) in the control group, (p=0.85).

Variable	All Patients	DP DSA	Control	P-value		
Number	31 (100%)	17 (55%)	14 (45%)			
DGF	12 (39%)	7 (41%)	5 (50%)	0.756		
1yr Rejection Free Survival	49.5%	33.6%	66.6%	0.071		
1 yr Graft Survival	86.4%	86.3%	85.7%	0.587		
Renal Function (eGFR) Median (IQR)						
3-month	40.5 (34.75)	46 (31)	43 (28)	0.721		
6-month	44 (32)	39 (33)	51 (30)	0.394		
1-year	44 (34.5)	43 (39)	48.5 (38.5)	0.358		
2-year	41 (38)	29 (49.5)	47 (21)	>0.99		
Proteinuria-UPCR median(IQR)						
3-month	34 (56.4)	46 (73)	35 (29.7)	0.347		
6-month	30 (110.6)	31.45 (120)	27.4 (35)	0.601		
1-year	26.7 (33.9)	10.8 (22.5)	26.7 (45.2)	0.620		
CMV viraemia	4 (14%)	3 (19%)	1 (8%)	0.390		
BK viraemia	3 (10%)	2 (13%)	1 (8%)	0.672		
Medication Adherence (CNI variability)						
0-3 months	29.4 (13.02)	29.1 (7.5)	31.1 (9.7)	0.56		
>3months	28.2 (10.4)	25.1 (6.7)	33.1 (13.7)	0.07		

Table 1: Clinical Outcomes

CMV viraemia occurred in a higher proportion of DP-DSA patients (p=ns). One graft was lost due to BK nephropathy in the DP-DSA group.

Discussion: DP incompatible transplants should not be considered standard risk. Current laboratory tests are unable to risk-stratify patients, therefore vigilance is required when transplanting across this barrier.

Removing low risk previous transplant mismatch in definition of unacceptable HLA listing improves opportunity of transplant offer in highly sensitised patients on waiting list

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Background: Defining unacceptable HLA antigens when listing patients is important risk stratification. This reduces positive cross match results and avoids untoward transplant outcomes (rejection and graft loss). However the chances of a patient receiving a transplant offer declines as the breadth of unacceptable antigens increases. A previous transplant HLA mismatch can be defined as high risk if it resulted in an antibody response in the recipient, or if the patient had a graft nephrectomy. In such instances, repeating a mismatch is associated with a potential memory response, and increased risk of adverse outcomes. Alternatively, a low risk mismatch has generated no antibody response.

Methods: We revised our local policy and removed low risk previous HLA mismatches from the list of declared unacceptable antigens. cRF before and after the policy change were calculated, and these were compared with offer rates following policy implementation.

Results: Low risk mismatches were identified and delisted in 29 patients. 59% were male, with mean age of 44 years. 45% were blood group 'O'. 28/29 were highly sensitised prior to the revised policy compared to 24/29 after de-listing. The cRF was 97.2% (73 – 100) and 91% (0-100) pre-and post-change, with a 7% reduction in overall cRF. This intervention resulted in the increased appearance of 5 patients (17%) on the matching runs. Two patients received an offer of a kidney.

cRF	Pre	post
< 85%	1	6
85-95%	4	3
96-99%	10	10
100%	14	10

Table 1: Change in proportions of cRF following revised policy on previous transplant mismatch.

Conclusion: Delisting antigens that represent low risk repeat mismatches can lead to the modest reduction in cRF of HSPs and improve the opportunity for transplant offer. Transplant teams should re-assess their previous mismatch policies to improve opportunities in HSPs. Such cases may require close immune surveillance and augmented immunosuppression therapy.

Comparison of porcine kidneys during normothermic machine perfusion in open and closed circuits

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Introduction: Normothermic machine perfusion (NMP) of kidneys may offer the opportunity to assess kidney viability before transplant. NMP circuits can be 'open', with the renal vein draining directly into a reservoir, or 'closed', with the vein cannulated and connected to the circuit. Closed circuits may be more physiological. Our aim was to compare open and closed NMP circuits.

Methods: Slaughterhouse pig kidneys were retrieved, flushed and transported at 4°C. The renal artery was cannulated and kidneys underwent hypothermic machine perfusion for 60-90mins. They were then allocated to open or closed circuit NMP, using oxygenated, leukocyte-depleted whole blood for seven hours. TPN, insulin and bicarbonate were added according to perfusion analysis and urine output was replaced with Ringers lactate. Perfusate, urine and renal biopsies were collected. Perfusion parameters including renal blood flow, arterial pressure and resistance were continuously analysed. LDH, free haemoglobin and markers of renal function were also measured.

Results: There was no difference in warm ischaemic time (19 vs. 15min) kidney weight (218 vs. 187g) or cold ischaemic time (4.5 vs. 4h). Kidneys in both groups showed an increase in flow and reduction in resistance during HMP. There was no difference in mean renal blood flow (157 \pm 52 vs. 158 \pm 48ml/min) or renal resistance (0.49 \pm 0.18 vs. 0.49 \pm 0.2ru) during NMP. Metabolic parameters including pH, pCO₂ and pO₂ and lactate were not different. Mean cumulative urine output was higher in the closed circuit (7 vs. 74ml; P=0.02). Mean LDH levels were no different between groups (1.68 vs. 0.5: P=0.08). Haemolysis, functional results and histology scoring are in progress.

Discussion: Early data comparing open and closed NMP circuits demonstrate no difference in perfusion or metabolic parameters except urine production, which was higher in closed circuit NMP. The closed circuit increases venous pressure and may be more physiological (results pending).

The use of 16S ribosomal RNA PCR to investigate donor derived transport fluid infections in patients undergoing renal transplantation: A retrospective audit of 55 deceased donors.

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Introduction: 16S ribosomal RNA (rRNA) gene polymerase chain reaction (PCR) is emerging as a novel, high-yield molecular method for the detection and identification of bacterial pathogens in clinical specimens with a high suspicion for infection. 16S rRNA PCR has been investigated as an alternative approach to conventional microbiological cultures in various clinical settings. 16S rRNA has the potential of providing results faster than conventional culturing

Methods: Transport fluid was obtained from 55 deceased donors and was assessed by two different methods. 16S rRNA PCR was compared with conventional microbiological culture for the detection of potential pathogenic bacteria.

Results: Of 55 deceased donor transplants 39 had 16S rRNA PCR performed. 18 (of 39) transplants had a positive culture (46%). 5 (of 39) transplants has a positive 16S rRNA result (13%). Compared with conventional culturing 16S rRNA demonstrated 100% specificity and 28% sensitivity for the detection of pathogens. The positive predictive value (PPV) for 16S rRNA compared to culture for detection of pathogens was 100% The negative predictive value for 16S rRNA was 62%.

Discussion: Transplant associated infections are associated with high levels of morbidity and mortality. 16S rRNA PCR offers the possibility of rapid high yield analysis of transport fluid for pathogens before the results of conventional culture. Despite the low sensitivity demonstrated, 16S rRNA PCR still demonstrates potential clinical utility as 28% of transport fluid with a positive culture could be detected at an earlier stage, additionally low sensitivity of 16S rRNA PCR may be an advantage due to reduced risk of detecting contaminants.

Conclusion: There is limited understanding of regarding the use of 16S rRNA PCR for detection of infection in deceased donors. 16S rRNA analysis of transport fluid is a novel technique which shows potential clinical utility in the detection of pathogens. Further investigation is required to explore this in more detail.

Machine perfusion parameters of small paediatric kidneys do not conform to the adult perfusion pattern

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Introduction: Kidney transplant from infant and neonatal donors are increasingly performed in the UK. First neonatal donor kidney transplant was performed in 2014. These kidneys are procured and transplanted en bloc. Inadequate in-situ flush is commonly observed in these kidneys. Once removed from the donor these kidneys can only be re-flushed after completion of back table surgery. Hypothermic Machine Perfusion (HMP) allows for a controlled flush of these kidneys. Normal Perfusion parameters for these kidneys are not known.

Methods: From May 2014 to October 2017, 17 pair of kidneys from infant and neonatal donors were perfused on LifePortTM machine using KPSI solution at a perfusion pressure of 20mmHg. The indication for HMP in all these kidneys was inadequate in situ flush at procurement.

Results: Of 17 machine perfused kidneys, the median donor age and weight were 28 days and 3.3Kg respectively. One pair was discarded due to no visible improvement of flush. A low flow and high resistance was observed from the start (14 ml/min and 1.5 respectively), which improved over 20-30 minutes. The flow and resistance at the end of perfusion were 21±9.7 ml/min and 1.05±0.52 respectively. In one kidney, the resistance persisted at 1.99, the maximum value permitted by the machine. Two grafts were lost due to early vascular thrombosis. DGF was observed in 4 patients and 10 grafts had primary function. The machine parameters did not correlate to immediate graft function.

Discussion: Inadequate in-situ flush is common in kidneys procured from infant & neonatal donors. HMP provides a safe and effective method of re-flushing these kidneys. These kidneys exhibit very high resistance and a predictable low flow rate. Such parameters did not correlate to immediate graft function. LifePort Machines are not calibrated for small paediatric kidneys and these values should be interpreted with caution.

In donation after circulatory death (DCD), can we identify patients most likely to benefit from ante-mortem interventions?

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Introduction: The UK transplant programme is an international outlier in not utilising ante-mortem interventions such as systemic heparinisation to improve transplant outcomes from DCD donors. The ethical issues inherent in prescribing potentially harmful treatments that will be of no benefit to non-proceeding donors may influence this. We aimed to determine if it was possible to identify a physiological 'cut-off' following treatment withdrawal beyond which it could be guaranteed the patient would proceed to donation.

Method: Physiological records from the donor care files of 408 consecutive DCD donors from eight UK organ donation teams between April and December 2013 were analysed. Systolic blood pressure (SBP) from time of treatment withdrawal, time to asystole and donation outcome were all reviewed.

Results: 255 DCD patients proceeded to donation, whilst 153 did not because of prolonged time to asystole. In the 255 proceeding donors the median time to asystole from the first recorded SBP <90mmHg was 8 minutes (mean 12.8 minutes, range 1-86 minutes) and from <50mmHg was 5 minutes (mean 5.9 minutes, range 1-56 minutes). Of the 153 non-proceeding donors, 13 had an episode of SBP <90mmHg and four had an episode of SBP <50mmHg within three hours of treatment withdrawal. Whilst all 17 of these non proceeding patients died during their hospital admission, there were 3 other non-proceeding patients who survived to discharge.

Discussion: Heparinisation at the time of treatment withdrawal exposes non-proceeding DCD donors to the risks of heparin but offers no benefit. This study demonstrates that donation becomes highly likely when significant hypotension occurs within the three hour window from treatment withdrawal (SBP<90mmHg, 255/268 patients [95.1%]; SBP <50mmHg, 255/259 patients [98.5%]). Such physiological thresholds may represent indicators of when organ retrieval is most likely to occur and when the benefits of ante-mortem interventions outweigh their potential harms.

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Hypothermic machine perfusion with RM3: role in graft outcome prediction

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Introduction: Use of marginal donors is one of the major challenges in transplantation with a need of post transplant function predictors. Aim of the present study was to evaluate renal outcomes based on Resistance Index (RI) during hypothermic machine perfusion (HMP) and its potential use in graft viability assessment.

Methods: Retrospective analysis of kidneys perfused with HMP (RM3; Waters Medical System) from 1.6.2015 until 13.02.2017. Delayed graft function (DGF) was defined as dialysis need within 1 week from transplant; eGFR was measured according to Modification of Diet in Renal Disease formula at 3, 6 and 12 months after transplant. Expanded criteria donor (ECD) was defined if age \geq 60, or \geq 50 with at least two from hypertension history, eGFR > 133 mmol/L, death from stroke. Statistics used the SPSS 20.0 version, setting a p-value <0.05 as significant.

Results: Seventeen kidneys were included: 7 males recipients, median age 55 years (29-77); median donor age 58 years (23-76), 9 DCDs, 6 ECDs, median Cold Ischemic Time 12 hrs (7-21), median Warm Ischemic Time 45 min (38-65). A statistical significant reduction in RI levels after 1 hour and 2 hours of HMP was observed; 2-hours RI≥0.45 mmHg/ml/min was predictive for DGF (area under the curve 0.76), with 80% sensitivity, and 59% specificity. Linear regression models showed higher values of 2 hours RI associated with ECD (p = 0.011). No correlation was confirmed between high RI values and 3, 6 and 12 months eGFRs. Median follow up was 12 months (8.1-29.2). One patient died and one lost his graft (both in low 2 hours RI group).

Conclusions: RI at 2 hours showed to be an early tool to predict DGF in transplanted kidneys, significantly correlated with ECD, an important resource to expand donor pool with no long term function effect.

The designing of a UK competency pack to guide non-medical organ care system operators (OCS) proceeding donation after circulatory death (DCD) hearts

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Introduction: Papworth Hospital introduced the OCS in February 2015 as a way of mechanical perfusion of a heart following donation after circulatory death (DCD). The OCS is currently operated by Transplant Surgical Fellows. Due to their movement through the Transplant service it has been decided that there is a need to train permanent non-medical National Organ Retrieval Service (NORS) members. Training of this staff group ensures a continuous workforce are trained to use this specialist equipment. The Competency pack is aimed for use by Donor Care Physiologist (DCP) and Transplant Practitioners (TP). The package includes a Standard Operating Procedure (SOP) as well several supporting documents.

Methods: Various training methods have been embarked upon, such as attending Transmedics Inc. headquarters in Andover and in-house training from the surgical team. This has initiated the development of a comprehensive competency pack providing support for non-medical staff in using the OCS for DCD hearts. Ensuring national standards are met the UK Competency Pack contains pictures and diagrams of the OCS kit to aid correct placement of equipment and to identify the necessary consumables. There is also a questions and answers section to assist with troubleshooting.

Results: Since February 2015 Papworth Hospital has placed 40 hearts onto the OCS. 36 recipients have received hearts following OCS perfusion. So far the results identify that 20 DCD heart transplant patients have survived more than one year.

Discussion: Papworth Hospital is the world's leading centre for clinical experience of DCD heart retrieval using the OCS. Development of the UK Competency Pack provides a benchmark for best practice and potentially offers support and guidance to other centres embarking on using the OCS for DCD hearts.

Donor renal artery barotrauma secondary to high pressure hypothermic aortic perfusion:-a potentially avoidable cause of sub intimal haematoma in renal arteries

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Introduction: A targeted national approach has led to an exponential increase in donation after circulatory death (DCD) in the last decade. In 2010 a National Organ Retrieval system protocol was introduced in order to standardize organ procurement. This involved high pressure (>250mmHg) in-situ hypothermic flush through the aorta. First introduced for DCDs, the pressured perfusion is now used for all deceased donation. It is widely accepted that cold preserved vessels are more prone to injury. This leads to the potential of vessel barotrauma which can cause sub-intimal haematoma, potentially making organs non-transplantable. We summarise a single centre experience of sub-intimal haematomas in donor renal arteries, since 2010.

Methods: The author maintained a prospective photographic record of all deceased donor kidneys with sub intimal haematoma received at their institution during the study period. All organs included underwent standard national protocol procurement. Outcome of these kidneys were analysed in binary terms, i.e. transplanted or discarded.

Results: Nineteen kidneys were received in our institution with sub intimal haematoma in the study period. All were received following the introduction of the new retrieval protocol in 2010. 13 were from DCD, 6 were from DBD donors, 6 left and 13 right kidneys. The mean donor age was 53 years, 7 male, 12 female. Degree of sub-intimal haematoma visible was graded. Two kidneys were transplanted after resection of the proximal segment containing the intimal damage. Fourteen kidneys were discarded.

Conclusions: Sub intimal haematoma in the donor kidney is associated with high risk of vascular thrombosis. Most such kidneys are discarded after retrieval. All kidneys with sub intimal haematoma in this cohort were procured after the introduction of the new retrieval protocol employing pressure during in situ hypothermic preservation. We suggest a randomised trial of current protocol vs 'non-pressurized' perfusion for hypothermic in-situ flush for DBD and DCD kidney procurement.

Memorandum of understanding between NHSBT, UK and Multi Organ Harvesting Aid Network Foundation, Chennai, India

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Multi Organ Harvesting Aid Network (MOHAN) Foundation (MF) entered into a landmark Memorandum of Understanding (MoU) with NHS Blood and Transplant (NHSBT), UK in January 2015 and was reaffirmed at the House of Lords in February 2016. The objective of the MoU was to promote collaboration and knowledge sharing between the two organisations with the aim of increasing organ donation rates in India and in the UK.

Many successful joint ventures have materialized since the MoU was signed. Collaborative working and sharing of good practices have had a positive impact in improving donation rates in both countries. Members from each organisation meet annually to discuss, share and implement ideas to help improve organ donation rates. MF assists NHSBT in improving organ donation rates among Black, Asian and Minority Ethnic (BAME) communities in the UK and NHSBT helps MF in increasing deceased donation rates in India.

Deceased donor transplantation is in its' infancy in India. There is no structured training for organ retrieval in India. Hence following the MoU, National Organ Retrieval Course was started in India with the help of surgeons from Oxford and Birmingham to help increase deceased donation rates in India.

Effective maintenance and optimisation of a potential organ donor remains a universal challenge. Donor Optimisation App is an offshoot of the collaboration. This app (Photographs 1 & 2) was developed, in India in partnership with MOHAN Foundation, to enable medical and paramedical personnel to have instant access to the latest evidence based guidelines for the management of potential organ donors. The app is being used by the health care professionals in both countries. The app is available for Android and iPhones and can be downloaded from the MOHAN Foundation website – www.mohanfoundation.org.

Photos 1 &2 - Donor Optimisation App





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How the MODST set about reducing 24 hour working for on-call specialist nurses (SN-OD's)

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Introduction: Due to the implementation of Specialist Requestors (S.R's) within the team we had the opportunity to re-evaluate the MODST rotas, examining the hours we worked when on-call, with the purpose of reducing 24 hour working. This allowed us to minimise 24 hour 'breaches' and remain in line with the EU working directive.

Method: A lead SN-OD was allocated and tasked with liaising with the team and a 'core group' of 5 SN-OD's met to discuss potential 'mock rotas' and proposed changes to on-call hours. Within a series of meetings involving all the team, these mock rotas were disseminated and a majority was reached in favour of one of the 3 examples. The Team Managers took the rota to H.R and Staff side for approval prior to the team trialling the newly proposed hours. The chosen rota commenced in November 2016 in line with the S.R role.

Results: 24 hour working has been reduced to 21 hours, 7 days a week with SN-OD's not commencing their working day when on-call until 12 midday. This in turn has been linked to the reduction in sickness levels within the team and we remain below the national average for sickness within the U.K SN-OD workforce. Within the last 12 months SN-OD retention has increased by 20.8% and although we have no comparative data for the year proceeding, the new rotas are believed to have influenced these figures. The MOSDT have had no recorded 24 hour 'breaches' since the implementation of the improved rota.

Discussion: The rotas have now been implemented for 12 months and have received positive feedback. This is a perfect time to formally evaluate the rotas, in the hope of reducing the on-call working hours further, from 21 to 15. We aim to provide the team with new mock rota examples by March 2018.

