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Abstract Book

26 – 28 February, SECC Glasgow

Wednesday 26th February
Lomond Auditorium – 12:30
Chairs: Dr Richard Baker and Dr Keith Rigg

O1

Antibody-mediated rejection in ABO-incompatible and positive crossmatch transplantations: a similar banff phenotype but a different outcome

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Introduction: Positive crossmatch (HLAi) and ABO-incompatible (ABOi) transplantations are becoming increasingly common, but their results appear very different. To date, there are few data directly comparing these two groups. The aims of this study were to compare the results, and in particular antibody mediated rejection (AMR), of ABOi (n=69) and HLAi (n=27) renal transplantations. We also analysed a third group of patients who received a combined ABOi+HLAi transplantation (n=10).

Patients and methods: 69 ABOi, 27 HLAi, and 10 combined ABOi/HLAi undergoing living-donor antibody incompatible transplants were included. All biopsies performed in the first 100 days after transplantation were reviewed and scored according to Banff criteria.

Results: One-year death-censored graft survival was better in ABOi than in HLAi and ABOi+HLAi patients (99%, 80%, and 80%, p=0.0002). Five-year death-censored graft survival was still better in ABOi than in HLAi and ABOi+HLAi patients (99%, 69%, and 64%, p=0.0002). Induction therapy with T-cell depletion (ATG/Alemtuzumab) was more frequently used in HLAi and ABOi/HLAi patients, while rituximab was mainly used in ABOi patients. However, the incidence of both clinical and histological antibody-mediated rejection was not significantly different between ABOi and HLAi (clinical: 16% vs 22%, p=05, histological 34% vs 52%, p=0.2); it was however higher in ABOi+HLAi patients (60% and 100%, p<0.05 versus ABOi and HLAi, respectively). After histological AMR, the percentages of patients experiencing a declining eGFR and graft loss were lower in ABOi than in both HLAi and ABOi+HLAi patients (declining eGFR: 29% versus 73% and 87%, p=0.05; graft loss: 6% versus 36% and 38%, p=0.04, respectively). This poor prognosis of AMR in HLAi and ABOi+HLAi transplantations was not explained by a higher severity of histological lesions (Semi-quantitative Banff scores were similar between the 3 groups).

Conclusion: The same AMR phenotype can lead to opposite outcomes according to the nature of the antigen and antibodies. An accommodation process could occur after AMR in ABOi transplantation while donor-specific HLA antibody commonly induces injury.

O2

Humoral allo- and auto-immunity in human lung transplant recipients

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Introduction: The development of autoantibody following lung transplantation has been associated with progression of Bronchiolitis Obliterans Syndrome (BOS), but the nature of the autoantibody response and, in particular, the specificity of target autoantigens remains unclear. Here, we evaluate humoral allo- and auto- immunity in lung transplant recipients.

Methods: Pre- and post-transplant sera obtained from lung transplant patients with either established grade 2-3 BOS (*n*=10) or without BOS (*n*=10) were assayed for the presence of donor specific alloantibody and autoantibody using Luminex Beads and Prospector Analysis of high-density protein micro-arrays comprising > 9000 human self-proteins.

Results: None of the study patients had detectable alloantibody, but we observed marked differences in patterns of autoantibody reactivity according to whether or not BOS had developed (Figure 1). BOS development was associated with the presence of class-switched autoantibody against a number of different target antigens that were, broadly, either lung-specific self-protein or related to lymphocyte and neutrophil activation. These responses were not present in the group of recipients with good graft function. Notably, for those patients who developed BOS, analysis of pre-transplant sera revealed that autoantibody to certain target self-proteins had already developed by the time of transplant. As before, these responses were not detectable in the pre-transplant sera of the patients who did not subsequently develop BOS.

Conclusion: Our results highlight that the development of BOS is associated with the generation of humoral autoimmunity against a number of different self-proteins. That some of these responses are present at the time of transplant suggests that prospective screening of lung-transplant recipients for autoantibody production may prove useful in predicting BOS development and may provide an opportunity to test whether the incorporation of anti-B cell therapies is effective at prolonging graft survival.

O3

Significance of tubuloreticular inclusions in renal allografts

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Tubuloreticular inclusions [TRIs] are commonly identified by electron microscopy [EM] in the endothelial cells and lymphocytes of patients with autoimmune diseases and viral infections such as SLE and HIV. TRIs are pathognomic of α- and β- interferon [IFN] production. The purpose of this study was to determine the relevance of TRIs in renal transplant biopsies.

We retrospectively analysed the histology reports of 2803 biopsy specimens from 1138 renal transplant recipients. 448 [16.0%] of samples from 306 patients were examined by EM. 37/306 [12.1%] patients were TRI+ and the remaining 269/306 [87.9%] TRI- patients served as controls. Mean follow up post index biopsy was 3.93 ± 2.22 years.

Patient survival was inferior in the TRI+ group compared with the TRI- group, 62.1% and 84.4% respectively [p=0.03]. Non-censored allograft survival was also inferior, 43.6% and 61.0% in the TRI+ and TRI- groups respectively [p=0.02]. Rejection free survival post index biopsy did not differ at 71.1% and 77.5% in the TRI+ and TRI- groups, p=0.97, although 20/37 [54.1%] TRI+ and 99/269 [36.8%] TRI- index biopsies had features of alloimmune injury, p=0.07. TRI+ patients were also more likely to have had prior rejection; 14/37 [37.8%] compared with 45/269 [16.7%], p=0.047, and also have class I DSA, 18/37 [48.6%] and 76/269 [28.3%], p=0.02. Evidence of the classic associations of TRIs, namely viral infections, autoimmune disease and malignancy were also investigated by multivariate analysis. Malignancy [OR: 7.08(1.01-49.50), p=0.049], viral infection [OR: 2.52(1.12-5.64), p<0.001] and DSA [OR: 2.51(1.12-5.62), p=0.025] were found to be associated with the presence of TRIs.

TRIs in renal transplant biopsies are not common but are associated with inferior patient and allograft outcomes. Viral infections at the time of biopsy are most strongly associated with TRIs. The novel finding of this study is that alloimmunity and specifically class I DSA are associated with TRIs.

O4

Molecular markers as diagnostic tools of donor organ quality and predictors of transplantation outcomes

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Background: As the demand for donor organs exceeds the supply more organs from older and high risk donors are currently accepted for transplantation. The ability to assess viability and quality of these organs prior to transplantation can be vital. Clinical proteomics has the potential to allow clinical and analytical validation of potential proteins as prognostic markers of organ quality and to identify novel therapeutic targets. We have investigated serum samples from three different types of donors to evaluate relevant molecular signatures of injury and repair associated with organ function and transplant outcome.

Method: Serum samples from living (LD), brain dead (DBD) and donors after circulatory arrest (DCD) were analysed using 'shotgun' proteomic approach. Samples from 10 donors per group were depleted of the 14 most abundant plasma proteins, precipitated and size-fractionated using SDS-PAGE. Protein bands were cut, digested with trypsin and analysed using tandem mass spectrometry (LC-MS/MS, LTQ Velos). The MS/MS spectra were analysed using using Progenesis and the 'in house' proteomic pipeline (CPF TPP).

Results: 305 proteins were significantly and differentially regulated across the three donor groups. A list of candidate proteins was differentially expressed among LDs, DBD, DCDs. There were 40 proteins that were uniquely expressed in the deceased donors only, 17 in the serum of DCDs only and 4 proteins in the DBDs suggesting the up-regulation of proteins of the coagulation and the inflammatory cascade when compared with living donors.

Conclusion: Our approach demonstrated that the proteomic signature of donors was informative to discriminate between donor groups suggesting that the identification of proteins that are related to organ quality and transplant outcome is feasible.

O5

HLA-incompatible transplantation – Do clinical phenotypes correlate with histology & DSA evolution to predict outcomes after positive crossmatch transplantation?

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Introduction: According to the Banff classification, histologically defined antibody mediated rejection (AMR) requires the presence of microcirculatory inflammation (MI), with C4d positivity and donor specific antibody (DSA), although this has been questioned and differing histological phenotypes identified[1]. This study aimed to correlate clinical outcomes with histological features after HLA incompatible transplantation.

Methods: A single centre, retrospective study of 25 patients requiring desensitisation due to a positive flow cross match. Protocol and 'for cause' biopsies performed within the 1st month, and at month 3 were re-scored according to the Banff classification by a single, blinded histopathologist. This was combined with clinical information including weekly eGFR & DSA monitoring. Patients were categorised into 3 groups: 'NORMAL'(eGFR >30ml/min at wk1, then stable n = 9)); 'DROP' (eGFR>30ml at wk1 followed by a significant drop, n = 8)) & 'LOW' (eGFR<30ml/min at wk 1, n=8).

Results: The 'LOW' group was strongly associated with poor long termlong-term graft outcome and graft loss compared to 'DROP' & 'NORMAL' (5yr GS DROP 100% vs LOW 62.5%p = 0.02). Risk factors associated with the 'LOW' group were a higher TFXCM at baseline & pre-tx; donor age; week 1 eGFR & month 3 eGFR. Histologically, AMR was present in all month 1 biopsies in both LOW & DROP groups, although mean MI scores were higher in the LOW group (3.0 +/- 0.5) compared to DROP (1.57 +/- 0.3) (p =0.04).

Discussion: We describe 2 clinical phenotypes of AMR with histologically similar features, but differing outcomes. Patients with an acute deterioration of graft function post transplant, appear to have a less severe phenotype of AMR which recovers with treatment and leads to improved long term outcomes compared to patients with a persistently low eGFR at week 1.

1.Mengel M, Sis B, Haas M, Colvin RB, Halloran PF, Racusen LC, et al. Banff 2011 Meeting report: new concepts in antibody-mediated rejection. Am J Transplant. 2012 Mar;12(3):563-70.

O6

Poor HLA matching and post-operative blood transfusions are associated with the development of de novo DSA post-renal transplantation.

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De novo donor specific antibodies [dnDSA] are associated with antibody mediated rejection and allograft loss. In the first study of its kind, we have undertaken a detailed multivariate analysis of pre- and post- transplant factors associated with the development of dnDSA.

We retrospectively analysed 871 ABO/HLA compatible renal transplant recipients who received a tacrolimus based immunosuppressive protocol with monoclonal antibody induction. 159/871[18.3%] patients developed dnDSA. Pre-transplant factors associated with dnDSA on univariate analysis were the presence of HLA Abs [OR: 1.48(1.0-2.17), p=0.049], being mismatched (MM) at both the class I and II HLA loci [OR: 3.84(2.52-6.36), p<0.01] and having a DQ HLA MM [OR: 2.96(1.92-4.54), p<0.01].

Post-transplant factors analysed included blood transfusion [OR: 2.15(1.33-3.49),p=0.002], delayed graft function [OR: 1.25(0.8-1.95),p=0.33], culture positive infection [OR: 0.95(0.63-1.42),p=0.80], non-compliance (assessed by the coefficient of variance of tacrolimus levels) [OR: 1.29(0.9-1.84), p=0.17] and biopsy proven rejection [OR: 1.81(1.16-2.84),p=0.01]. On multivariate analysis, factors found to be independently associated with dnDSA are shown below

Variable	Timing	OR (95% CI)	p value
Live transplants	Pre-transplant	0.63 (0.42-0.96)	0.03
Primary Allograft	Pre-transplant	1.77 (0.92-3.43)	0.09
Sensitisation	Pre-transplant	1.58 (0.97-2.59)	0.07
Not MM at CI+CII	Pre-transplant	0.35 (0.19-0.64)	0.0007
DQ matched	Pre-transplant	0.55 (0.33-0.93)	0.026
No Transfusion	Post-transplant	0.44 (0.26-0.76)	0.0032
Rejection	Post-transplant	1.76 (1.10-2.81)	0.018

Poor HLA mismatching and post-operative blood transfusions are strongly associated with dnDSA and are therefore potentially avoidable.

Wednesday 26th February
Alsh Suite – 12:30
Chairs: Dr Iain MacPhee and Prof David Taube

O7

Impact of donor and recipient CYP3A5, CYP3A4*22 and ABCB1 polymorphisms on Tacrolimus pharmacokinetics and clinical outcome in liver transplant recipients

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Background: Single nucleotide polymorphisms (SNPs) of the CYP3A subgroup and ABCB1 (encodes P-gp) influence Tacrolimus pharmacokinetics in renal transplant patients. As CYP3A is expressed predominantly in liver tissue, it is possible that donor rather than recipient genotype plays the more significant role in Tac pharmacokinetics.

Methods: 121 patients transplanted between 2007 and 2012 were included in the study. Donor and recipient DNA samples were genotyped for SNPs of ABCB1 exon 26 (3435C>T), CYP3A5 (6986A>G) and CYP3A4 intron 6 (CYP3A4*22) using a Taqman® drug metabolism genotyping assay and a real time PCR technique. Tac dose/trough levels were evaluated at 11 time points in the first month and at 3, 6 and 12 months post-transplant and correlated with clinical outcome data (acute rejection episodes, survival, incidence of adverse or side-effects).

Results: Patients receiving a liver from a heterozygote CYP3A5*3/*1 (GA) donor required significantly higher doses of tacrolimus and had a significantly reduced concentration/dose ratio (0.771 vs 2.10) throughout the first year of follow-up (Mann-Whitney U test, $p<0.01$). Donor CYP3A5*3/*1 expression also increased the time to reaching therapeutic concentration (8.04 days *3/*1 vs 5.26 days *3/*3, Mann-Whitney U test, $p=0.02$). There was a significantly higher incidence of biopsy proven acute rejection in patients receiving a liver from a donor with CYP3A5 *3/*1 genotype (50%, n=14) compared with *3/*3 genotype (19.6%, n=102), Chi-squared, $p=0.0001$. None of recipient polymorphisms nor the donor ABCB1 or CYP3A4*22 affected tacrolimus pharmacokinetics or the clinical outcome.

Conclusion: Donor rather than recipient expression of the *1 (A) allele of CYP3A5 reduces tacrolimus exposure. The recipients of these livers have a lower concentration/dose ratio of tacrolimus and take a longer time to achieve therapeutic levels. This translates into an increased incidence of acute rejection.

O8

DCD liver transplantation confers a significant survival advantage compared to waiting longer for a DBD organ

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Introduction: In the context of shortage of suitable organs for transplantation, it is often not clear whether a patient should receive a 'marginal' organ from a DCD donor which might adversely impact survival, or remain on the waiting list for a more 'optimal' liver from a DBD donor. We thus aimed to examine the consequence of waiting for an optimal organ by comparing the survival of patients after a DCD transplant to those who had a DBD transplant or remained on the waiting list (DBD/WL).

Method: Patients placed on the liver transplant waiting list in our centre from 1st January 2008 to 31st December 2011 were identified from a prospectively-maintained transplant database. Kaplan-Meier plots and log-rank tests were used to compare patient survival from the time of listing between DCD and DBD/WL recipients. To compare survival from time of transplantation, a matching algorithm was used: DCD patients were individually matched to up to 3 DBD/WL patients chosen at random. These DBD/WL patients had to be on the waiting list for the same length of time or longer to the matched DCD patient. Data was analysed using a Cox regression model stratified on matched sets to obtain a hazard ratio, adjusted for age at listing, UKELD score and HCC status. This matching process was repeated 1000 times to obtain a distribution of hazard ratios.

Results: 52 DCD patients and 386 DBD/WL patients were included in the analysis. A significant difference was detected between the survival time distributions from listing between the DCD and DBD/WL groups (log rank test p=0.040). Using a stratified Cox proportional hazards model, the risk of death was 79% lower in the DCD group than the DBD/WL group (HR=0.207 [95%CI: 0.045, 1.004]). Mortality of the cohort of patients who were on the waiting list but did not receive a transplant was 13% at 1 month, 23% at 6 months and 43% at 1 year.

Discussion: Receiving a liver transplant from a DCD donor confers a significant survival benefit compared to remaining on the waiting list for an 'optimal' DBD organ to become available.

O9

A national audit of donor after circulatory death physiology and withdrawal practice

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Introduction: Donors after Circulatory Death (DCD) have contributed to a significant increase in organs available for transplant in recent years. No national protocols for withdrawal location or practice exist, apart from the designated stand off time. However, there is a general acknowledgment that minimisation of functional warm ischaemia times is desirable. The aim of this audit was to examining withdrawal practice in Scotland and to assess donor or withdrawal factors that are associated with retrieval outcome.

Methodology: Core donor demographic and physiological data, details of functional warm ischaemia and withdrawal practice and was obtained from NHSBT on all potential DCD donors attended by the Scottish Organ Retrieval Team (SORT) between 01/04/2011 and 01/03/2013.

Results: 85 potential DCD organ donors were attended during the time period studied. 60 proceeded to an organ retrieval procedure with 112 kidneys, 24 livers and 12 pancreas organs retrieved. The mean age of donors was 52.2 (11-75yrs). The mean donor FiO2 requirement was 0.42 and 38% of donors were on inotropic support. 91% of potential donors had care withdrawn in ITU. 83% of donors were extubated and 95% had ventilatory support reduced or withdrawn. 83% of potential donors had sedative drugs continued or introduced. Differences noted in donor demographics and physiology between proceeding and non-proceeding donor included an increased percentage of proceeding donors on inotropic support (38.3% v 12% $p = 0.01$) and younger age (50.1 v 57.3 yrs. $p = 0.04$). A higher percentage of donors who underwent measures to relieve airway obstruction were observed in the non-proceeding group (13% v 36% $p = 0.01$).

Conclusion: Younger age and need for inotropic support does appear to be associated with an increased likelihood of proceeding to organ retrieval. This audit also demonstrates variation in airway management after withdrawal of care and maybe associated with a lower likelihood of proceeding to organ retrieval procedure.

O10

Belatacept-based immunosuppression for renal dysfunction post-intestinal transplantation

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Introduction: Calcineurin inhibitors have been linked to a higher incidence of acute renal failure due to its nephrotoxic effects, which may be related to its erratic area under the curve immediately after intestinal transplantation in patients with caval drainage of the grafts.

Methods: We identified the patients demonstrating a significant decline in their pre-transplant glomerular filtration rate (eGFR) after transplantation. The decline was quantified using the MDRD equation. EBV status of the patient was documented before the switch. Any episodes of rejection after the switch were recorded.

Results: From October 2008 to November 2013, 24 patients underwent intestinal transplantation. All had Campath induction and Tacrolimus monotherapy. Six (25%) demonstrated a mean decline of 45mls/min (range 25-70mls/min) in their eGFR from pre-transplant values. Decline was noted at a mean of 45 days (range 7-720 days) post transplantation. All 6 patients were switched to Belatacept. All patients had a positive EBV serology at the time of the switch. Mean time post-transplant to switch was 208 days (range 23-1195 days).

The switch was accompanied with Azathioprine (50mg OD) and Prednisolone (10mg OD) n=2, Low dose tacrolimus (levels<3) n=2, No other maintenance therapy n=2. One patient (17%) demonstrated moderate rejection, 15 days post switch to Belatacept. This patient was switched to Belatacept monotherapy at 5mg/kg. This patient later succumbed to an Aspergillus brain abscess related to the step up in immunosuppression to treat rejection.

Discussion: Majority of patients demonstrated a significant improvement of their eGFR. One patient demonstrated moderate rejection. Belatacept may be a valid option for patients demonstrating significant decline in their eGFR after transplantation. Belatacept as monotherapy may be a high-risk strategy for rejection.

O11

Infections after living kidney donation: prevalence and impact

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Introduction: Hand assisted laparoscopic nephrectomy (HALDN) is the most commonly utilised modality for living kidney donation in the UK. Despite this, there is a paucity of data on infectious complications and their potential modifiable risk factors. Consequently current BTS guidelines are unable to provide definitive recommendations for infection prevention. We conducted a retrospective analysis - aided by primary care and hospital patient records - of infection episodes.

Methods: 826 consecutive HALDNs between 2003 and 2012 were included. Applying the healthcare protection agency's criteria for surgical site infections (SSIs) and a clinician diagnosis of infection for other infectious complications, we recorded all infections occurring in the first 30 postoperative days. Data was also collected on patient demographics; operative surgical practices (incision type, use of surgical drains, length of surgery); antibiotic prophylaxis; biochemical indices of the postoperative inflammatory response and healthcare resource utilisation.

Results: The cohort comprised of 52% females with mean age 44.6 years (SD11.5). 133/826 (16%) donors had a documented postoperative infection; this included 86 (10.4%) SSIs, 29 (3.5%) urinary tract infections, and 30 (3.6%) chest infections. 95% received antibiotic prophylaxis. Outpatient healthcare utilisation was increased twofold in donors with infections (2.18 v 1.1 visits, $p<0.0001$) and total inpatient hospital stay was also increased (4.73+/-0.18 v 3.85+/-0.05 days $p=0.01$). Univariate analyses revealed no associations with age, BMI, length of surgery; use of surgical drains; main incision site; laterality of surgery or prophylactic antibiotics. Day 2 CRP was raised in the infection group (133 v 111 $p=0.04$), although median time to infection presentation / diagnosis was 10 days.

Discussion: Postoperative infection rates in HALDN patients are high and impact greatly on healthcare resources. No associative clinical factors are identified. A greater inflammatory response to surgery (as measured by day 2 CRP) may be implicated. In the context of such a high event rate further research into predictive statistical modelling and the health economic cost of donor infection is warranted.

O12

Ischaemia/reperfusion injury on time-zero biopsies and relevance to long-term liver transplant outcomes

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Introduction: Ischaemia /reperfusion injury (IRI) that develops after liver implantation may prejudice long-term graft survival, but is poorly understood and evaluation of the initial severity of IRI is difficult. Here we correlate the severity of IRI, as determined by histological grading of 'time-zero' biopsy, with long-term patient and liver graft outcomes.

Methods: Time-zero biopsies of 474 liver transplants, performed following graft revascularisation and carried out at our centre between 2000 and 2010, were graded as: nil (10.5%), mild (58.8%), moderate (26.1%) and severe (4.6%).

Results: Severe IRI was associated, on multivariate analysis, with donor age, donation after circulatory death, prolonged cold ischaemia time, and liver steatosis. The severity of IRI on biopsy correlated closely with graft outcome. In particular, a severe IRI grade was associated with significantly greater post–transplant morbidity compared to the other 3 groups, with markedly higher rates of primary non-function (9.1% vs 0.9%; p=0.006), early graft dysfunction (55% vs 21% p<0.0001) and the need for re-transplantation within 90 days (14% vs 2.6%; p=0.02). Longer-term outcomes in the severe IRI group were also poor, with five-year graft and patient survival of only 38% and 51% (compared with 74% and 81% for the remainder). Notably the degree of steatosis on biopsy did not correlate with graft survival (p=0.37), re-transplantation within 90 days (p=0.82) or PNF rate (p=0.07), suggesting severity of IRI to be an independent predictor of graft outcome.

Severe IRI on time-zero biopsy was a better predictor of one year graft loss than liver-steatosis, early-graft-dysfunction syndrome, and high first-week alanine aminotransferase, with a positive predictive value of 43.5% and diagnostic accuracy of 85.9%.

Conclusion: Time-zero biopsies predict adverse clinical outcomes following liver transplantation and severe IRI on biopsy signals the likely need for early re-transplantation.

Wednesday 26th February
Boisdale Suite – 12:30
Chairs: Dr Maria Hernandez-Fuentes and Linda Barber

O13

Blood and urinary cell messenger RNA levels samples can potentially stratify risk of acute rejection in renal transplant recipients

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Background: Identification of molecular biomarkers in blood and urine samples has the potential to revolutionize post transplantation management. Such biomarkers could help risk stratify patients and reduce the need for invasive testing with biopsies to diagnose acute rejection (AR). Furthermore, changes at molecular level are likely to precede both histological findings and graft dysfunction, allowing earlier diagnosis and treatment to limit graft damage. The aim of our study is to identify and characterize biomarkers that can diagnose and predict AR in renal transplant recipients.

Methods: Serial Blood and urine samples are collected from recipients before the transplant and over the first year post-transplant at 26 time-points and during episodes of graft dysfunction. RNA was extracted from blood samples collected into Tempus Blood RNA tubes and from urine sediment cells. cDNA was synthesised and pre-amplified for urine. Quantitative real time PCR was done for 20(blood) or 23(urine) target and 4 control genes.

Results: A pilot study consisting of 18 biopsy proven acute rejection (BPAR) and 26 stable patients revealed a significant over- expression of 5 genes in blood (SEMA7A, PF4, TGFB1, ITGAM, C6orf25) at week 2 after transplantation in the BPAR group, thereby predicting the subsequent development of rejection episodes occurring up to one year post-transplantation (Wilcoxon test, $p<0.05$, false discovery rate <5%). Using the expression of these 5 genes in a multivariate prediction model returned a probability score that predicted BPAR with a sensitivity of 0.7, specificity of 0.95, and an AUC of 0.80. Rise in SEMA7A ,TGFB1 and IP-10 gene expression in blood of BPAR is 3-4 weeks before the biopsy compared to the increase in creatinine which is 1 week pre-biopsy. For urine, the difference of gene expression 1-2 weeks and 3-4 weeks pre-biopsy was analysed in 14 BPAR and 14 stable samples at matched time points. Preliminary analysis suggests that differences in expression for perforin and FasL were detected between these groups. This suggests that it might be possible to use a urine test to predict a rejection episode with high specificity and sensitivity up to 4 weeks before it occurs.

Conclusions: Our pilot study suggests that measurement of mRNA levels in blood and urine could help risk-stratify patients for AR in kidney transplant recipients before clinical evidence of rejection allowing better management and potential individualisation of anti-rejection therapy. Validation of these findings in a larger cohort is clearly needed.

O14

Development of machine perfusion preservation and normothermic reperfusion and viability assessment models in pre-clinical porcine and human pancreases

Karim Hamaoui[1,3], Daniel Casanova[1,2], Terry Cook[3], Ara Darzi[1], Vassilios Papalois[1,3]

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Background: The advantages of hypothermic machine perfusion (HMP) over cold-storage for organ preservation include facilitating thorough vasculature washouts; delivery of oxygen/nutrients, removal of toxic metabolites, and opportunities for real-time viability assessment and pharmacological intervention. HMP is increasingly being utilised in Kidney preservation - especially for extended criteria and DCD allografts. Experimental studies into HMP for whole organ pancreatic preservation are lacking, and may be related to fundamental differences in pancreatic flow characteristics. The pancreas is physiologically a low-flow organ, thus attempts to establish pancreatic perfusion models are challenging. Our group has investigated several models of porcine pancreatic MP - including hypothermic perfusion and normothermic reperfusion (NMR) used for organ viability assessment. Here we report our preliminary data in development of pre-clinical HMP models of pancreas preservation using porcine pancreases, as well as human pancreases unsuitable for clinical transplantation (NRES/NHSBT approval gained).

Methods: Six pancreases (WI=30mins) were retrieved from landrace-pigs. Pancreases (n=3, SCS) either underwent 24 hours of SCS, were benched and then underwent 2 hours of viability assessment on an isolated NMR circuit; or (n=3, HMP) 24 hours of SCS then 5 hours of HMP re-conditioning with UW solution on a Waters Medical RM3 perfusion machine followed by NMR. NMR was accomplished using autologous whole oxygenated blood at 30-40mmHg systolic perfusion pressure. Perfusion dynamics were monitored throughout. Human pancreases (n=2, H-HMP) were used in development of a direct pre-clinical model and underwent 56h of SCS, followed by 5h of HMP and then 2h of NMR using a krebs henseleit buffer based reperfusion solution.

Results: HMP pancreases demonstrated improving perfusion indices during HMP at low pressures (<20mmHg), with minimal weight gain (15.3 +/- 7%). During 2hours NMR SCS pancreases exhibited overall higher (1.1 ml/min/100g/mmHg) but deteriorating (35% decline) perfusion dynamics compared to HMP pancreases which displayed lower (0.58 ml/min/100g) and stable perfusion. Human pancreases demonstrated stable perfusion (PFI 0.43 +/- 0.35 ml/min./100g) during HMP, with minimal oedema (9.3% weight gain). During NMR perfusion indices were stable (1.18 +/-0.52 ml/min/100g/mmHg PFI). Functional assessment during NMR by addition of glucose demonstrated islet beta cell viability by increased insulin secretion in all pancreases. Human pancreases demonstrated exocrine function with production of pancreatic secretions, but not porcine models.

Conclusions: HMP of porcine pancreases is feasible using low perfusion pressures with minimal oedema. Pancreases undergoing SCS for 24h then a period of HMP exhibited stable perfusion dynamics during NMR compared to organs undergoing 24h SCS only. Functional assessment of islet beta cells of perfused pancreases during NMR is feasible. Fundamentally the use of human pancreases with identical protocols demonstrates similar perfusion and functional characteristics to porcine models. HMP and NMR of whole pancreas allografts is feasible and development of these models could be beneficial in improving pancreas preservation prior to transplantation.

O15

Metabolomic analysis of cadaveric kidneys stored by hypothermic machine perfusion

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Background: Hypothermic Machine Perfusion (HMP) provides an opportunity for assessment of cadaveric kidneys prior to transplantation. The aim of this study was to use Nuclear Magnetic Resonance (NMR) spectroscopy to assess the metabolomic profile of perfusate from cadaveric kidneys with both immediate and delayed graft function (IGF/DGF).

Methods: Perfusate was sampled at 45 minutes and 4 hours of HMP. 1-D NMR spectroscopy was used for sample analysis. Resultant NMR spectra were examined using Chenomx profiling to identify metabolites and their concentrations. Clinical parameters were recorded to correlate with the profiles. Data were analysed using IBM SPSS 19 (IBM Corp. Armonk, NY).

Results: Samples were analysed from the perfusate of 29 cadaveric kidneys. Glucose concentrations were significantly lower in DGF kidneys compared to those with IGF at both 45 minutes (8.045 v 9.829 mM, p=0.006) and 4 hours (8.219 v 10.626 mM, p=0.003). Concentrations of inosine and leucine were significantly different between DGF and IGF kidneys at 45 mins (0.002 v 0.013 mM, p=0.009 and 0.010 v 0.006 mM, p=0.036) and gluconate levels were also significantly different at 4 hours (51.152 v 57.258 mM p=0.009).

Discussion: NMR spectroscopy can identify differences in the metabolic profile between DGF and IGF kidneys. Glucose metabolism may be an important pathway in the development of post-transplant DGF. This type of analysis may help to identify markers to indicate the quality of kidneys prior to transplant.

O16

Renoprotection and mechanism of CHBP on ischemia-reperfusion and ciclosporin A-induced renal injury in a mouse model

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Introduction: Ischemia reperfusion (IR) injury and cyclosporine A (CsA) nephrotoxicity affect acute and chronic post-transplant renal allograft function and survival. Helix B surface peptide (HBSP, derived from erythropoietin) remains tissue protection without erythropoiesis. In this study, the effect and mechanism of a novel metabolic stable cyclic HBSP (CHBP) were investigated in a transplant injury-related mouse model.

Methods: The both renal pedicles were occluded for 30 min followed by reperfusion for 2 or 8 weeks, with or without CsA 35 mg/kg gavage daily, and/or CHBP 24 nmol/kg intraperitoneally injection every 3 days. The ratio of urinary protein/creatinine was measured. Tubulointerstitial damage and renal fibrosis were examined on H&E and Masson's trichrome stained sections respectively. Finally, a slide-based antibody array was used to further explore involved intracellular signal pathways.

Results: The ratio of urine protein/creatinine was significantly lower in the group treated with CHBP compared with that in the IR group with or without CsA treatment at both time points. The tubulointerstitial damage and interstitial fibrosis were improved by CHBP in CsA treated group only at 2 weeks ($P<0.05$). In addition, the expression of mTOR, HSP27 and SAPK/JNK protein was decreased by CHBP in the IR kidneys at 2 weeks ($P<0.05$).

Conclusions: CHBP protected the kidney against IR and CsA induced injury in the mouse model, which might be associated with the reduction of mTOR, HSP27 and SAPK/JNK protein.

O17

Ischaemic postconditioning reduces renal warm ischaemia reperfusion injury in an experimental large animal model

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University of Leicester, Leicester, UK

Background: Ischaemic conditioning, using short repeated sequences of intermittent ischaemia, is a novel strategy that may ameliorate renal transplant ischaemia reperfusion injury. The aim of this study was to assess the effects of direct and remote ischaemic conditioning in a porcine model of renal warm ischaemia reperfusion injury.

Methods: Female landrace pigs weighing 45-50Kg underwent laparotomy and cross clamping of the left renal pedicle for 60 minutes. Animal were randomised into one of three groups; untreated controls (n=7); direct postconditioning involving 6 x 15 second cycles of clamping then releasing the left renal artery, performed immediately following the 60 minutes ischaemia (n=6); or remote periconditioning involving 4 x 5 minute cycles of clamping then releasing the left common iliac artery, performed 20 minutes after renal pedicle clamping (n=7). Following left renal clamp release a right nephrectomy was performed and animals were recovered for 5 days. Sham animals (n=2) underwent right nephrectomy only.

Results: The area under the serum creatinine curve (direct 1071±136 vs. control 1722±973µmol/L.day; P=0.025) and peak creatinine levels (direct 312±49 vs. control 519±268µmol/L; P=0.008), were significantly lower in the direct group compared to control. Remote periconditioning did not improve renal function compared to control (P=0.515). There was no mortality in any of the groups and no complications directly related to either conditioning technique.

Conclusion: In this *in vivo* large animal model direct renal artery ischaemic postconditioning protected kidneys against warm ischaemic injury. This straightforward technique could easily be translated into clinical practice.

O18

Calcineurin activity in renal proximal tubule epithelial cells

Seema Jain[1,2], Iain MacPhee[2], Mysore Phanish[1,2], Mark Dockrell[1,2]

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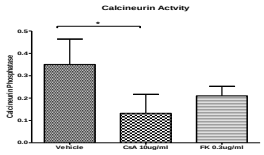
I**ntroduction:** Ciclosporin (CsA) and Tacrolimus (FK) are widely used immune modulators in organ transplantation. They act on T-lymphocytes by indirectly inhibiting the calcium-dependent serine-threonine phosphatase calcineurin (CN), which when active, phosphorylates the transcription factor NFAT leading to its translocation into the nucleus where it promotes the synthesis of Interleukin 2. Unfortunately their prolonged use is also associated with nephrotoxicity, classically described histologically as striped interstitial fibrosis and tubular atrophy with vasculopathy. The extent to which toxicity is dependent on inhibition of CN in renal tubular epithelial cells is unknown. We have investigated the impact of CsA and FK on CN activity and markers of toxicity in renal proximal tubule epithelial cells.

Methods: Primary human renal proximal tubule epithelial cells (PTEC) were treated with CsA (10µg/mL) and FK (0.3µg/mL) for 24-144hrs. Protein analysis was done using western immunoblotting and phosphatase activity was determined using a BIMOL green phosphate assay. Immunofluorescence was used to visualise NFAT translocation.

Results: We demonstrated the presence of CN, NFAT 1, 3 and 4 in primary human PTEC. Calcineurin phosphatase activity was inhibited by CsA and FK (see graph below). Both inhibitors reduced nuclear translocation of NFAT1 when the cells were stimulated with the calcium ionophore Ionomycin; the rise in $[Ca^{2+}]_i$ has been demonstrated to activate CN.



(* p≤0.05)

However at the concentrations used, only CsA caused a loss of the adherens junction protein, K cadherin (n=3, p≤0.05) which is important in maintaining the integrity of the human renal proximal tubule epithelium. We have previously demonstrated K cadherin loss in biopsy material from patients diagnosed with chronic interstitial fibrosis with tubular atrophy. There was no significant acute cell death, as determined by cellular LDH release.

Discussion: We have shown that the Calcineurin-NFAT pathway is active in PTECs and that it is inhibited by the CN inhibitors CsA and FK. However loss of K Cadherin was only observed with CsA and not FK at these doses, thus suggesting that it is not responsible for the nephrotoxicity caused by these agents.

Wednesday 26th February
Lomond Auditorium – 15:00
Chairs: Prof John Kirby

O19

Autoantibody responses to a heart allograft augment allograft vasculopathy by amplifying conventional cellular and humoral alloimmune effector mechanisms

Ines Harper, Jason Ali, Simon Harper, Kourosh Saeb-Parsy, Eleanor Bolton, J Andrew Bradley, Gavin Pettigrew

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Introduction: Although transplant-related autoantibody responses are reported increasingly, their contribution to graft failure remains poorly understood. We used a MHC-mismatched murine heart transplant model in which passenger donor CD4 T cells trigger recipient autoantibody to examine the hypothesis that humoral autoimmunity contributes to allograft vasculopathy (AV) by amplifying conventional alloimmune responses.

Methods: A new donor strain (bm12.K^d.IE) was created, to incorporate additional MHC class I (H-$2K^d$) and class II (I-E) target alloantigens. IgG allo- and auto-antibody responses were measured weekly. Indirect-pathway CD4 T cell responses were assessed by transfer of CFSE-labelled TCR75 T cells, CD8 cytotoxic responses were measured by ELISPOT. Donor CD4 T cell were depleted with anti-CD4 antibody (YTS 191.1) AV was assessed morphometrically.

Results: Heart allografts from unmodified donors provoked long-lasting indirect-pathway CD4 T cell responses and strong, class-switched alloantibody responses against the mismatched K^d class I alloantigen. Moderate CD8 T cellular cytotoxicity was also observed. These were associated with development of progressive allograft vasculopathy and eventual graft failure. In contrast, alloimmune responses were barely above background following grafting with CD4 T cell-depleted hearts that did not trigger autoimmunity, with only minimal vasculopathy development and indefinite graft survival. The contribution of donor CD4 T cells to graft rejection was not due to a direct effect on the graft, because they are killed within days after transplantation, but instead to the humoral immunity that they trigger; in the absence of recipient B cells, donor T cell responses remained vigorous, but host CD4 T cell alloimmunity was diminished and no longer influenced by the presence of donor CD4 T cells.

Conclusions: Concurrent humoral autoimmunity contributes to allograft rejection by augmenting conventional alloimmunity, and is triggered by even transient donor T cell survival.

O20

Impact of de novo HLA antibodies on retransplantation and outcome following islet transplant alone

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Most pancreatic islet transplant alone (ITA) recipients undergo subsequent 'top-up' islet transplants within a restricted timeframe to achieve sustained graft function. Retransplantation could therefore, be compromised by the development of HLA antibodies following the first graft. The aim of this study was to determine the incidence of HLA sensitisation following islet transplantation and to assess the impact of post-transplant donor-specific HLA antibodies (DSA) on islet transplant outcome. 31 ITAs were performed in 21 patients at our centre between 2008 and 2013. In this cohort, 12 patients received 1 graft, 8 patients 2, and 1 had 3 grafts. Prospective post-transplant HLA antibody monitoring was performed using Luminex technology after 1 month and then 3 monthly, and additionally during clinical events. Before transplantation, 8/21 (38%) patients were sensitised with defined HLA antibodies (cRF >5%). Post-transplant antibody monitoring was available for 28/31 (90%) transplants. De novo HLA antibodies developed after 7/28 (25%) transplants, in 7/20 (35%) patients, of which 4/7 (57%) were sensitised prior to transplant. De novo DSA were detected following 4/28 (14%) transplants, in 4/20 (20%) patients, of which 2/4 (50%) were pre-sensitised. In all 4 cases the DSA developed after a first transplant with a significant increase in overall cRF. Although 2/4 of these patients received islet preparations of lower purity, there was no clear association with donor parameters. The development of DSA was associated with decreased graft function, 2 patients experienced rapid loss of function, while 2 had a slower deterioration. 2/4 patients have subsequently received top-up islet transplants, but the other 2 are now highly sensitised and remain on the transplant list. In conclusion, the rate of HLA antibody formation following islet transplantation is comparable to that in our whole pancreas transplant programme and not greater than in other organ transplants. De novo DSA following islet transplant were associated with poorer outcome. Increased cRF post-transplant restricts access to subsequent transplants, and therefore the immunogenicity of HLA mismatches should be considered in donor selection.

O21

Evaluation of HLA-class I single antigen beads and iBeads™ to discriminate between clinically relevant IgG binding to intact HLA proteins and clinically irrelevant binding to denatured HLA proteins

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Introduction: The advent of Luminex-single antigen bead (SAB) technology has been instrumental in revealing the critical role of donor HLA-specific antibodies in the pathogenesis of acute and chronic allograft injury. The clinical application of SAB, however, is hampered by the detection of clinically irrelevant 'natural' antibodies against cryptic epitopes expressed on denatured HLA proteins that arise during the SAB manufacturing process. To overcome this limitation, One Lambda has produced 'iBeads' that are largely devoid of denatured HLA.

Methods: We tested One Lambda HLA-class I SAB and iBeads using W6/32 and HC-10 monoclonal antibodies to detect intact and denatured HLA protein expression respectively on corresponding bead populations. In addition, sera obtained from five patients with no previous alloantibody priming events and five patients with prior HLA alloantigen exposure were tested.

Results: W6/32 showed similar binding to intact HLA-class I proteins expressed on different SAB populations (median MFI 2694,SD+/- 638), but there was overall lower and widely different binding to intact antigen on iBeads (median MFI 3730, SD+/- 585). In contrast, HC-10 binding showed high levels of denatured HLA-class I on SAB populations (median MFI 17293,SD +/- 6977), but minimal binding to denatured HLA protein on iBeads (median MFI 1079,SD +/-1011). Evaluation of patient sera demonstrated three antibody binding patterns to corresponding HLA specific bead populations: positive with SAB and negative with iBeads; negative with SAB and positive with iBeads; positive with both SAB and iBeads.

Discussion: SAB populations express comparable amounts of intact HLA-class I on all bead populations, but many beads carry high levels of denatured antigen that may cause a false positive HLA specific antibody assignment. In contrast, iBeads express variable but overall lower levels of intact HLA molecules and low levels of denatured HLA protein. When used in combination, the relationship between antibody binding to clinically relevant (intact) and irrelevant (denatured) HLA can be determined and provides important insight into their clinical relevance.

Wednesday 26th February
Lomond Auditorium – 17:00
Chairs: Prof Alan Jardine and Dr Phil Mason

O22

Eculizumab (Ecu) improves renal function in atypical haemolytic uraemic syndrome patients with and without kidney transplant

Neil Sheerin[1], Thorsten Feldkamp[2], Denis Fouque[3], Richard Furman[4], Osama Gaber[5], Larry Greenbaum[6], Timothy Goodship[1], Maria Herthelius[7], Maryvonne Hourmant[8], Christoph Licht[9], Antonella Trivelli[10], Camille L. Bedrosian[11], Chantal Loirat[12]

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Introduction: Ecu inhibits complement-mediated thrombotic microangiopathy (TMA) in patients (pts) with atypical haemolytic uraemic syndrome (aHUS). Case reports have suggested that TMA and graft loss is inhibited by Ecu in transplanted pts with aHUS. These results can now be supplemented by clinical trial data.

Methods: Ecu safety and efficacy from 37 aHUS pts aged ≥12 years (both non-transplant [NT] and prior transplant [T]) in two single-arm, 26-week, phase 2 trials with long-term extensions were analysed. One trial enrolled pts with progressing TMA (>25% decrease in platelet count despite ≥4 plasma exchange/infusion [PE/PI] sessions in the week prior to screening; median Ecu duration 100 weeks). The other trial enrolled pts with long disease duration (receiving chronic PE/PI on a stable regimen with no platelet count decrease >25% during an 8-week observation period before Ecu treatment; median Ecu duration 114 weeks).

Results: Ecu improved renal function (estimated glomerular filtration rate [eGFR]) in all groups (Table), with greater improvement in NT than T pts with progressing TMA (P=0.0165). Baseline eGFR did not predict change. Ecu was well tolerated and no graft loss was seen in the 2 years extension study of chronic treatment.

Discussion: In pts with aHUS treated for 2 years with Ecu, treatment was well tolerated and renal function improved both in NT and T pts. Earlier initiation of Ecu was associated with greater improvement in renal function (P<0.05) regardless of transplant status, supporting early initiation of Ecu for better outcomes.

	Progressing TMA*		Long disease duration†	
	NT (n=10)	T (n=7)	NT (n=12)	T (n=8)
Mean±SD baseline eGFR, mL/min/1.73m^2	27.0±14.8	17.1±12.9	25.9±16.6	38.2±21.0
Mean±SD eGFR increase mL/min/1.73m^2	48.3±38.4	14.8±18.7	7.3±7.5	3.9±23.8

Table: Renal function in Ecu-treated aHUS pts with and without kidney transplant

*median duration Ecu 100 weeks †median duration Ecu 114 weeks

023

24hr Ambulatory blood pressure monitoring (ABPM) risk stratifies hypertensive kidney transplant recipients (KTRs)

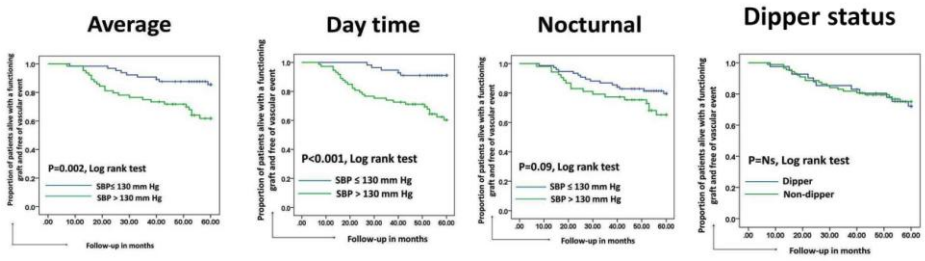
Santhanakrishnan Balasubramanian, Aravind Cherukuri, Andrea Rhodes, Richard Baker

Leeds Teaching Hospitals NHS Trust, Leeds, UK

Background and methods: Systolic hypertension has been shown to be associated with adverse clinical outcomes after renal transplantation. In non-transplant patients, 24hr ambulatory blood pressure monitoring (ABPM) has been shown to be a superior predictor of clinical outcomes when compared to clinical blood pressure readings alone. In this study we have prospectively analysed129 kidney transplant recipients (KTR) diagnosed with hypertension based on the clinic blood pressure (CBP) of >130/80mm Hg. All these patients underwent ABPM and groups were stratified based on ABPM systolic (>/<130mm Hg) and diastolic blood pressure (</>80mm Hg) values (SBP & DBP). The primary outcome measure was a composite of graft loss, cardiovascular event or death over a 5year follow-up.

Results: Of the 129 KTRs, only 64 had average 24hr SBP>130 mm Hg on ABPM. Overall, CBP significantly overestimated SBP even in the true hypertensive KTRs based on ABPM (CBP, 164± 16 mm Hg, ABPM, 143± 9 mm Hg, P<0.0001). Based on the ABPM readings, 33% of hypertensive KTRs required an increase in their anti-hypertensive therapy (P=0.01). Day time (P=0.002) and 24hr average SBP (P<0.001) were strongly associated with the composite end point in a univariate Kaplan Meier analysis. Whilst the 24hr average DBP (P=0.03) was significantly associated with poor event free survival, nocturnal dipper status was not significant. The influence of 24hr average SBP on event free survival was more significant in KTRs with diabetes (P=0.02), lower eGFR (P=0.001), proteinuria (P=0.007), who are younger (P=0.02) and female (P=0.01). Similar non-significant trends were seen with DBP as well. Despite a significant improvement in CBP in both the groups over 5 years, eGFR and proteinuria remained significantly worse in the true hypertensive group based on the assessment of ABPM during this period.

Conclusions: To conclude, 24hr ABPM helps to risk stratify apparent hypertensive KTRs based on CBP. True hypertensives based on ABPM represent a significantly high risk population with adverse medium term outcomes despite appropriate therapy.



O24

Hypertension is not a contraindication to living kidney donation

Rawya Charif, Dimitrios-Anestis Moutzouris, Jack Galliford, Jen McDermott, Harvinder Dulku, Honeylet Orr, David Taube, Marina Loucaidou

Imperial College Kidney and Transplant Centre, Hammersmith Hospital, London, UK

The increasing numbers of patients with ESRF on a waiting list for a kidney transplant has been the main driving force for expanding the donor pool. We undertook living kidney donor transplantation from hypertensive donors after initial reports in the literature than short-term outcomes are safe. We report 5-yr data in this group and compare these with the outcomes of non-hypertensive donors from our centre.

Data were prospectively collected on 555 consecutive live donors from 2000-2012 at their annual follow-up visits. The hypertensive group consists of donors presenting with a pre-existing diagnosis of hypertension, well-controlled on at least one antihypertensive agent and without evidence of end-organ damage. We analysed 5-yr follow-up data for 24 hr. Creatinine Clearance (CrCl) and protein excretion as well as blood pressure control.

Of 555 donors 50 were hypertensive (H) and 505 non-hypertensive (NH). In the H group 33(66%) were Caucasian, 9(18%) South Asian (SA) and 5(10%) Afrocaribbean (AC) and 3 (6%) of other ethnicity. There was a higher percentage of Caucasians in the hypertensive group (66%) but similar in the SA and AC. Mean age was 45.5 years (H=54.6, NH=44.9, $p<0.001$). Mean Body Mass Index was H=28.9, NH=26.9, ($p=0.002$). The mean CrCl in mls/min was 110.1 (H=117.4, NH=n109.4, $p=0.114$) at time 0 and 90.4 (H=92.5, NH=90.1, $p=0.762$) at 5 years. We did not find any evidence of developing proteinuria in with 24-hour protein excretion of 0.12 (H=0.17, NH=0.12, $p=0.02$) g/24hrs at 5 years. Blood pressure remained well-controlled in the hypertensive group at 5 years at 135/85 vs 135/81 in the non-hypertensive group ($p=0.971$ and 0.158). 43 donors in the non-hypertensive group developed hypertension post donation.

We conclude that donor nephrectomy in well-controlled hypertensive donors with no evidence of end-organ damage is safe and does not result in poorer outcomes compared to non-hypertensive donors.

O25

Transplant recipient risk stratification by a RAG system

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North Bristol NHS Trust, Bristol, UK

I**ntroduction:** Over recent years we have seen a rise in 30 day mortality rates amongst recipients of deceased donor kidney transplants. Analysis of these cases showed a significant inter-clinician variability in deciding what level of co-morbidity is acceptable for entering the waiting list.

Method: A Red-Amber-Green (RAG) traffic light system was developed using evidence from analysis of UKRR data looking at the factors that predict mortality at 1 and 5 years in 30000 incident RRT patients. The analysis indicated age at commencement of RRT, cause of ESRD, and presence of some comorbidities predicted mortality and appropriate weight was given for each of these variables in developing the risk score. . The total score was then divided into categories of green for unconditional listing, amber being equivocal with possible need for further investigation or discussion and red, not suitable to be listed.

Results: On a point prevalent analysis the system would have green-lighted 71% of our local waiting list population (130 patients), with 27% scoring amber and 2% red. A 2 year retrospective analysis based on recipient phenotype at our centre demonstrated that the score has 100% sensitivity and 98% specificity to predict 30 day mortality. The scoring system would have reduced our 30 day mortality to zero but we would have also not performed 1.6% of our successful transplants (3 out of 183).

Discussion: The Bristol RAG recipient scoring system has acceptable sensitivity and specificity enabling clinician buy in in order to reduce inter-clinician variability whilst listing patients for renal transplantation. Following implementation of the scoring system we plan to audit outcomes prospectively.

O26

Cytomegalovirus is associated with increased long-term mortality but not cancer risk after organ transplantation

Rajeev Desai[1], Dave Collett[1], Christopher Watson[2], Philip Johnson[3], Paul Moss[4], James Neuberger[1]

[1]NHS Blood and Transplant, Bristol, UK, [2]Addenbrooke's Hospital, Cambridge, UK, [3]University of Liverpool, Liverpool, UK, [4]University of Birmingham, Birmingham, UK

The impact of Cytomegalovirus (CMV) infection on patient survival and the risk of cancer following transplantation is uncertain and based on small numbers. We therefore evaluated the effect of CMV on outcomes in patients receiving a solid organ transplant.

We identified recipients of kidney, liver and cardiothoracic transplants done in the UK between 1987 and 2007. We included 22461 recipients in whom donor and recipient CMV IgG status was known. Recipients were grouped into: donor negative recipient negative (D-R-), D-R+, D+R+ and D+R-. The ten-year post-transplant survival in D-R- recipients (73·6% [95%CI 72·3, 74·9]) was significantly higher (p<0·0001) than in other recipients (66·1% [65·3, 66·9]). Compared with the D-R- group, the risk-adjusted hazard of death within ten years of transplantation for D+R- group was 14% higher for kidney recipients (p=0·0495), 13% higher for liver recipients (p=0·16), 34% higher for heart recipients (p=0·01) and 35% higher for lung recipients (p=0·006). The proportion of recipients with a cardiovascular cause of death was higher (p=0·03) among the CMV positive recipients (18%) compared to the CMV negative (16%). The unadjusted incidence of all cancers was 8·8% (7·9, 9·6) among D+R+ group, 7·0% (6·0, 7·9) among D+R- group, 9·1% (8·1, 10·1) among D-R+ group and 6·4% (5·5, 7·3) among D-R- group and this difference was statistically significant (p<0·0001). However, there was no statistically significant difference in the risk-adjusted incidence of all cancers between these groups following correction for age, gender and the transplanted organ.

The results from this large study demonstrate that Cytomegalovirus is associated with a significantly increased long-term mortality after kidney and cardiothoracic transplantation and an increased risk of cardiovascular death and should allow clinicians to focus interventions to reduce the mortality in these groups of patients.

O27

Risk factors for hypertension post donor nephrectomy: 8-year analysis

Dimitrios-Anestis Moutzouris, Rawya Charif, Jack Galliford, Jen McDermott, Andrew Achilleos, Harvinder Dulku, Honeylet Orr, David Taube, Marina Loucaidou

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Kidney transplantation from a living donor is the treatment of choice for patients with end stage renal failure. However, data is limited regarding risk factors for developing hypertension (HTN) post donor nephrectomy. We investigated the prevalence and the risk factors for HTN post donor nephrectomy. We compared data among patients who developed HTN (H) or not (NH).

Data were prospectively collected on 555 consecutive live donors from 2000-2012 at their follow-up visits. HTN was defined as BP above 140/90mmHg or use of antihypertensives. Borderline HTN was defined as not requiring treatment with BP measurements not consistently above 140/90 mm Hg. We performed logistic regression of risk factors for developing HTN. We compared 8-yr data for 24 hr Creatinine Clearance (CrCl) and protein excretion between the groups.

43 developed HTN post donor nephrectomy (22 male, 21 female). In the H group 27 (62.8%) were Caucasian, 6 (14%) South Asian (SA) and 9 (20.9%) Afrocaribbean (AC). 18.8% of AC developed HTN ($p=0.018$). The patients who developed HTN were older (51.5±11.3 vs 44.2±13.6 years, $p<0.001$) and had a longer time since donation (7.5±2.5 vs 5.7±6 years, $p<0.001$). There was no difference regarding BMI (H=27.3±4.7 vs NH=27±5.1, $p=0.643$). Risk of hypertension increased with age at donation ($p<0.001$), years from donation ($p<0.001$), AC race ($p=0.014$) and history of borderline HTN ($p<0.001$). The mean CrCl in mls/min was H=106.2±26, NH=109.7±33, ($p=0.541$) at time 0 and H=89.9±20, NH=90.2±25, ($p=0.949$) at 5 years. No significant proteinuria developed (24-hour protein excretion H=0.13±0.12 and NH=0.10±0.06 g/24hrs, $p=0.175$) at 5 years. Diastolic BP was higher in H group at donation (H: 83±9 vs 78.7±9 mmHg, $p=0.004$). Systolic and Diastolic BP was higher in the H group at 5 years (H:144/85 vs 134/80, $p=0.001$ and 0.028 respectively).

AC patients, older patients and patients with pre-donation borderline HTN are at increased risk for developing HTN post donor nephrectomy. However, kidney function and proteinuria are not different from those who remain normotensive.

O28

New onset diabetes after transplantation despite the use of a steroid-sparing regime is associated with a higher mortality from cardiac causes

Dimitrios-Anestis Moutzouris, Christopher Baker, Nicola Kumar, Michelle Willicombe, Richard Corbett, Neil Duncan, Jack Galliford, Adam McLean, David Taube

Imperial College Renal and Transplanta Centre, Hammersmith Hospital, London, UK

New-onset diabetes after transplantation [NODAT] is associated with increased cardiovascular risk and reduced patient survival. We have also shown that patients who develop NODAT despite the use of a steroid sparing immunosuppressive regime also have reduced patient survival.

In a retrospective, single centre study, we reported the outcomes of 920 patients [552m, 368f, mean age 47±13.3 yrs, range 18-78, mean follow up 57.6±30 mos], receiving a steroid sparing, tacrolimus based regime after monoclonal antibody induction. Steroids were stopped 7 days post transplantation and only introduced to treat rejection. We excluded patients with history of diabetes mellitus. Overall, 169/920 [18.4%] patients developed NODAT defined as diabetes requiring diet control [19.9%], oral hypoglycaemics [62.0%], insulin [15.7%] or both [2.4%].

Cumulative patient survival in the NODAT+ and NODAT– free group at 1, 3, 5 years post transplant was 98.2%, 93.6%, 90.2% and 98.5%, 97%, 94.8%, respectively (p=0.032). Cumulative graft survival in NODAT and in NODAT-free group at 1,3 and 5 years was 98.2%, 92.3%, 87% and 95.7%, 92%, 87.9%, respectively (p=0.547). The cumulative incidence of NODAT was 9.5%, 14.2% and 16.5% at 1, 3 and 5 years after transplantation, respectively. During follow up, there were 71 cardiac events, of which 22 occurred in patients with NODAT [1 STEMI, 9 non-STEMIs, 9 episodes of cardiac arrhythmia and 3 cardiac deaths). In NODAT-free patients, there were 49 cardiac events (4 STEMI, 18 NSTEMI, 24 episodes of cardiac arrhythmia and 3 cardiac deaths). NODAT + group had an increased risk of cardiac events (12.4% vs 6.5%, p=0.009) and death (10.1% vs 4.9%, p=0.011). Patients with NODAT had reduced coronary event-free survival (log rank p=0.017) and overall survival (log rank p=0.032). Older age (p<0.001) and development of NODAT (p=0.041) increased the risk for a cardiac event.

This study shows that patients who develop NODAT despite the use of a steroid-sparing regime have a higher incidence of cardiac events and impaired patient survival.

O29

New onset diabetes after transplantation [NODAT] despite the use of a steroid-sparing regime

Dimitrios-Anestis Moutzouris, Christopher Baker, Nicola Kumar, Richard Corbett, Michelle Willicombe, Neil Duncan, Adam McLean, Jack Galliford, David Taube

Imperial College Renal and Transplant Centre, Hammersmith Hospital, London, UK

Because NODAT is associated with increased cardiovascular risk and reduced patient survival, we have used a steroid-sparing regime since 2002.

In this retrospective, single centre study, we report the outcomes of 920 patients [552m, 368f, mean age 47 ± 13.3 years, range 18 - 78, mean follow up 57.6 ± 30 months], receiving a steroid sparing, tacrolimus based maintenance regime after monoclonal antibody induction. Steroids were stopped 7 days post transplantation and only re introduced to treat rejection. We excluded patients who had a history of diabetes mellitus before transplantation. Overall, 169/920 [18.4%] patients developed NODAT defined as diabetes requiring diet control [19.9%], oral hypoglycaemics [62.0%], insulin [15.7%] or both [2.4%].

Cumulative patient survival in the NODAT+ and NODAT – free group at 1, 3, 5 years post transplant was 98.2%, 93.6%, 90.2% and 98.5%, 97%, 94.8%, respectively ($p=0.032$). Cumulative graft survival in NODAT and in NODAT-free group at 1,3 and 5 years was 98.2%, 92.3%, 87% and 95.7%, 92%, 87.9%, respectively ($p=0.547$). The cumulative incidence of NODAT was 9.5%, 14.2% and 16.5% at 1, 3 and 5 years after transplantation, respectively. The incidence of NODAT was increased in non-Caucasoids; 29.8% of South Asians, 22.6% of Afro Caribs and 11.9% of Caucasians developed NODAT [$p<0.001$]. Steroids were reintroduced in 188/920 [20.4%] of patients and 28.2% of patients on steroids developed NODAT vs. 15.9% of patients who were not on steroids [$p<0.001$]. Those who developed NODAT were older compared with those who did not [50.8±11.7 vs. 46±13.5 years, $p<0.001$]. By Cox-regression analysis, risk of NODAT was associated with steroid use [$p<0.001$, Exp (B) 2.265], South Asian [$p<0.001$, Exp (B) 3.136], Afro Carib race [$p=0.002$, Exp (B) 2.218] and older age [$p<0.001$, Exp (B) 1.035]. This study shows that patients receiving a steroid-sparing regime still have a significant risk of NODAT associated with reduced patient survival. Steroid re introduction, ethnicity and age are major risk factors.

O30

Alemtuzumab induction in renal transplantation is not associated with increased replication of opportunistic viral pathogens

Aravind Cherukuri, Matthew Welberry-Smith, Richard Baker

St. James's university Hospital, Leeds, UK

Introduction: There is conflicting evidence for the incidence of opportunistic viral infections and their outcomes after alemtuzumab induction in Kidney Transplant Recipients (KTRs). In a RCT of two steroid avoidance regimes comparing alemtuzumab induction with tacrolimus monotherapy and basiliximab induction with tacrolimus and MMF maintenance therapy, we compared the replication rates of four opportunistic viral pathogens (CMV, BK, EBV and JC) viruses in the urine and blood during the first post-transplant year and analysed the impact of their replication on medium term graft outcomes.

Methods and results: Longitudinal analysis of the replication of CMV, BK and JC viruses at 1, 3, 6, 9 and 12 months after transplantation by RT-PCR revealed that alemtuzumab group was associated with a modestly reduced prevalence of both viruria and viremia through the first year, although none of these results were statistically significant. With regards to the CMV infection, 22.4% of KTRs in the alemtuzumab group and 19% in the basiliximab group were in the high risk group (D+R-). These patients received prophylaxis with valganciclovir. A further 40% of patients in the alemtuzumab group who were in the intermediate group (D+R+, D-R+) also received prophylaxis. All the viral replication analysis was blinded to the clinical teams. No patients were treated based on the viral replication results alone. In this study, only one patient developed CMV disease and no patients had BK nephropathy. Interestingly, prevalence of none of these opportunistic viruses in the blood or urine was associated with a decreased graft survival for the entire study population over a five year follow-up period (Kaplan Meier survival analysis). Especially, opportunistic viral replication was not associated with adverse graft survival in the alemtuzumab group over a 5 year follow-up period. Rejection rates were comparable in the presence or the absence of these viruses either in the blood or urine.

Conclusions: To conclude, alemtuzumab induction with tacrolimus monotherapy was not associated with higher prevalence of opportunistic viral replication in the first year after renal transplantation. Importantly, viral replication was not associated with adverse graft outcomes.

Wednesday 26th February
Alsh Suite – 17:00
Chairs: Prof John Forsythe and Dr Richard Baker

O31

Ex-vivo normothermic perfusion in marginal donor kidney transplantation

Sarah Hosgood, Adam Barlow, James Hunter, Michael Nicholson

University of Leicester, Leicester, UK

Background: *Ex-vivo* normothermic perfusion (EVNP) is a novel method of preservation that restores circulation and allows an organ to regain function prior to transplantation. This study reports the outcome of EVNP in kidneys from marginal donors.

Methods: Thirty six kidneys from marginal donors underwent a short period of EVNP immediately before transplantation. Kidneys were perfused with a plasma free red cell based solution at a mean temperature of 34.7°C.

Results: Twenty three kidneys were from extended criteria donors (ECD), 8 from donation after circulatory death (DCD) donors and 5 from standard criteria donors (SCD) that suffered a hypoxic brain injury. The average donor age was 56 ± 14yr and recipient age 57 ± 12yr. Kidneys were perfused for an average of 62 ± 12min. The mean renal blood flow during perfusion was 67 ± 28ml/min and the total amount of urine produced 160 ± 115ml. All kidneys were transplanted successfully with no complications. The total cold ischaemic time was 11.3 ± 4.5h and total ischaemic time 13.2 ± 4.7h.

There were no incidences of primary non function and the delayed graft function rate (DGF) was 4/ 36 patients (11%). eGFR at day 7 and at 1 and 12 months was 40 ± 21, 47 ± 17 and 52 ± 15ml/min respectively. Patient survival was 100% and graft survival at 12 months 97%.

Conclusion: This first series of EVNP in ECD, DCD and marginal donor kidney transplantation supports the concept that restoring circulation and function prior to transplantation is a safe and feasible method of kidney preservation. EVNP was associated with good early graft function despite the marginal nature of the kidneys.

O32

A national registry analysis of kidney allograft preservation with Marshall's solution in the United Kingdom

John O'Callaghan[1,2], Simon Knight[1,2], Robert Morgan[1], Peter Morris[1,2]

[1]Centre for Evidence in Transplantation, London, UK, [2]Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK

Background: The most commonly used preservation fluids for static cold storage of renal allografts in the UK are University of Wisconsin Solution (UW, approximately £120 per litre) and Marshall's Solution (Hyper-osmolar Citrate, approximately £10 per litre). These two fluids have never been compared in a randomised controlled trial. The aim of this study was to compare the outcomes of renal allografts preserved with either fluid using data from the national transplant registry held and maintained by NHSBT.

Methods: Data regarding deceased donor kidney transplants performed during the period January 1st 2005 to December 31st 2008 was requested from the Kidney Advisory Group at NHSBT, with three years' follow up (n=5,027 kidneys). Details were requested from each retrieval and renal transplant team in the UK regarding preservation protocols used during the inclusion period. Following univariate analysis, multivariate logistic and linear regression models were fitted in a stepwise fashion to analyse relationships between donor, recipient and transplant factors and outcomes.

Results: Marshall's Solution was used as the initial aortic flush in 52% of kidney retrievals and as a storage fluid for 80% of kidney allografts. The use of Marshall's Solution as a kidney storage fluid was associated with longer CIT ($p<0.001$), older donors ($p<0.001$), non-liver donors ($p<0.001$), non-pancreas donors ($p<0.001$), donors with hypertension ($p<0.001$) and donation after brain-death ($p<0.001$).

After adjusting for confounding factors, the choice of storage fluid was not associated with the risk of PNF ($p=0.770$), DGF ($p=0.420$), acute rejection ($p=0.300$), renal function at one year ($p=0.204$) or graft loss ($p=0.823$ in DBD, $p=0.229$ in DCD).

Conclusions: Marshall's solution has been used for the preservation of large numbers of kidneys in the UK. It is associated with transplant outcomes that are equivalent to those with UW Solution. Thus on the basis of cost a strong case can be made for the continued use of Marshall's Solution for renal preservation.

O33

Impact of the new fast track kidney allocation scheme (FTKAS) for declined kidneys in the United Kingdom

Alan White[1], Heather Roberts[1], Clare Ecuyer[1], Katherine Brady[1], Brendan Clarke[1], Matthew Wellberry-Smith[1], Alex Hudson[2], Samir Pathak[1], Magdy Attia[1], Lutz Hostert[1], Richard Baker[1], Niaz Ahmad[1]

[1]St James' University Hospital, Leeds, UK, [2]National Health Service Blood and Transplant, Bristol, UK

Introduction: A 'new' Fast Tract Kidney Allocation Scheme (FTKAS) was implemented by the NHSBT in Nov 2012 for simultaneous offering of previously declined kidneys. We evaluated the impact of the FTKAS in overall effectiveness of utilization of previously declined kidney and its outcome in a single largest user centre.

Methods: We surveyed all 23 adult renal transplant centres for their views on the system. Overall utilization was evaluated by data obtained from NHSBT. Outcome in a single centre was analysed using a prospective database.

Results: All 23 centres responded to our 8-item questionnaire. Ten centres participated in the scheme. Other centres cited graft and patient outcome concerns and inadequate logistical support for their non-participation. During Nov 2012 and Apr 2013, a total of 124 kidneys were offered through the FTKAS (102 DBD, 22 DCD). Of the 124 kidneys offered, 85 kidneys were transplanted in 10 participating centres, 39 kidneys were discarded (utilization rate 68%). Five of the ten participating centres utilized 90% of FTKAS kidneys. Our institution was the largest single user of the system accounting for 30% of total utilization. In comparison, 166 kidneys were offered through previous 'declined kidney scheme' in a five-year period (2006-2011), 65 utilized in 59 transplants (39%) with five centres accounting for 90% of utilization. Of the 34 kidneys accepted by our centre via the FTKAS, 31 were subsequently allocated and 25 kidneys (16 DBD, 9 DCD) were transplanted in 23 recipients. Six kidneys were deemed unsuitable and were not transplanted by us or by any other centre. Of the 25 kidneys transplanted, 4 were dual transplants in 2 recipients and 21 were single kidney transplants. There was 1 incidence of primary non-function, 7 patients with delayed graft function and 15 with primary function. There were no cases of recipient mortality and no biopsy proven acute rejection in the first six-month follow up period. Six month graft and patient survival were 95% and 100% respectively with 3 months median serum creatinine of 150umol/L (IQR 79.0-322.0). These results were comparable to a matched group of kidney transplant during the same period.

Conclusions: The implementation of the FTKAS has led to effective utilization of the declined kidneys with outcome comparable to kidneys allocated through standard scheme. Utilization seems to be concentrated in few centres. Non-participation in the scheme based on outcome concerns is mostly subjective whilst logistical issues need to be addressed.

Thursday 27th February
Lomond Suite – 10:10
Chairs: Mr Nizam Mahmode and Dr Varuna Aluvihare

O34

Three years of altruistic kidney donors: kind kidneys or costly MOT?

P C Munipalle, M Crockett, N K Hamilton, T Fleming, J D Morgan, A G Edwards

Dept. of Surgery, Southmead Hospital, Bristol, UK

Introduction: Altruistic kidney donation is expected to gain more significance with increasing public awareness - the initial contact rate by potential donors to our unit has nearly doubled from 2009 to 2012. We reviewed our experience of managing the altruistic donation with the aim of highlighting the reasons for failure to proceed and need for further studies to improve efficiency.

Methods: All the offers of altruistic kidney donation were prospectively recorded and the data were analysed. The cost of each stage of work-up was calculated with input from relevant departments.

Results: Over the last six years, 105 altruistic donors made initial contact with our unit. So far 11 successfully donated, 49 are under work-up and 45 failed to proceed with donation - the main reasons being the donor being medically unsuitable (21) and donor choice (17). 4 of them opted out after the completion of stage 3; the total cost of working up the 17 potential donors till they pulled out was £19,864. In addition, valuable time of transplant co-ordinators was spent on their initial consultation with this cohort.

Discussion: The assessment of potential altruistic donors who withdraw their offer to donate puts considerable pressure on resources of the unit. Further work is needed to investigate the reasons behind this to enable not only resource allotment and workload management but also a better understanding of what we can do to reduce the rate of non-proceeding.

Ethical issues arising from detection of unsuspected medical conditions in this cohort need to be addressed.

O35

UK Donation Ethics Committee (UKDEC) draft guidance on pre-mortem interventions to optimise organ quality & improve transplant outcomes in DCD

Antonia Cronin[1], Dale Gardiner[3], Penney Lewis[2]

[1]MRC Centre for Transplantation, King's College, London, London, UK, [2]Centre of Medical Law and Ethics, King's College, London, London, UK, [3]Nottingham University Hospitals NHS Trust, Nottingham, UK

Background: In 2009, the Dept of Health (DH) issued guidance on the legal issues relating to DCD, stating that if a person (P) wished to be a donor, actions which facilitate donation may be in their best interests (BI) if they do not cause or place them at a material risk of experiencing harm or distress. Since then the number of DCD transplants performed in the UK has more than tripled. Reports vary, but the consensus is that pre-mortem interventions that optimise organ quality also improve transplant outcomes. This has prompted further consideration of the BI test in this context.

Methods: A UKDEC legal working group undertook a review of the existing guidance and doctrinal analysis of primary and secondary legal sources. A clinical working group was appointed and conducted a review of relevant literature relating to pharmacological and mechanical pre-mortem interventions. The findings of the two groups were combined and new guidance was drafted.

Results/Discussion: The UKDEC now proposes new guidance to apply when the continuation of life-sustaining treatment is no longer in P's BI & organ donation would be in P's BI. It states that to decide if an intervention would be in P's BI, the potential benefits to P must be balanced against the potential (risk of) harm or distress. The potential benefits encompass both the prospective benefit of knowing their wishes will be facilitated, and the future benefit attaching to their legacy. P will usually have an interest in the well-being of their loved ones and so may also be benefitted indirectly if the donation helps them come to terms with their loss. Examples of potential harm include pain, discomfort, shortening P's life & worsening P's medical condition. Examples of potential distress include feelings of suffocation, panic, & invasion of privacy. Factors affecting the balancing assessment include: the strength of P's desire to become a donor; the potential of an intervention to optimise donor organ quality & improve transplant outcomes; & the possibility of the alleviation of symptoms or avoidance of distress. Examples of pharmacological and mechanical pre-mortem interventions, such as the administration of heparin & extubation will be used to test the draft guidance.

Thursday 27th February
AIsh Suite 10:10
Chairs: Mr Gavin Pettigrew

O36

HLA derived T regulatory epitopes (Tregitopes) – a potential therapeutic target in transplantation and autoimmunity

Seema Jham[1,2], Helen Smith[2], Shazia Shabir[1,2], Richard Borrows[1], Simon Ball[1]

[1]Queen Elizabeth Hospital Birmingham NHS Trust, Birmingham, UK, [2]University of Birmingham, Birmingham, UK

Introduction: Our laboratory has documented renal transplant recipients' (RTR) T cells responses to non-polymorphic peptides derived from HLA class I. We now demonstrate HLA class II derived peptides are potential Tregitopes, responses to which are seemingly skewed from regulatory to effector in RTR. This may underlie a shift of $CD4^{+}CD25^{Hi}$ T cell phenotype associated with graft dysfunction.

Methods: Class II binding peptides from the β-2 domain of HLA class II were defined using the epimatrix algorithm. Cell surface phenotype of $CD4^{+}CD25^{Hi}$ T cells were analysed in 39 RTR & 17 healthy controls using a standardised flow cytometric gating strategy. PBMC's from 8 RTR, already identified to make γ-IFN in response to 1 of 3 HLA derived peptides, were cultured with & without peptide, with & without sorted autologous $CD4^{+}CD25^{Hi}CD45RO^{+}CD127^{Hi}CCR7^{-}$ (activated memory) T cells or $CD4^{+}CD25^{Hi}CD45RO^{+}CD127^{Lo}$ (T regulatory cells). Culture supernatants were analysed at 48^{0} using cytokine multiplex assays.

Results:

1. Activated memory T cells are increased in RTR compared to healthy controls.
2. Activated memory T cell numbers are associated with allograft (dys)function.
3. Activated memory T cells produce γ-IFN, IL2 & TNF-α in response to non-polymorphic HLA derived peptides defined in silico as likely to bind MHC class II promiscuously.
4. Addition of T regulatory cells was associated with suppression of peptide specific production of pro-inflammatory cytokines and importantly, peptide specific production of IL10

Conclusion: These data imply that HLA derived self-peptides act as Tregitopes, responses to which are altered in the setting of transplantation so that effector responses dominate, potentially contributing to graft damage. Although Tregitopes need not be derived from non-polymorphic sequences or bind class II promiscuously, the use of such peptides facilitates their easy identification and potentially development of universal therapies not requiring personalisation. This is relevant to therapy for a range of disease processes not only transplantation.

O37

A novel assay to detect donor-specific memory T cells in potential renal transplant recipients

Olivia Shaw[1,2], Maria Hernandes-Fuentes[2], Robert Vaughan[1,2]

[1]GSTS Pathology, London, UK, [2]Kings College London, London, UK

Introduction: 36% of patients receiving an HLA antibody incompatible renal transplant suffer T cell mediated rejection (TCMR). In this group of patients, whilst antibody mediated rejection (AMR) can be anticipated, there are no assays available pre-transplant to accurately predict future early TCMR. We have developed an assay aimed at detecting donor specific memory T cells in potential HLA antibody incompatible renal transplant recipients to predict future TCMR episodes.

Methods: 32 potential donor and recipient pairs were identified for testing, 6 unsensitised controls and 26 sensitised. Donor derived HLA molecules isolated from lymphocytes were immobilised onto the wells of a microELISA plate using the MicroAMS ELISA kit (immucor GTI diagnostics) following kit instructions and recipient peripheral blood mononuclear cells were introduced, in addition to soluble CD28. A cell only negative control, a positive control with additional CD3/28 stimulating beads and separate wells containing donor derived and 3rd party derived HLA molecules were included. Supernatant was assayed at 18, 72 and 120 hours for the presence of IFNγ, TNFα, IL-2, IL-4, IL-5, IL-10 and IL-17 using the Fluorokine MAP multianalyte profiling kit from R&D Systems.

Results: No correlation was found between an overall response, or individual cytokine responses, and the presence of a repeat HLA mismatch, sensitisation status or gender ($p=0.293 – 1.000$). 16 of the patients went on to be transplanted with an organ from the stimulating donor. 4/16 were diagnosed with TCMR on biopsy. All four had produced IL-17 by 72 hours in response to donor stimulation only ($p=0.0021$). None of the remaining 12 patients had produced this cytokine.

Discussion: Our results confirm previous reports that the presence of memory T cells cannot be accurately predicted by HLA antibody sensitisation. Here we describe a novel assay system which appears, in our small patient group, to accurately predict future TCMR episodes. IL-17 and Th17 cells have been linked to TCMR episodes. This assay could offer a more complete risk assessment prior to transplantation, particularly in HLA antibody incompatible pairs.

O38

Immunogenicity of DQ7 HLA antigens in renal transplantation

Michelle Willicombe, Paul Brookes, Matthew Blow, Eva Santos-Nunez, David Taube

Imperial College Kidney and Transplant Centre, London, UK

De novo DQ donor specific antibodies [DSAs] are associated with chronic antibody mediated rejection and allograft failure. The aim of this study was to analyse the incidence of specific DQ DSA post renal transplant and determine if there is a difference between the immunogenicity of individual donor DQ antigens and the pathogenicity of the reciprocal DQ antibodies.

We retrospectively studied 871 patients with a mean follow up of 3.89 ± 2.10 years. No patient had detectable DSA at the time of transplantation.

159/871 [18.3%] patients developed de novo DSA of which 70/159 [44.0%] developed DSA against DQ antigens. 30/70 [42.9%] had DQ7 DSA, which were detected more frequently than other DQ DSA specificities. The table below shows the frequency of DSA development adjusting for DQ antigen mismatch and analyses the risk of development of DQ7 DSA compared with other DQ DSA.

DQ Allele	Mismatch frequency (No.)	Corresponding DSA No. (%)	OR (95% CI)	p value
DQ7	144	30 (20.8)	1	
DQ6	151	14 (9.3)	0.39 (0.2-0.77)	0.0065
DQ8	61	6 (9.8)	0.41 (0.16-1.05)	0.06
DQ9	42	0 (0)	0.04 (0.002-0.74)	0.03
DQ5	134	10 (7.5)	0.31 (0.14-0.66)	0.002
DQ4	37	1 (2.7)	0.11 (0.01-0.80)	0.03
DQ2	120	13 (10.8)	0.46 (0.23-0.93)	0.03

Once a DQ DSA developed there was no difference in clinical outcome; subsequent allograft loss [OR: 0.61(0.2-1.7), p=0.34], rejection [OR: 0.87(0.3-2.3), p=0.78] and TG [OR: 2.22(0.6-6.3), p=0.22] risk was not increased in patients with DQ7 DSA compared with DQ DSA of other specificities.

This study suggests that the DQ7 allele is more immunogenic than other DQ alleles. However once developed, anti DQ7 DSAs do not appear to be more pathogenic than DQ DSA of other specificities.

Thursday 27th February
Lomond Auditorium – 11:00
Medawar Medal
Chairs: Prof Anthony Warrens and Prof Derek Manas

M1

Interleukin-10 producing regulatory B cells require B cell receptor ligation, but not cognate T cell help for effective prolongation of allograft survival.

Mekhola Mallik, Margaret C Negus, Sylvia Rehakova, Eleanor M Bolton, J Andrew Bradley, Gavin J Pettigrew

University Department of Surgery, NIHR Comprehensive Biomedical Research Centre, Cambridge, UK

Introduction: Although operationally tolerant kidney transplant patients have increased frequencies of peripheral B cells with transitional cell phenotype, regulatory B cells (Bregs) have yet to be clearly identified in vascularised organ transplantation. Here, we examine the potential for Bregs to improve graft outcomes in a mouse model of chronic cardiac allograft rejection.

Methods: Bregs were generated in vitro by treating C57Bl/6 (B6) B cells with anti-CD40 monoclonal antibody for 3 days. The impact of $2x10^7$ Bregs on graft rejection kinetics, effector autoantibody responses and development of allograft vasculopathy (AV) in B6 recipients of MHC class II-mismatched hearts (n=9 animals) was compared to untreated controls (n=14). The importance of IL-10 expression, T cell interaction and BCR engagement was assessed by instead transferring, respectively, IL-$10^{-/-}$ (n=11), MHCII$^{-/-}$ (n=6) and hen egg lysozyme (HEL)-specific B cells (n=4). The effect of $2x10^6$ Bregs enriched for a transitional $CD19^+CD21^{hi}CD23^{hi}$ phenotype (n=5) was compared to treatment with an equivalent number of non-transitional ($CD19^+CD21^{lo}CD23^{lo}$) Bregs (n=3).

Results: B6 recipients of bm12 hearts receiving no treatment demonstrated slow graft rejection [median graft survival time (MST)=43 days], and developed strong autoantibody and severe AV. Treatment with IL-10-/- and HEL-specific “Bregs” made no appreciable difference to graft outcomes. Surprisingly, MHCII-/- “Bregs” were as potent as B6 Bregs at prolonging allograft survival (MST>100 days, $P<0.01$ vs untreated controls) and abrogating the development of autoantibody ($P<0.01$) and AV ($P<0.05$). Finally, although the non-transitional ($CD21^{lo}CD23^{lo}$) fraction of the cultured ‘Bregs’ inhibited autoantibody responses, the inhibition achieved with the transitional $CD21^{hi}CD23^{hi}$ fraction was much more marked.

Conclusion: Our results indicate that IL-10 Bregs may prove effective cellular therapy for prolonging clinical allograft survival. Bregs may be enriched within the $CD21^{hi}CD23^{hi}$ B cell fraction and BCR ligation, but not cognate T cell help, is necessary for effective control of alloimmunity.

M2

In-situ normothermic regional perfusion (NRP) for controlled donation after circulatory death

Lucy V Randle[1], Paolo Muiesan[2], Andrew J Butler[1], Ian Currie[3], Thamara Perera[2], John L Forsythe[3], Christopher JE Watson[1], Gabriel C Oniscu[3]

[1]Addenbrooke's Hospital, Cambridge, UK, [2]Queen Elizabeth Hospital, Birmingham, UK, [3]Royal Infirmary of Edinburgh, Edinburgh, UK

Introduction: Organs recovered from DCD donors have a greater risk of dysfunction and complications after transplant. This study presents the initial UK experience investigating the use of in-situ normothermic regional perfusion (NRP) for organ retrieval from Maastricht category 3 DCD donors.

Methods: 16 NRP DCD retrievals were performed at 3 UK centres. NRP was established post-asystole via laparotomy, aortic and IVC cannulation and maintained for two hours prior to organ retrieval. Lung retrieval was carried out with isolated cold thoracic perfusion. Blood gases and biochemistry were monitored every 30' to assess organ function.

Results: 47 organs (29 kidneys, 8 livers, 4 pancreata and 3 lung pairs) were recovered (2.93/donor vs 2.6 national average) and transplanted in 37 recipients. The median donor functional warm ischaemic time was 23' (15'-31') whilst the time from asystole to NRP was 16' (10'-23'). The median donor age was 46 years old (19-74). Two donors were on CVVHD at the time of retrieval.

24 patients received a kidney transplant (3 double) with a median cold ischaemic time (CIT) of 12h22' (5h25'-18h22'). The median creatinine at 1, 3 and 6 months was 110µmol/L, 109µmol/L and 98 µmol/L respectively. 5/24 recipients had delayed graft function (20.8% vs 50% national average).

8 patients received a liver transplant with a median CIT of 4h10' (2h49'-6h21'). The median peak ALT during 1st week was 257 (58-3043). One patient had PNF. All other livers have a minimum 6 months follow-up with no evidence of ischaemic biliary damage. Two SPK and three double lung transplants were performed with primary function

The rate of organs transplanted from all potential organs was higher than the current national rates for kidney (93% vs 82%), liver (50% vs 30%) and lungs (18% vs 4%).

Conclusions: NRP appears to increase organ recovery with beneficial short-term outcomes compared to standard cold perfusion DCD retrievals.

M3

Understanding heterogeneity in indirect pathway alloresponses may inform development of immunoregulatory therapies

Jason Ali, Margaret Negus, Thomas Conlon, Eleanor Bolton, Kourosh Saeb-Parsy, J. Andrew Bradley, Gavin Pettigrew

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Introduction: The indirect pathway is generally considered a single entity. Here we address how indirect responses against different alloantigens differ in their strength and longevity, and how this knowledge may be used to direct immunoregulatory therapy with antigen-specific regulatory T cells (Tregs).

Methods: A murine model of cardiac transplantation was used [bm12.Kd.IE to C57BL\6]. Indirect CD4 T-cell allorecognition of donor MHC class I and II, and H-Y minor alloantigen was assessed by quantifying proliferation of adoptively transferred monoclonal T-cell receptor transgenic T-cells (TCR75, TEa and Mar respectively) at various time points. Antigen presentation by dendritic cells (DC) and B cells was assessed by selective depletion using diphtheria toxin or depleting anti-CD20 mAb. Tregs were generated by in vitro culture.

Results: Indirect pathway responses were heterogeneous. Whereas the indirect response against class I alloantigen was long-lived and persistently strong, the class II indirect response was remarkably short-lived (decaying within two weeks), because it is dependent upon donor B-cells and DC's as a source of class II alloantigen, and these are cleared rapidly by the recipient. The longevity of the class I indirect response reflected on-going antigen presentation, but notably host B-cells played an increasingly important role, perhaps reflecting antigen-specific expansion. The indirect response against minor H-Y antigen was long-lived but weakened progressively. In keeping with the long-term dominance of the anti MHC class I indirect response in this model, transfer of class I antigen specific Treg, either at the time of transplant, or three weeks later, abrogated germinal centre alloantibody responses and blocked development of allograft vasculopathy.

Conclusions: Although thought of as a single entity, our results highlight that indirect allorecognition comprises a number of responses that vary in duration and strength according to target alloantigen. Specific targeting of those dominant, long-lived responses may be particularly effective at preventing chronic rejection.

M4

Quality assessment of human kidneys using *ex-vivo* normothermic perfusion

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Background: The suitability of kidneys for transplantation is currently assessed primarily using donor characteristics. Even with the addition of other measures such as macroscopic appearance, histological examination and hypothermic perfusion parameters assessment of viability is difficult. Because of this uncertainty, about 15% of donated kidneys are declined for transplantation. Ex vivo normothermic perfusion (EVNP) allows a functional assessment of kidney viability and may allow more accurate prediction of graft outcome.

Methods: Sixty five human kidneys deemed unsuitable for transplantation after retrieval underwent 60 minutes of EVNP with an oxygenated red blood cell based solution at 36.0°C. Renal blood flow and urine output were the primary functional parameters. Receiver operating characteristic (ROC) curves were used to identify thresholds of these variables for kidney viability. These thresholds, along with macroscopic appearance, were incorporated into a viability score (renal blood flow <63mls/min =1; urine output <50ml/hr =1; macroscopic assessment of perfusion: good =1, patchy =2, poor=3), with a possible total score of 1 to 5.

Results: Of the 65 discarded kidneys 20 had a viability score of 1 (high predicted viability), 14 scored 2, 13 scored 3, 5 scored 4 and 13 had a viability score of 5. When the viability score was applied to a series of 36 marginal kidneys transplanted after EVNP, 26 had a viability score of 1-2, 10 scored 3-4 and none scored 5. The delayed graft function rate was 3.8% in kidneys scoring 1-2 and 30% in those scoring 3-4 (P = 0.056). eGFR was significant lower in kidneys with a score of 2-3 up to 3 months post-transplant compared to those scoring 0-1 (35 ± 11 vs 53 ± 17mls/min; P = 0.005). On this basis, of the 65 discarded transplant kidneys, 52 were deemed viable and suitable for transplantation.

Conclusion: Functional parameters and visual assessment of a kidney during 60 minutes of EVNP may be used to reliably assess graft quality. The technique may be used to increase transplant rates by decreasing the number of discarded kidneys, whilst safeguarding against primary non function.

M5

Contribution of donor and host CD4 T cell populations to initiation and diversification of transplant-associated autoantibody responses

Muhammad Saeed Qureshi, R Motallebzadeh, Eleanor M Bolton, J Andrew Bradley, Gavin J Pettigrew

University Department of Surgery, NIHR Comprehensive Biomedical Research Centre, Cambridge, UK

Introduction: The triggers for transplant-associated autoantibody are unclear. Here, we studied the role of host and donor CD4 T cell populations in initiating and diversifying humoral autoimmunity following murine heart transplantation.

Methods: Bm12 allografts were transplanted into either wild type (WT) or T-cell deficient ($TCR^{-/-}$) B6 recipeints. Germinal centres (GCs) were quantified by calculating percentages of PNA and GL 7 positive B cells follicles.

Results: Whereas bm12 hearts transplanted into B6 recipients triggered long-lasting GC (68±3%) antinuclear autoantibody responses, and developed progressive allograft vasculopathy (AV) (76±6%, MST 56d),depletion of CD4 T cells in the donor abrogated autoantibody generation. Autoantibody was still generated in $TCR^{-/-}$ recipients, but GC activity (2±1%) was not observed and grafts survived indefinitely (MST >100d) with minimal AV development. Reconstitution of the $TCR^{-/-}$ recipients with host CD4 T cells restored graft rejection and GC activity and was associated with development of a late anti-vimentin autoantibody response ((63±1-wk7 to 195±1%-wk15, *p=.01* vs 60±2-wk7 to 75±1%-wk15 in bm12 to $TCR^{-/-}$, *p=0.3)*. The critical role of host CD4 T cells in mediating autoreactive GC activity was further supported by the observations that host CD4 T cells were the only population that localised to splenic GC areas and acquired the characteristic $CXCR5^{hi}$,$PD1^{hi}$ and CXCR5hi,ICOShi T follicular helper (T_{FH}) cell phenotype. Similarly, reconstitution of $TCR^{-/-}$ recipients with T_{FH}-defective SAPKO B6 CD4 T-cells did not restore GC activity. Finally, bm12 heart transplantation into BM chimeric B6 mice with an isolated defect in B cell antigen presentation resulted in low levels of IgG autoantibody, but late anti-vimentin antibody was not generated and graft survival was prolonged (MST 91d vs 56d; *p= 0.04*). **Conclusion:** Passenger donor CD4 T cells within the heart allograft initiate humoral autoimmunity, but its maintenance is mediated by host CD4 T cells that provide cognate T_{FH} cell recognition for autoreactive GC formation and late diversification of the response. The GC response is critical for progression of AV.

M6

Abdominal wall transplantation to complement intestinal transplantation

Georgios Vrakas, Genevieve Casey, Charlotte Bendon, Srikanth Reddy, Rubens Macedo Arantes, Peter Friend, Henk Giele, Anil Vaidya

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Introduction: The advent of abdominal wall transplantation (AWTx) offered a potential solution to the often-challenging closure of the abdominal wall at the time of intestinal transplantation (ITx). Besides facilitating closure, the AWTx is proving a promising asset for early, patient led rejection monitoring.

Methods: We performed a retrospective case notes analysis of all patients undergoing intestinal and abdominal wall composite tissue allograft transplantation. Clinical presentation of rejection was correlated with histology, stoma output, citrulline levels and endoscopy findings.

Results: From October 2008 to November 2013, 24 patients underwent ITx in our institute. Mean age 42±2.8 years (range 23- 73). M/F: 14/10. Median follow up 485 days (range 29-1879) for surviving/ 85 days (range 28- 823) for non-surviving patients. All patients had Campath induction followed by Tacrolimus monotherapy. Eight patients received an AWTx in addition to ITx.

Two episodes of AWTx rejection were documented in 2 patients (25%, 2/8). These patients presented to the hospital with neutropenia and a peri-follicular, micro-papular pink rash limited to the AWTx at a median of 61 days (range 55- 68). Histology revealed grade II-III rejection in each case. Both patients were systemically well, had normal stoma output (<20mls/kg/24 hours), citrulline levels >25 µmol/l and endoscopically healthy bowel. Initial ileal biopsies on one patient revealed histologically normal mucosa. However, the second patient (presented 10 days after appearance of rash) showed signs of mild acute intestinal rejection in the bowel.

Discussion: We report on a series of combined AWTx and ITx. The skin component may be useful in a patient led monitoring of the ITx graft since it is visible and presents the earliest and only sign of rejection.

M7

Endothelial targeted anticoagulation in renal allografts using preclinical ex-vivo machine perfusion models

Karim Hamaoui[1,4], Sally Gowers[2], Richard Smith[3], Terry Cook[4], Anthony Dorling[3], Ara Darzi[1], Vassilios Papalois[1,4]

[1]Department of Surgery, Imperial College London, London, UK, [2]Department of Bioengineering, Imperial College London, London, UK, [3]MRC Centre for Transplantation, Kings College London, London, UK, [4]Imperial College Renal and Transplant Centre, Hammersmith Hospital, London, UK

Background: Allograft thrombosis is a severe complication in renal transplantation. It is implicated worldwide in up to 7% of early adult graft loss, and ~35% in children, with the pathogenesis related to preservation & recipient/donor factors, with 'marginal' kidneys at higher risk. Microvascular thrombosis in particular is implicated in reperfusion injury and damage. The only preventative measure is systemic anti-coagulation, conferring bleeding risks upon patients. An ideal more effective method would be localised anticoagulation directly within an allograft. Our group has developed a series of novel endothelial binding hirudin-anticoagulant fusion-proteins (FP). We hypothesise kidney preconditioning with FP will ameliorate deteriorations in perfusion seen in an established ex-vivo renal thrombosis model. We report our pre-clinical findings using porcine and human ex-vivo perfusion models testing FP.

Methods: 36 kidneys were retrieved from cadaveric pigs (warm ischaemia=15mins) and transported to the laboratory (transport cold ischaemia = 5h). Paired kidneys acted as controls. Kidneys first underwent machine perfusion (MP) on a Waters Medical RM3 perfusion machine, with 4˚C UW solution (4h). Controls then underwent treatment via MP with either unmodified perfusion solution (Negative Control Group, NCG=14) or solution with Inactive-FP (absent anticoagulant effect, Positive Control Group, PCG=4). Test kidneys were perfused with FP treated perfusion solution (FP-Group, FPG=18). All kidneys then underwent autologous whole-blood normothermic perfusion (6h).

Results: Kidneys demonstrated similar perfusion dynamics during initial UW perfusion. During the normothermic phase there was reduced deterioration of perfusion in FPG vs. All Control kidneys, with superior flow (26.3 vs. 19.7ml/min/100g, $p<0.05$) and perfusion indices (0.51 vs. 0.43 ml/min/100g/mmHg, $p<0.05$) in FPG kidneys. Subgroup analysis indicated similar superior perfusion dynamics in FPG compared to the PCG and NCG ($p<0.05$). Perfusate analysis demonstrated less ($p<0.05$) fibrin generation in FPG vs. Controls correlating with perfusion results. Rapid sampling microdialysis for cortical lactate during reperfusion demonstrated lower detected levels in FPG vs. NCG kidneys.

A pair of human kidneys (NRES/NHSBT approval gained) was used in development of direct translational pre-clinical model using a similar treatment protocol. Similar efficacy was demonstrated with superior perfusion dynamics, lower fibrin generation and lower microdialysis cortical lactate levels in the treated vs. control group.

Conclusion: We demonstrate that organ preconditioning with localising anticoagulants allows amelioration of deterioration in perfusion dynamics seen in ex-vivo thrombosis models. There is high potential for the development and application of this translational strategy to deliver locally-active anti-coagulants directly within the allograft where it is needed, and decrease the development of microvascular thrombosis, while avoiding systemic anticoagulation and its associated risks.

M8

National study of logistical factors influencing cold ischaemia times in deceased donor kidney transplants

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Background: Prolonged cold ischaemia time (CIT) is associated with a significant risk of short and long term graft failure in deceased donor (DD) kidney transplants as demonstrated by recent national and international studies. Several logistical factors may influence CIT across the kidney timeline. The aim of the present study was to undertake a comprehensive review of these factors in UK transplant centres and to determine their impact on CIT.

Methods: This is a prospective longitudinal study of DD kidney transplantation in the UK. Data was collected over 14 months from donor and recipient coordinators/transplant surgeons in 16 transplant centres, Histocompatibility and Immunogenetics (H&I) staffs in all 19 H&I laboratories, transport providers and ODT to determine whether there are specific areas to focus efforts to reduce CIT.

Results: Data for 1822 transplants were included; 40.3% were DCD and 10% SPK transplants. The overall median CIT was 13.48hr (shortest 10.75hr, longest 18.55hr) with significant centre variation. The factors that significantly influenced CIT were donor type, distance travelled by organs, method of histocompatibility testing, i.e., prospective pre-transplant crossmatching (pXM) vs virtual crossmatch (vXM) and type of recipient sample and donor sample used for pXM test ($p<0.0001$). Median CIT for transplants that went ahead with a vXM was 3hr shorter compared to pXM ($p<0.0001$). There was a delay of median time of 3hr in starting transplant surgery despite organ, recipient and pXM result being ready.

Conclusion: This study identifies several logistical factors relating to donor, transport, crossmatching, recipient and theatre that impact significantly on CIT in DD renal transplantation in the UK. A number of these factors are potentially modifiable. It is, therefore, imperative to address these factors to enable optimal utilisation of available kidneys.

Thursday 27th February
Alsh Suite – 16:00
Chair: Mr Colin Wilson

S1

A decade of hand assisted laparoscopic donor nephrectomy – lessons learnt from 870 cases

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Guy's and St Thomas NHS Foundation Trust, London, UK

Introduction: Hand assisted laparoscopic donor nephrectomy (HALDN) is a procedure still in its relative infancy within wider surgical practice. This mandates robust data collection on perioperative and long term outcomes.

Methods: A retrospective analysis of all 870 HALDNs in one institution – from May 2003 until May 2013 - was undertaken. Data was collected on baseline characteristics; 30 day major complications (need for reoperation or unplanned postoperative critical care, blood loss requiring transfusion, need for open conversion, pulmonary embolism) and minor complications (any other deviation from a normal postoperative course including infections and wound complications). Recurring longer term complications were also recorded. To account for temporal changes in practice and the learning curve effect, all outcome measures were stratified by 4 subgroups over time. The potential effect of training on patient outcomes was also assessed in a specific subgroup of 200 cases.

Results: The mean age of donors was 44.7yrs (SD11.6) and 52% were female. Mean hospital stay was 3.9 days (SD1.4). A major complication occurred in 3% (n=27) of which 5 (0.6%) underwent open conversion and 20 (2.3%) underwent reoperation. Frequency of minor complications was 22.6%. The frequency of total complications did not change over time (17 v 19 v 20 v 25 %, p=0.060). Longer term complications included an incisional hernia rate of 5.5% (median time to presentation: 8 months) and 32 (7.6%) male donors presented with ipsilateral orchalgia. In a subgroup of 200 patients, 40 procedures were identified as training cases. On univariate analysis training did not increase complication rates (p=0.73) or hospital stay (p=0.76).

Discussion: This data provides the most comprehensive assessment yet of HALDN operative outcomes in the UK; giving a robust basis for informing patients. The lack of a temporal change, or an effect of training, suggests that the procedure can be learnt quickly, and provides a safe method for training juniors.

S2

Hypercoagulability in potential pancreas transplant recipients-the value of thromboelastography

Mari Kilner[1], Colin Wilson[2], Tina Biss[2], Kate Talks[2], John Hanley[2], Bryon Jaques[1], Derek Manas[1], Steve White[1]

[1]Institute of Transplantation, Newcastle-upon-Tyne, UK, [2]Dept. of Haematology, Newcastle-upon-Tyne, UK

Introduction: Graft thrombosis following pancreas transplantation (PTx) is a devastating complication and remains the most common cause of early graft loss. Thromboelastography (TEG) is an established haematological technique which evaluates both the rate and strength of clot formation.

Methods: Since 2012 we have changed our haematological work up and pre-operative investigations to incorporate routine TEG's. Data were collected on our most recent patients including PTA (n=1) or SPK (n=9). TEG and a standard coagulation screen were performed. Control data were collected from healthy volunteers (n=29).

Results: Hypercoagulability was demonstrated in all diabetic patients being assessed for PTx with TEG's. Three patients had slightly raised fibrinogen levels The rest (n=7) had a normal basic coagulation screen.

Conclusions: Diabetic patients assessed for PTx demonstrate hypercoagulability. Anti-coagulation post PTx with TEG monitoring is essential to reduce the risk of graft loss due to thrombosis.

Table 1. (mean ± SD)

Variable	Diabetics (n=10)	Controls (n=29)	*t*-test(*p*-value)
r time (start of clot formation secs)	5.2 ± 0.6	8.4 ± 2.3	<0.0001
α angle (speed of clot formation, degrees ◦)	67 ± 8.5	59 ± 6.9	<0.01
K value (time to 20 mm of clot formation, seconds)	1.1 ± 0.3	2.3 ± 0.6	<0.0001
Maximum amplitude (final strength of clot mm)	69 ± 8.4	62 ± 5.5	<0.01

S3

A retrospective study of Initial graft function and biliary complications in recipients of DCD liver grafts receiving streptokinase pre-flush during procurement

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St James's University Hospital, Leeds, UK

Introduction: Liver transplantation using grafts from donors after circulatory death (DCD) have doubled in the last decade in UK. The extent of primary warm ischaemia time and the quality of graft perfusion at the time of organ procurement and upon reperfusion determines subsequent graft function & biliary complications. Pharmacological modulation with anti-fibrinolytic agent streptokinase at the time of procurement has shown to improve hepatic microvascular perfusion in animal models.

Aim: We reviewed our experience of using streptokinase for DCD liver procurement over a period of 3 years (September 2009- September 2012) on initial graft function and biliary complications.

Methods: 61 DCD liver transplants have been performed in our centre since Jan. 2008.Streptokinase (1,500,000 units) pre-flush was introduced to our DCD retrieval protocol in September 2009 and discontinued in Oct. 2012 with introduction of the National standards for organ retrieval. In this time period the streptokinase pre-flush was administered in 28 DCD Livers and outcome of those grafts were compared with 31 DCD liver transplants with no pre-flush. Initial poor function was defined according to the Ploeg-Maring criteria

Results: In our cohort one patient (3.6%) in streptokinase pre-flush group had primary non function compared to 2 patients (6.2%) in no pre-flush group. Initial poor function based on day 2-7 serum Transaminase and Pro-thrombin time was higher in no pre-flush group but failed to reach statistical significance (24% vs 29% p0.67). Biliary complications were observed in 10 patients (31%) in no pre-flush group and 6 Patients (21%) in pre-flush group.

Conclusion: In view of smaller numbers the effects of streptokinase pre-flush was not shown to be significant in our cohort. However, the incidence of ischaemic type biliary strictures and poor initial function showed a trend towards improvement in streptokinase pre-flush group

Friday 28th February
Alsh Suite – 09:30
Chairs: Dr Maria Hernadez-Fuentes and Ms Lorna Marson

O39

Transitional B cell T1/T2 ratio is a marker for graft dysfunction in human kidney transplant recipients (KTRs)

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Accumulating evidence supports a regulatory role for human transitional B cells (TrB) in renal transplantation. TrB cells are clearly heterogeneous with variable cytokine expression. In this study we have analysed the functional and clinical significance of human TrBs and subsets.

1. The phenotype of TrBs was established in 15 healthy volunteers. TrBs demonstrated cytokine polarization with relatively higher IL-10 expression when compared to TNF-α (high IL-10/TNFα ratio) and exhibited regulatory properties *in vitro* by selectively suppressing Th1 cytokine expression by mitogen stimulated autologous Tconv cells ($CD4^{+}CD25^{lo}$) in an IL-10 and TNF-α dependent fashion. Within the TrB population, phenotypically distinct subsets were identified - T1 ($CD24^{+++}CD38^{+++}CD20^{+++}IgM^{++}CD10^{++}$) and T2 ($CD24^{++}CD38^{++}CD20^{++}IgM^{+}CD10^{lo}$). T1 cells had a significantly higher IL-10/TNF-α ratio and were thereby more polarized towards IL-10.
2. TrB mediated immune regulation was confirmed in 88 KTRs. Patients with biopsy proven antibody mediated rejection (CAMR, n=25) had significantly lower absolute B cell numbers, lower TrBs, relative depletion of T1 TrBs (i.e. lower T1/T2 ratio) and a lower IL-10/TNF-α ratio within the TrBs when compared to either healthy volunteers (n=15), patients with stable graft function (n=41) or graft dysfunction in the absence of CAMR (n=22). In fact a lower IL-10/TNF-α ratio within the TrB of patients with CAMR paralleled the T1/T2 ratio. Both TrB-IL-10/TNF-α ratio and TrB-T1/T2 ratio were effective in distinguishing patients with stable function from those with rejection on ROC curve analysis (AUC= 0.83 and 0.88, P<0.001 respectively).
3. When patients were divided into tertiles based on either TrB-IL10/TNF-α ratio or TrB-T1/T2 ratio, patients in the lowest tertiles of both groups had significantly worse deterioration in renal function (Δ eGFR over 3 year follow-up) and a significantly higher proportion of KTRs with DSAs. 4. Since TrB-T1/T2 ratio paralleled TrB-IL-10/TNF-α ratio in its ability to predict graft outcomes, its utility as a potential marker of graft dysfunction was validated in two independent random samples (50 transplant recipients each) acquired from an RCT comparing alemtuzumab and basiliximab induction in renal transplantation. In both these validation sets, patients in the lowest tertile of TrB-T1/T2 ratio had the worst deterioration in eGFR and more DSAs.

To conclude, with these experiments we provide evidence for TrB mediated immune regulation which is dependent on both IL-10 and TNF-α. The cytokine polarization within TrBs paralleled the ratio of T1/T2 subsets and this ratio could potentially be used as a biomarker for allograft dysfunction.

O40

Tertiary structure and electrostatic potential of HLA B-cell epitopes reveal the molecular basis for alloantibody binding and epitope immunogenicity

Dermot Mallon[1,2], Peter Winn[3], Eleanor Bolton[1,2], J. Andrew Bradley[1,2], Craig Taylor[1,2], Vasilis Kosmoliaptsis[1,2]

[1]Department of Surgery, University of Cambridge, Cambridge, UK, [2]Addenbrooke's Hospital, Cambridge, UK, [3]Department of Biosciences, University of Birmingham, Birmingham, UK

Introduction: The potential of donor HLA B-cell epitopes to induce recipient humoral alloimmunity depends on their structural and physiochemical properties. We determined the three-dimensional structure and electrostatic potential of two widely-expressed HLA B-cell epitopes and examined the impact of amino acid mutations on HLA antibody reactivity.

Methods: Tertiary protein models of high frequency HLA-B alleles (n=24) expressing either the Bw4 or Bw6 epitope (defined by sequence motifs at positions 77-83) were generated using comparative structure prediction based on crystallographically-resolved HLA structures. The electrostatic potential in three-dimensional space encompassing the Bw4/Bw6 epitope, for each HLA-B molecule, was computed by solving the Poisson-Boltzmann equation for macromolecules and quantitatively compared with one another to form dendrograms that cluster epitopes with similar electrostatics properties. Amino acid mutations within the 77-83 sequence motifs were also examined.

Results: Comparison of the electrostatic potential in the space surrounding residues 77-83 allowed tight clustering of HLA-B molecules according to Bw4 or Bw6 epitope expression, independent of epitope amino acid composition and variability in the structural context of epitope expression, providing a molecular basis for known patterns of serological cross-reactivity. Critical amino acid mutations that abrogated antibody binding to Bw6-expressing HLA-B*07:02 (G83R, R79G, R82L) induced distinct electrostatic potential changes displacing the mutants from the Bw6 epitope cluster; in contrast, mutation N80T did not affect antibody binding and had negligible physiochemical effect.

Conclusion: This study suggests that HLA B-cell epitopes are characterised by distinct topographic patterns of electrostatic potential explaining HLA-specific antibody binding and enabling novel insights into HLA immunogenicity.

O41

A stratified approach to antibody removal in HLA antibody incompatible renal transplantation

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[1]GSTS Pathology, London, UK, [2]Guys and St Thomas NHS Foundation Trust, London, UK, [3]Kings College London, London, UK

Introduction: The HLA antibody incompatible (HLAi) renal transplant programme at Guys hospital has been running for 9 years. Initially patients identified as candidates for HLAi transplants underwent twice weekly plasma exchange (PEX) with post treatment low dose IVIg (0.5g/KG) with the aim of reducing the T & B cell flow cytometric crossmatch (FXM) to negative prior to proceeding with the transplant. In approximately 50% of patients the antibodies did not reduce to the required level despite long and costly treatment periods. To streamline the process a more stratified approach was developed.

Methods: Patients identified as candidates for HLAi transplant from a living donor were treated with a single plasma volume PEX. Serum samples taken immediately pre and post the treatment were subject to serial dilution and FXM against potential donor cells. The reduction in both the relative median fluorescence (RMF) at neat and the titre at which the FXM became negative were recorded. Where a reduction in one or more dilutions was observed, the predicted number of pre transplant PEX required were calculated. Neat serum samples were also tested using LABScreen Single Antigen Beads (Onelambda) (SAB) and the cumulative donor specific antibody median fluorescence intensity (MFI) calculated.

Results: 117 potential pairs were treated as described and 31 patients were subsequently transplanted. No patients approved for HLAi transplant using this method subsequently failed to receive a graft following antibody removal. Comparison of the predicted and actual PEX required pre transplant by linear regression gave an R^2 of 0.87 ($p=<0.0001$). Neither the pre treatment T & B cell RMF at neat, or titre, or the SAB MFI values were indicative of the number of PEX required pre transplant. Confirming the need for the test PEX procedure.

Discussion: We have developed a successful testing rationale to aid work up of patients requiring HLAi transplantation. This process gives a personalised approach and allows for efficient planning of these transplants from booking theatre slots to preparing the donor, enabling the best use of the resources available.

O42

Targeting the BAFF/APRIL signalling axis for prevention of antibody-mediated allograft rejection

Manu Chhabra[1], Margaret Negus[1], Sylvia Rehakova[1], Jing Garland[1,2], Mekhola Mallik[1], Saeed Qureshi[1], Jason Ali[1], Eleanor Bolton[1], Andrew Bradley[1], Gavin Pettigrew[1]

[1]Department of Surgery, University of Cambridge, Cambridge, UK, [2]Department of Medicine, University of Cambridge, Cambridge, UK

Introduction: B cell activating factor (BAFF) and its related cytokine APRIL are critical for B cell maturation. Here we study how their blockade influences heart graft survival in murine models of chronic antibody mediated rejection (AMR).

Methods: BAFF blockade and combined Anti-BAFF/APRIL blockade was achieved by administering BAFFR-Ig or TACI-Ig. The impact of this blockade was examined in two models of chronic AMR (MHC class II mismatched and MHC class I + II mismatched). Kinetics of graft rejection were monitored and humoral alloimmunity assessed by: immunohistochemical appraisal of splenic germinal centre (GC) activity; quantification of splenic and bone marrow (BM) plasma cells (PCs); and assay of serum effector antibody.

Results: BAFFR-Ig or TACI-Ig treatment of naive B6 mice induced profound depletion of mature B cells, and produced a B profile similar to that of mice genetically-deficient for BAFF-receptor. In either transplant model, even though B cell depletion was sustained, challenge with a heart allograft surprisingly provoked long-lasting class-switched effector antibody responses that resulted in endothelial C4d deposition, development of AV and eventual graft failure. In both models, GC responses were abrogated by BAFF blockade, with either marked reductions in, or a virtual absence of, antigen-specific BM long-lived PCs following administration of BAFFR-Ig or TACI-Ig, respectively. The source of antibody instead appeared to be splenic extrafollicular responses, because numbers of antigen-specific splenic PCs were not affected by BAFFR-Ig therapy, and only slightly reduced with TACI-Ig therapy. This escape and extrafollicular activation of alloreactive B cells does not reflect sub-optimal BAFF and APRIL blockade, because similar responses were observed following challenge of BAFF-receptor deficient mice.

Conclusion: Even though BAFF blockade can effectively deplete the mature B cell compartments and prevent GC humoral immunity, concurrent alloantigen challenge provokes a limited extrafollicular response that can nevertheless mediate chronic AMR and lead to eventual graft failure.

O43

Depletion of B cells ameliorates renal chronic allograft damage through inhibition of intra-allograft germinal centre formation

George Tse[1], Chris Johnston[1], David Kluth[1], Mohini Gray[1], Jeremy Hughes[1], David Gray[2], Lorna Marson[1]

[1]MRC Centre for Inflammation Research , The University of Edinburgh, Edinburgh, Scotland, UK, [2]Institute of Immunology and Infection Research, The University of Edinburgh, Edinburgh, Scotland, UK

Introduction: Nodular B cell rich infiltrates have been identified in chronically rejected renal allografts and have been associated with the development of tertiary lymphoid tissue. However their significance is unclear, with conflicting published data. We have investigated the role of B-cells in a mouse model of renal chronic allograft damage (CAD).

Methods: We have used congenic strains with donor C57BL/6^{BM12} kidneys transplanted into C57BL/6 recipients; such transplants develop interstitial fibrosis and tubular atrophy. B cells were depleted 4 weeks following transplantation by intravenous injection of anti-CD20 monoclonal antibody versus Rituximab (anti-human-CD20). Mice were culled at 8 and 12 weeks after transplantation and histological outcomes determined; viable tubules, collagen deposition (Picrosirius red), B cell (B220+), T cell (CD3+) infiltration, and germinal centre formation (GL7+). Additionally B cells were analysed by flow cytometry.

Results: At 4 weeks following renal transplantation tubular injury is minimal, however B220+ B cells accumulate within the cortex of the kidney with subsets (follicular CD23+ IgM+, marginal CD23- IgM+, transitional CD23- IgM-) that are CD86 activated. B cell depletion by anti-CD20 protected against the development of CAD with a greater number of viable tubules ($p<0.05$) and reduced deposition of collagen ($p<0.05$). Furthermore B cell depletion resulted in a reduction in the number of germinal centres per mm2 tissue area ($p<0.05$), these B cells in the germinal centres co-localised on immunofluoresence for B220+ IgM+ IgG+ GL7+ furthermore plasma cells were apparent based on CD138+. These B cells produced multiple cytokines mediating inflammation and chemotaxis of macrophages and T cells.

Conclusion: In this mouse model of CAD we have shown that B-cells form germinal centres within the transplanted kidney. Furthermore depletion of these B-cells following transplantation inhibits progression of injury and the key features of interstitial fibrosis and tubular atrophy.

O44

CYP3A4*22 genotype but not POR*28 predicted tacrolimus dosage at day 7 post transplantation

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Background: Tacrolimus has a narrow therapeutic index with wide variation between individuals in the blood concentration achieved for a given dose that is, to a large extent, dependent on the level of expression of the drug metabolising enzymes cytochrome P450 3A4 (CYP3A4) and A5 (CYP3A5). A pharmacogenetic strategy with initial drug dosing based on *CYP3A5* genotype which predicts CYP3A5 expression resulted in only marginal improvement in the number of patients achieving target blood concentrations of tacrolimus within 3 days of starting treatment. Recently, it has been reported that the SNPs *CYP3A4*22* and *POR*28* may affect tacrolimus dose requirements.

Methods: DNA samples from patients commenced on tacrolimus post transplant at our centre were analysed by rapid realtime PCR using a LightCycler 2.0 Carousel System to identify expression of the polymorphisms *CYP3A4*22* and *POR*28*. Statistical analysis was performed using SPSS 17.0 (IBM).

Results: 174 samples were analysed: 33% Female, 66% Caucasian, 13% Black., 14% South Asian; 7% Mid East. 10 (5.6%) were carriers of the *CYP3A4*22* SNP (mutant CT genotype) which predicts reduced *CYP3A4* activity. Tacrolimus blood concentrations on day 7 post transplant were measured and adjusted for dose. Concentrations for *CYP3A4*22* carriers were compared with those for those with the wild-type CC genotype using the Mann-Whitney U test. The distributions were significantly different with $p<0.05$. Mean concentration for CT at day 7 was 13.4 ng/mL (SD 7.9) and for CC was 9.2 (SD 6.3) ($p<0.05$). 82 were carriers for *POR*28* (48%) which has been associated with increased tacrolimus dose requirement in CYP3A5 expressors. *POR*28* expression was not associated with *CYP3A5* expression (p= non significant). *POR*28* expression did not affect the distribution nor mean value of tacrolimus concentration 7 days post transplant (p = not significant).

Conclusions: *CYP3A4*22* but not *POR*28* genotype may add value to generation of algorithms to predict the optimal initial dose of tacrolimus.

Posters
Moderated Poster Session
Wednesday 26th February – 18:30
Lomond Auditorium

Category: **Hystocompatibility & Immunogenetics**

P1

Assessing the impact of virtual crossmatching four years after introduction: a single centre audit

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Whilst kidney transplant is an effective treatment for End Stage Renal Disease, delayed graft function (DGF) following ischaemic/re-perfusion injury remains a significant challenge. Transplantation can proceed without a prospective crossmatch (pXM) in patients where a negative XM may be predicted from allosensitising events and antibody screening. Such a virtual XM (vXM) policy was introduced in our centre in July 2009. This single centre audit aimed to determine whether the introduction of vXM has led to reduced cold ischaemic time (CIT) and incidence of DGF.

Data from 328 patients from January 2008 to September 2013 receiving kidney donations after brain death (DBD; n=237) and circulatory death (DCD; n=91) and simultaneous kidney pancreas transplants were collected and analysed. Three groups were compared: 211 patients receiving vXM from July 2009 to September 2013 (DBD=148; DCD=63), 53 patients eligible for vXM (pre-vXM era) from January 2008 to June 2009 (DBD=36; DCD=17), and 64 patients receiving pXM from July 2009 to September 2013 (DBD=53; DCD=11). DGF was defined as the need for dialysis within the first 7 days post-transplant except for hyperkalaemia.

In vXM patients mean CIT was 12.1 ± 0.25 hr (n=209), 1.75 ± 0.6 hr (p= 0.0012) less than the pre-vXM group and 2.6 ± 0.6 hr (p=<0.0001) less than the pXM group. DGF in vXM patients was 22% (n=211), significantly less than the 35% (n=53) in pre-vXM patients (p=0.0486), but not significantly less than the pXM group (DGF=19%; n=64).

Introducing vXM has reduced CIT, but by less than the time taken to perform pXM, indicating this is not the rate-limiting step. The lack of a significant reduction in DGF between the vXM and pXM groups, despite similar CIT between the pre-vXM and pXM groups indicates that additional factors influence DGF.

P2

Impact of pre-formed and de-novo MICA antibodies on renal allograft outcomes in transplant recipients sensitised by pre-formed, donor-specific HLA antibody

Philippa Dodd, Michelle Willicombe, Paul Brookes, Eva Santos-Nunez, Nicola Gunby, Rawya Charif, Candice Clarke, Jack Galliford, David Taube

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Pre-formed, donor-specific antibodies directed at human leucocyte antigens (HLA) are associated with antibody mediated rejection and inferior allograft outcomes. The MHC class I-related chain A (MICA) are polymorphic gene sets closely linked to the HLA-B locus located on chromosome 6, are expressed on a variety of cell types including endothelial cells and have been considered a plausible target of an allograft response. However, their broad clinical importance has not been clearly defined. The aim of this study was to determine the prevalence of MICA antibody, the association between MICA and HLA antibodies and the effect of MICA antibodies on renal allograft outcome.

We undertook this study to investigate MICA antibody status in patients with pre-formed, donor-specific HLA antibodies who underwent renal transplantation between 2006-2011 (n=63). Sera sampled immediately prior to-, at 3, 6 & 12 months post-transplantation and at rejection episodes were examined using LABScreen® Luminex® assay technology. Additional data in respect to allograft function (serum creatinine), HLA mismatch, HLA antibody status, donor type, rejection epsiodes and allograft failure were also collected. Uni- and multivariate analyses were performed.

7.9% (5/63) recipients tested positive for pre-formed MICA antibody and remained positive post-transplantation, 25.3% (16/63) devloped MICA antibody de novo and 66.6% (42/63) tested negative for MICA antibody. Neither pre-formed or de novo MICA antibodies were significantly associated with allograft rejection (p=0.52), survival (p=0.96) or function (p=0.34).There was no significant association between MICA antibodies and pre-transplant sensitisation with HLA class I (p=0.897), class II (p=0.937) or class I+II (p=0.753) donor-specific antibodies. In this cohort of patients MICA antibodies, detected up to one year post transplantation, had no impact on renal allograft outcomes.

P3

Results of the C1qscreen assay and comparison with serum cytotoxicity - a matter of synergy?

David Lowe[1,3], Sunil Daga[3,4], Daniel Zehnder[3,4], Curtis McMurtrey[2], William Hilderbrand[2], Clare Collins[1], Rob Higgins[4], David Briggs[0]

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Introduction: Recently single antigen bead (SAB) based C1q fixing assays (C1qScreen) have been introduced and a number of studies have found associations between C1q+ antibody specificities and increased AMR. However, inconsistencies have been reported between standard SAB assays, the C1qScreen assay and CDC results. This study explores these disconnects and aims to identify factors determining serum cytotoxicity.

Methods: Fifty-one donor recipient pairs who underwent HLA incompatible transplant (HLAi) were analysed.In the pre-transplant CDC crossmatch16 were positive, and 35 were negative, but all had demonstrable DSA by standard SAB. IgG subclass testing was performed in all patients and CDC results were also correlated with presence of DSA in the C1qScreen.

Results: CDC positive cases showed a significantly increased median MFI in all IgG subclass groups, however of these cases only 8/16 showed a C1q fixing DSA by C1qScreen Assay. Epitope specific antibody preparations showed that antibody specific for a single epitope in isolation was poorly reactive in the CDC assay. Addition of a second antibody specificity led to greatly enhanced CDC reactivity, i.e synergy. This synergy was enhanced if the distance between the respect epitope positions was greater.

Discussion: IgG subclass specific DSA levels were significantly raised in CDC positive cases, but the C1qScreen assay detected DSA in only 50% of cases. Furthermore, we show that HLA-specific antibodies act in a synergistic manner to more effectively cross-link C1q and bring about a cytotoxic reaction. This synergy is dependent upon the physical location of the epitopes on the HLA molecule.

P4

Recipient transplant nephrectomy is associated with higher pre-sensitization for subsequent renal transplantation

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There is a lack of consensus about the impact of recipient nephrectomy on sensitization to donor antigens and future transplant outcomes. In this study, we have retrospectively analysed all the recipient nephrectomies (Group-N) performed between 1988 and 2009 at our centre and compared them to patients with a failed transplant and no nephrectomy (N0). In this period there were a total of 207 kidney transplant recipients (KTRs) who were re-listed after a failed transplant of whom, 86 (41%) underwent graft nephrectomy. Patients with graft nephrectomy had higher levels of HLA pre-sensitization detected by Luminex screening prior to the subsequent renal transplant. The mean calculated PRA was significantly higher for Group N in comparison to Group-N0 (Group-N, 62±42; Group N-0, 53.9±4; P=0.02; Mann Whitney U test). When this was analysed as a cumulative number of detected antibody specificities, again, Group-N had significantly higher specificities detected on the Luminex platform (Group N, 18.5; Group-N0, 11.6; P=0.02; Mann Whitney U test). Patients in Group-N0 had slightly lower cumulative anti-donor HLA specific antibodies to the failed graft when compared to the Group-N (Group-N0 1.07, Group-N 1.34; P=0.3). Of the 86 patients with nephrectomy data for pre and post nephrectomy HLA antibodies was available for 43 and in these patients; there was a significant increase in the cumulative HLA antibody specificities post-nephrectomy (cumulative HLA specific antibody specificities; pre nephrectomy 4.2 vs. post nephrectomy 12.1, P<0.0001). When the total DSA specificities were analysed based on the timing of nephrectomy, patients who had nephrectomy within 30 days of transplantation had significantly lower cumulative DSA specificities in comparison to those who had nephrectomy after 30 days (cumulative DSA specificities, nephrectomy <30 days, 1.0 vs. nephrectomy>30 days 12.1, P=0.03). Interestingly, despite the higher levels of HLA allo-sensitization in the nephrectomy group, there was no significant difference in the time to re-transplantation in these re-listed KTRs. Despite, the higher levels of pre-sensitization as determined by the PRA, KTRs who underwent nephrectomy (Group-N) had comparable incidence of early acute rejection (Group N, 14.9%; Group-N0, 17.7%, P=Ns) DGF (Group-N, 32.8%; Group-N0, 35.4%; P=Ns) and their graft survival at 1 year (Figure-1B) was also comparable to those without nephrectomy. To conclude, with this retrospective analysis, we show that recipient graft nephrectomy is associated with higher levels of allosensitization but this was not associated with adverse clinical outcomes following the subsequent transplantation.

P5

Inhibition of the single antigen bead assay in the presence of the C5 monoclonal antibody eculizumab

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Introduction: Eculizumab is a humanised monoclonal antibody that targets the C5 component of the complement cascade and is currently undergoing clinical trials for use in protection against antibody mediated rejection in HLA incompatible (HLAi) kidney transplantation. Anecdotal evidence suggest that the presence of eculizumab in patient sera can inhibit *in vitro* HLA-specific antibody detection in the Luminex-single antigen bead (SAB) assay and may cause a misleadingly low assessment of donor specific antibody (DSA) levels during post-transplant antibody monitoring.

Methods: Serum samples obtained before and after HLAi kidney transplantation obtained from four patients (two randomised to receive Eculizumab and two conventional therapy) were tested using HLA class I and II SAB. In addition, pre-transplant sera obtained before Eculizumab therapy were tested untreated and following ex vivo addition of Eculizumab at doubling dilutions 1:5,000 to 1:80,000 to examine its effect on HLA class I and II SAB binding.

Results: Patient sera obtained post-eculizumab therapy showed a substantial inhibition of antibody binding to HLA class I DSA (mean inhibition 94% (range 92 – 97%)). This was considerably greater than when compared to patients undergoing HLAi transplantation who did not receive eculizumab which showed a mean inhibition of antibody binding to HLA class I DSA of 40% (range 34 -63%). The ex vivo addition of eculizumab to pre-transplant sera resulted in a reduction of antibody binding to both HLA class I (24% inhibition) and II (28% inhibition) SAB with inhibition at around 1:10,000 dilution.

Discussion: The presence of eculizumab in patient sera causes non-specific inhibition of antibody binding to HLA class I SAB but has little effect on binding to HLA class II SAB. Our results support previous anecdotal evidence that post-transplant HLA class I DSA monitoring in patients receiving eculizumab may give misleadingly low assessment of antibody levels.

P6

A prospective analysis on the use of different immunosuppression regime and the development of donor specific antibodies in renal transplant patients

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Introduction: Antibodies (Abs) against Human Leucocyte Antigen (HLA) that appears following transplantation play an important role in renal transplantation. The aim of this study is to analyse in detail the development of Donor Specific Antibodies (DSA); and to establish whether they are related to use of different immunosuppression regimes. Outcome in terms of rejection rates are then compared.

Methods: Prospective study of renal transplants performed in a single Centre from January 2009-December 2010. All patients were transplanted with negative cross match (Complement dependent cytotoxicity assay and Flow Cytometric Analysis) and did not have DSA pre-transplant. Sera samples were collected at Day 10, 1 month, 3 months and thereafter at 3 months interval. They were screened using Luminex based technology and positive findings (MFI>500) were subsequently tested with Single Antigen Beads to look for presence of DSA (positive if MFI>1000).

Results: 177 patients with sera samples collected from January 2009-June 2012. Basiliximab was used as part of the transplantation induction regime in 142 patients (80.2%) and 11 of these developed DSA Abs (7.7%). On the other hand, 33 patients had Alemtuzumab (19.8%) and 5 of these developed DSA (15.2%). Incidence of DSA is almost twice as high in the Alemtuzumab group. Majority of the DSA were of HLA Class I. Patients with DSA have higher rejection rates (29% versus 18%) compared to those who did not develop them.

Conclusions: Our study shows that the use of Basiliximab versus Alemtuzumab has a role in the development of DSA post-transplantation which then found to affect rejection rates.

P7

HLA-specific antibody titration analysis

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Introduction: Due to the increasing demand for more accurate and meaningful data in antibody detection assays, which includes quantitative measures of antibody titers, we evaluated a series of serological specimens to demonstrate the benefit of antibody titration analysis. We show that by identifying the linear range of the assay, semi-quantitative observations are possible where titer comparisons can be easily made and saturation issues such as “prozone effects” are eliminated.

Methods: To determine linear range and half maximal effective concentrations (EC50), serological specimens from highly sensitized patients were diluted to eight different concentrations and their MFI signal determined using an in-house, 120-allele Luminex-based single specificity solid phase assay platform.

Results: Our results show that individual, single-allele titration curves can be generated to establish optimal performance range. We found that titration analysis has two major benefits: (1) eliminating serological interferences at high concentrations, and (2) semi-quantitative observations within the linear range. According to our test series, most sera will cause interferences and high background if tested undiluted. Accurate determinations can only be made by applying serial dilutions to reach highest signal-to-background ratios.

Discussion: Since the physiological responses of the adaptive immune system against an HLA target are highly variable and antibody composition is distinct to each individual, accurate determination of specificities, titer and strengths of antibodies has been extremely difficult. Titration analysis offers the possibility to evaluate several of such functional traits of antibodies to any given HLA molecule allowing better interpretation of individual antibody populations in a quantitative matter. This project will likely lead to a better assessment of HLA titers and generate new insights for post-transplant monitoring and early recognition of immunologic rejection.

P8

Evolution of de novo HLA response (IgM and IgG) following kidney transplantation and effect on graft outcomes

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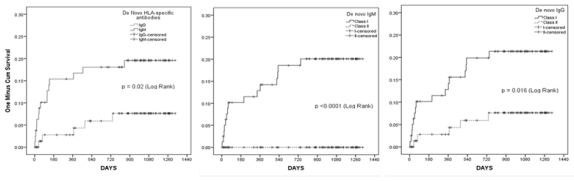
Background: It has generally been accepted that IgM class HLA-specific antibodies pre-transplantation is not a contraindication for transplantation. However, the role of IgM class HLA-specific antibodies of de novo origin remains controversial. The purpose of this study is to describe the evolution of immune response early following kidney transplantation, and relate this to adverse outcome during initial years post-transplantation.

Methods: 80 cases with negative cross-match and HLA-specific antibodies on Single Antigen Beads (Luminex) were studied. Serum samples were collected daily/1st week, weekly/1st month, monthly/1st year and then three monthly. 19 cases with ABO-incompatible kidney transplantation were included in this study.

Results: 18.7% and 26.25 % developed de novo IgM and IgG HLA-specific responses respectively. See figure, demonstrate evolution of de novo response with time. Table demonstrate the outcome in relation to class/es of antibodies. Group with de novo IgG and prior rejection had poor graft function compared to group with de novo IgG alone (p =0.03).



Group (=x)	IgM & IgG negative (1)	IgM alone positive (2)	IgG alone positive (3)	IgM & IgG positive (4)
N	48	9	17	6
No events	28 (58%)	7 (77%)	12 (71%)	2 (33%)
Failure	4 (8%)	0	1 (6%)	1 (17%)
Death	2 (4%)	0	1 (6%)	1 (17%)
Rejection	16 (33%)	1(11%)	5 (29%)	3 (50%)
ACR	12 (25%)	1(11%)	3 (18%)	2 (33%)
AMR	3 (6%)	0	2 (12%)	1 (17%)
Proteinuria*	10 (21%)	1 11%)	1 (6%)	1 (17%)

Conclusions: This three year prospective study of 80 cases following kidney transplantation showed that early de novo response for both IgM and IgG de novo HLA-specific response did not increase adverse events in short term. Similar to IgG, there was epitope spreading noted in IgM response however they did not correlate in terms of specificity suggesting different mechanistic of Isotype response. There was no IgM response to class II HLA, this needs to be confirmed in larger prospective studies with longer follow-up periods.

P9

Changing profile of the workload of the H&I laboratory in support of a living donor kidney transplant programme over one decade

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Introduction: Changes in legislation and advances in the technology used by H&I Laboratories have transformed Living Donor Kidney Transplant Programmes (LDKP) in the last decade. The aim of this abstract is to demonstrate the differences in the complexity and workload of a H&I Laboratory in support of a LDKP by comparing two Living Donor (LD) cohorts a decade apart.

Methods: Data related to the laboratory's workload generated by the LDKP has been prospectively recorded on a Microsoft Access database. The database was interrogated to compare a cohort of LD pairs referred to the laboratory in the 2002/03 fiscal year to a cohort referred in 2012/13.

Results: In 02/03 151 LD were referred for 88 recipients (1.7 donors per recipient) compared to 375 LD referred for 216 recipients (1.7 donors per recipient) in 12/13. An increase of 426%. In addition 35 altruistic donors were referred to the laboratory in 12/13, a donor route that did not exist in 02/03.

134 (88.7%) LD were genetically related to their recipient in 02/03 compared with 66.1% (248) in 12/13. The laboratory performed 0 virtual crossmatches, 45 preliminary flow cytometry crossmatches (FCXM) and 35 immediate pre-transplant FCXM on the 02/03 cohort compared to 83, 42 and 64 respectively for the 12/13 cohort. 35 (23%) LD pairs from the 02/03 cohort progressed to transplant compared to 64 (17%) in the 12/13 cohort. 101 of the 12/13 LD pairs are in work up. 3 have LD transplant dates. 2 of the 12/13 ABOi LD pairs proceeded to transplant compared to 0 in the 02/03 cohort. 36 of the 02/03 recipients received a cadaveric kidney transplant (41%) compared to 23 (11%) in 12/13.

Discussion: Changes in legislation and the promotion of LD have increased the work load of the H&I Laboratory in the last decade. This increase has been effectively managed by the changes in technology employed by H&I laboratories. Most importantly these changes have increased the number of LD transplants. 23 LD transplants were performed at this centre in 02/03 compared to 112 in 12/13; an increase of 500%.

Category: Rejection

P10

Outcome of early antibody-mediated histological lesions in blood group-incompatible kidney transplantation

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Introduction: Antibody-mediated rejection (AMR) is defined by microcirculation inflammation (MI, g+ptc) and C4d deposition (C4d+MI+). It is associated with early graft loss in ABO-incompatible transplantation (ABOi). However, the incidence and the outcome of C4d-negative AMR (C4d-MI+) and C4d deposition without morphological evidence of rejection (C4d+MI-) needs to be clarified. . The goal of our study was to describe these different histopathologic patterns on early biopsies and to correlate them with outcome.

Patients and methods: Sixty four early biopsies in 50 ABOi patients were scored according to the Banff classification and classified according to the presence of MI and C4d deposition.

Results: 13 (26%), 17 (34%), 6 (12%), and 14 (28%) of patients were C4d+MI-, C4d+MI+, C4d-MI+, and C4d-MI-, respectively. Patients with C4d+MI+ or C4d-MI+ biopsies had a lower 3-month eGFR (45 ± 11 mL/min and 37 ± 16 mL/min) when compared with patients with the C4d-MI- phenotype (60 ± 16 mL/min, p=0.02 and p=0.03, respectively). Beyond 3 months, more patients in the C4d+MI- group experienced a declining eGFR when compared with the C4d+MI+, C4d-MI+, and C4d-MI- groups (69%, 29%, 33%, and 29%, p=0.03, respectively). In the C4d+MI- group, interstitial inflammation was strongly associated with a declining eGFR (i>0:100% versus i=0:43%, p=0.03). Finally, 87% of the C4d-positive patients had baseline antibody titre ≥ 1/16, versus 55% in the C4d-negative group (p=0.01).

Conclusion: Beyond three months, stability in eGFR is a common occurrence in ABOi transplantation, even after AMR and this could fit the definition of accommodation. However, isolated C4d deposition associated with interstitial inflammation may lead to chronic graft dysfunction and should not be considered as accommodation. In the future, characterisation of this indolent inflammatory process may influence post-transplant treatment.

P11

How much is a living donor kidney worth? Treating AMR with eculizumab

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Introduction: In patients undergoing HLA-incompatible transplantation, early aggressive AMR has previously proved difficult to treat, and risk of early graft loss is high. Complement inhibition with Eculizumab has been reported to be successful in treated antibody mediated rejection (AMR). Eculizumab treatment is costly, and funding is not currently agreed by NHS England for the treatment of AMR. One 300mg vial of Eculizumab costs £3150. After initial loading (1200mg £12,600), treatment is given weekly (900mg £9450) for a total of 5 weeks, although if plasmapheresis is used in addition, a replacement dose of 600mg (£6300) is given due to a reduction in plasma concentrations.

Case report: We report the outcome of an HLA-incompatible recipient who, after undergoing desensitisation with 2 sessions of double filtration plasmapheresis (DFPP) and Campath induction received a transplant from a relative. Post transplant the patient developed oligoanuria and acute graft dysfunction and donor specific antibody rise (DSA) on Day 5. Treatment was commenced with DFPP, however there was no response to treatment. Because of the risk of graft loss, a decision was made to treat with Eculizumab on Day 6. Funding was secured for a maximum of £75,000. The patient received a total of 5 sessions of DFPP, replacement Eculizumab & IvIg post transplant, and a total of 4 weeks of Eculizumab (£75,600). Post treatment renal function improved and eGFR on discharge was 44ml/min/1.73m^2.

Discussion: Prompt early treatment of aggressive AMR and imminent graft loss with Eculizumab and DFPP was successful, and costly. This case raises questions about respect for patient autonomy, as well as distributive justice for the NHS. Additionally the transplant team has a duty to respect the autonomy of the donor. Donors give their kidney freely, and this act in itself benefits not only the recipient, but also the NHS.

P12

Rescue of ABOi transplants with antibody-mediated rejection. A single centre experience.

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ABO incompatible transplants were previously deemed too high risk and costly but have now become an effective way of shortening waiting times. They do however provide an extremely difficult management problem when antibody mediated rejection (AMR) occurs.

Four complex ABOi cases have been encountered in our centres where pre-operative antibody titres were low enough to avoid immuno-absorption (IA) but which developed AMR shortly post-op. In the first case recognition of raised antibody titres was delayed until day 6 and once methylprednisolone was given on day 7 IgM titre increased to 256 and the graft was lost on day 13. The second patient had microangiopathic haemolytic anaemia (MAHA) so Tacrolimus levels were kept low post-operatively resulting in rejection and IgM titres reached 512 despite methylprednisolone and the kidney rapidly infracted without IA. The third patient had SLE with antiphospholipid syndrome and rising antibody titres from day 6 which did not respond to IA and methylprednisolone Ecluzimab was given on day 9 but just after urine output had declined and this treatment was too late to prevent graft infarction. Nephrectomy was performed on day 11. The fourth patient had rising antibody titres from day 6 and treatment with Therasorb IA was initiated. Ecluzimab was given earlier than the previous case; on day 7 at first signs of a rising creatinine (100umol/L from 76umol/L previous day) together with 8 Glycorex IA treatments. Further doses of Ecluzimab were given on day 17 and 24 and titres reduced down to 32 (IgG) and 16 (IgM) by day 27 and creatinine of 205 umol/L. This kidney was successfully rescued and remains functioning with a baseline creatinine of 90umol/L.

Development of antibodies post ABOi renal transplant requires attention to detail and rapid initiation of treatment. Our salvaged transplant case would suggest that if Ecluzimab is to be used this should be early rather than late (case four as opposed to case three).

P13

High acute cellular rejection rate in early steroid withdrawal protocol

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Introduction: Steroid avoidance or withdrawal is part of different immunosuppressive minimisation protocols in low immunological risk kidney transplant recipients. In our centre we applied early steroid withdrawal protocol within the first week for low risk live donor kidney transplant recipient. 1ry endpoint of the study was to audit the incidence of rejection within the first 3months.

Methods: 51 live donor kidney transplant performed from August 2012 to August 2013. 20 patients [15 males and 5 females with mean age 43 years (SD 14.12)] defined as low immunological risk were included in the early steroid withdrawal protocol and 31 recipients were excluded due to presence of anti-HLA antibodies, ABOi, or HLAi. The standard protocol used was a quadruple therapy including Basilixmab, preloaded Tacrolimus, preloaded MMF and prednisolone which was given intraoperatively 500 mg then 20mg postoperative from day 1until tapering to withdrawn on day 7. Biopsy was performed if there was evidence of delayed graft function up to day 7, unsatisfactory drop of the creatinine, or unexplained rise of creatinine >20% after satisfactory drop.

Results: 12 live related and 8 live unrelated, including one altruistic and one from the pool exchange program, were included in the study. All patients had early drop in their creatinine. Unsatisfactory drop of creatinine was observed in 1 patient due to biopsy proven ATN. Unfortunatly 7/20 (35%) patients developed biopsy proven cellular rejection that fulfilled the Banff criteria while 3/20 (25%) developed borderline rejection. 5 patients developed the rejection between day 7 and 10 post transplant, 4 patients in 2^{nd} week and 1 patient at 12 weeks. 1/10 developed more than one attack of rejection. 2 patients had Banff 1b, 1patient had 2a, and 3 had border line rejection. 4 patients had combined vascular rejection and cellular rejection. Patients with rejection were treated with Methylprednisolone and started on prednisolone 20mg which tapered over the next 21 weeks to 5mg. 1 patient need addition of ATG to treat the rejection.

Discussion: Although there are several report showing safety of early steroids withdrawal in low immunological risk kidney transplant recipient in our experience we observed an high incidence of acute rejection despite preloading the live donor recipient with Tacrolimus an MMF that lead us to stop the use of this protocol.

P14

Ultrastructural features of chronic antibody-mediated damage in highly sensitised patients with or without C1q-activating anti-HLA antibodies

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HLA incompatible (HLAi) transplantation after desensitisation is associated with a higher incidence of antibody mediated rejection (AMR). We previously found that in recipients with a positive donor cell-based flow cytometric cross match (FXM+) prior to desensitisation, the presence of C1q+antibodies pretransplant is indicative of an increased risk of AMR, with acute AMR occurring in 100% of patients with C1q+antibodies and in 25% of the patients with C1q- antibodies pretransplant. All pre-transplant C1q- patients who developed acute AMR had detectable C1q+antibodies at the rejection episode.

We performed ultrastructural analysis of follow-up biopsies in our retrospective cohort of 17 HLAi patients who had IgG anti-HLA donor specific antibody (DSA) with FXM+ prior to desensitisation. We compared patients with C1q+ antibodies (9 patients; 4/9 C1q+DSA; 5/9 C1q+HLA (non DSA)) to those with no C1q activating antibodies (8 patients, $C1q^-$) pretransplant. All but 2 of the 17 patients had more than 1 biopsy and the last biopsy available to date in 15/17 was assessed for features of chronic AMR (cAMR).

Amongst C1q+ patients, 6/8 had features of cAMR by 35.3±8.33 (median 37.5) months post transplantation. In 3/6, cAMR was diagnosed by transplant glomerulopathy (TG) on light microscopy (LM). In 3/6, cAMR was only visible on electron microscopy (EM) (cg 0.5 in 1, ptcbml in 1, cg0.5+ptcbml in 1). In C1q- patients, 4/7 had features of cAMR by 42.3±27.9 (median 33.5) months post transplantation. In 1/4 cAMR was diagnosed on LM (TG). In 3/4 cAMR was only visible on EM (cg 0.5 in 1, ptcbml in 2). The C1q- patient with TG had developed a C1q-fixing antibody post-transplantation, but the other 3 had not.

Ultrastructural analysis increases detection of early features of cAMR in patients with antiHLA antibodies. In this analysis of a small cohort of patients, ultrastructural findings of early cAMR are present in both C1q+ and C1q- patients. Longer follow up times are necessary to see whether all progress to TG and/or long-term graft loss.

P15

Class I HLA-IgM donor-specific antibodies are associated with antibody-mediated rejection after renal transplantation

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Preformed and de novo IgG donor specific HLA antibodies [DSA] are associated with acute and chronic antibody mediated rejection [AMR] and inferior renal allograft survival. These DSAs are readily identified by single antigen bead assays. A proportion of patients with AMR have no detectable circulating IgG HLA DSAs and it is presumed that these antibodies are either absent or bound to the allograft. IgM HLA antibodies are traditionally thought to be harmless auto-antibodies and there are few studies attributing a more pathogenic role for these antibodies in renal transplantation.

In this study we show that a significant proportion of patients with biopsy proven AMR and no detectable IgG HLA DSA have Class I IgM HLA DSA. 24 patients [17m, 7f, mean age 43.7 years] with biopsy proven AMR were studied. 17/24 patients had evidence of either focal or diffuse C4d deposition on indicative biopsy. Sera from these patients, sampled pre and post transplantation, including at the time of indicative biopsy, were screened using LABScreen® Luminex® mixed and single antigen bead assays for the presence of IgG and IgM HLA and DSA. None of the patients had IgG HLA or DSA antibodies. However 17/24 [70.8%] screened positive for the presence of IgM antibodies and 12/24 [50%] were identified as having class I IgM DSA.

These preliminary findings suggest that IgM HLA antibodies may have a significant pathogenic role in AMR, particularly in those patients who are IgG DSA negative. These findings may also have significant therapeutic implications as patients with IgG DSA negative AMR may not be plasma exchanged because traditionally no circulating antibodies have been identified for removal. If these patients have IgM DSA, they may well respond to appropriate forms of plasma exchange.

Category: Surgical 1

P16

The inflammatory and complement mediated response to EVNP in human kidneys

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Background: The inflammatory response to a short period of *ex-vivo* normothermic perfusion (EVNP) has not been fully characterised. The aim of this study was to quantify and compare the inflammatory effects of EVNP in donation after circulatory (DCD) and donation after brain death (DBD) kidneys.

Methods: Sixty human kidneys that were deemed unsuitable for transplantation after retrieval underwent 60 minutes of EVNP at 37°C. Thirty five kidneys were from DCD donors and 25 from DBD donors. Perfusion parameters, urinary biomarkers, cytokines and C4d were measured in the plasma, urine and tissue during perfusion.

Results: The mean warm ischaemic time was 13 ± 4min in the DCD kidneys. The mean cold ischaemic time was 28 ± 13 and 34 ± 17h in the DCD and DBD kidneys (P = 0.102). Kidneys from DCD kidneys had a higher level of proteinuria (0.73 ± 0.52 vs 0.46 ± 0.22pg/ml). However, there was no significant difference in the perfusion parameters (mean renal blood flow, DCD 75 ± 35 vs DBD 65 ± 27ml/min/100g;P=0.238) or total urine output (DCD 88 ± 75 vs DBD 103 ± 83ml; P = 0.443). There was also no significant difference in the urinary markers of tubular injury, KIM-1 and NGAL, between the groups (P = 0.178, 0.551). Levels of TNFα were not detectable in the plasma pre or post perfusion in either group. Urinary IL-6 levels were also similar in both groups (P = 0.526). Diffuse tissue expression of C4d (>50%) was similar in both groups after cold preservation (P = 1.000). There was no change in C4d expression after EVNP in either group.

Conclusion: A short period of EVNP does not appear to up-regulate inflammatory or complement pathways in human DCD or DBD kidneys.

P17

The effect of body mass index on kidney transplantation – size doesn't matter

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Introduction: Kidney transplantation in obese patients (body mass index [BMI] >30 kg/m^2) with end-stage renal disease is controversial, with many centres setting an upper limit on BMI when considering patients for transplantation. Excluded patients however will be precluded from the benefit of transplantation over dialysis. A detailed analysis is required to determine if surgical complications and in particular, graft and patient survival outcomes, are worse in obese patients.

Methods: All recipients of kidney-only transplants (n=1090) between 2002 and 2012 in our centre were included. Surgical complications (e.g. wound infection, haemorrhage, vascular thrombosis), graft loss and patient survival were identified from a prospectively maintained database. Comparisons were made on the basis of the following BMI categories: <26 (n=439), 26-28.9 (n=169), 29-31.9 (n=128), >32 (n=65). Multivariate regression analysis was used to determine risk factors for surgical complications and patient and graft survival.

Results: Surgical complications occurred in 253 (23.2%) recipients. In multivariate analysis, higher recipient BMI (OR=1.05 per unit increase in recipient BMI, p=0.01) and recipient diabetes (OR=1.78, p=0.02) were significantly associated with overall surgical complications; however higher recipient BMI was only a significant risk factor for wound infection (p=0.002). Obesity was not a risk factor for urinary, vascular or lymphatic complications. 5-year patient and graft survival were comparable among the different BMI groups (p=0.82 & p=0.91 respectively).

BMI	<26	26-28.9	29-31.9	>32
Patient survival	94.8%	95.3%	95.3%	93.8%
Graft survival	88.2%	87.6%	89.1%	89.2%

Discussion: Although higher recipient BMI was associated with increased risk of wound infection, there was no negative impact on graft or patient survival. Obese patients should not be denied transplantation on the basis of BMI alone.

P18

Defluxing the renal transplant ureter – a management option for transplant reflux with pyelonephritis

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Introduction: Transplant pyelonephritis (TxP) is an important post transplant complication that may lead to graft scarring and potentially graft loss. We believe that there is a rationale to prevent or correct transplant vesicoureteric reflux (TxR) associated with TxP. We evaluate the use of endoscopic injection of dextranomer/hyaluronic acid copolymer (Deflux) to the transplant ureter to correct TxR and a history of TxP.

Methods: All patients with TxP were placed on prophylactic antibiotics. A MCUG and DMSA were performed to assess the degree of TxR and transplant scar. Deflux was indicated when a break-through infection occurred despite prophylactic antibiotics. Transplant Deflux was approved by our Institution New Procedures Committee in 2011. We prospectively assessed all patients undergoing Deflux to the transplant ureter from December 2011 to October 2013. All patients received peri-operative antibiotic cover.

Results: 84 renal transplant patients had TxP between 2007 and 2013 were assessed with MCUG and DMSA scans. 12 female patients were assessed for Deflux to the transplant ureter after break-through infections. 1 patient declined the procedure and remains on prophylactic antibiotics; 2 patients are awaiting the procedure. 9 patients have undergone transplant Deflux. 1 patient had scarring on DMSA but no TxR on MCUG. 3 patients had Grade I–II TxR; 5 patients had Grade III-V TxR. Cystoscopic injection of Deflux was achieved in all cases (0.5ml to 1.5ml Deflux / case). 3 patients had culture proven UTI within one month post Deflux; all successfully treated with outpatient antibiotics. 1 case has persistent grade I TxR; 2 cases have reduced TxR and 3 cases no longer have TxR; 3 await post Deflux MCUG assessment. No cases of transplant ureteric obstruction were seen.

Conclusion: Endoscopic injection of Deflux to the transplant ureter appears to be a safe and attractive minimally invasive technique to correct TxR. Further long-term data is required to determine if it will prevent further episodes of TxP and renal transplant scars.

P19

Obesity and living donor nephrectomy: short and medium term outcomes

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Introduction: Laparoscopic living donor nephrectomy is now an established procedure such that some UK centres are now advocating an "extended eligibility criteria" for living donation including accepting obese kidney donors. We aimed to investigate the rationale for including obese patients in UK living donor programmes by studying their postoperative and medium-term clinical outcomes.

Methods: A case control study of 111 obese (BMI>30) donors who were age, sex and race matched (1:1) with normal weight (BMI<25) donors undergoing hand assisted laparoscopic donor nephrectomy at one institution was carried out. Perioperative outcomes, kidney function and blood pressure were all assessed. Mean follow up was 26 months. Statistical analysis was calculated using the t-test and chi squared test using SPSS version 16.

Results: Mean donor age was 49 years and 58% of the cohort was female. The mean BMI for obese donors was 31.8 (SD10) and 23.6 (SD 9) for normal weight donors. There were no significant differences in operation time: 194 v 198 mins; open conversion: 0.9% v 0.9%; 30 day postoperative infection rate: 16/111 v 11/111, hospital stay: 3.89 v 3.97 days ($p>0.05$). However obese patients did experience significantly more wound complications (9/111 v 19/111 $p=0.026$) and incisional hernia rates (2/111 v 10/111 0.012). There was no significant difference in kidney function (mean eGFR 65 v 63mls/min/1.73m^2 $p=0.931$) or those considered to be hypertensive (14 v 16% $p>0.05$) between the groups at two years.

Discussion: Obese donors have comparative perioperative outcomes compared to their normal weight counterparts. Incisional hernia and wound complication rates are notably increased. Longer term parameters of cardiovascular risk (BP) and chronic kidney disease (eGFR) are equivalent to non-obese donors. The utilisation of obese living kidney donors is safe but requires appropriate patient counselling. Further longitudinal follow up of kidney function and CV risk parameters is also necessary.

P20

Safety and potential benefits of early ureteric stent removal tied with urinary catheter after renal transplantation

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Introduction: The use of double-J ureteric stents after kidney transplant is a well consolidated practice in many transplant units. In this single centre retrospective study we evaluate the safety and potential benefits of early (5 days) and standard (6-weeks) removal of ureteric double-J stents.

Methods: Ureteric stents were tied to Foley catheter prior to the fashioning of a neo ureteric-cystostomy in 42 patients (Group A). We identified in our database 42 frequency and donor type matched recipients of renal transplants as a control group, where the stent was removed with planned cystoscopy after 6 weeks (Group B). Both groups received similar antibiotics and immunosuppression. Primary endpoints were successful removal of stents and incidence of urinary leaks. Secondary endpoints were incidence of UTIs in the first 6 weeks post transplant and at 12 weeks. UTI was defined as a significant bacteriuria of 10^5 colony forming units (CFU) per millimetre (CFU/mL). Chi-square test was performed.

Results: All stents in Group A and in Group B were successfully removed. We did not observe any urinary leak in Group A; three (7.1%) were diagnosed in Group B; p=0.03. One case in Group B required re-implantation. In the first 6 weeks post-transplant we observed in Group A one (2.3%) and in Group B seven (16.6%) UTIs; p= 0.01. After 12 weeks there were in Group A five (11.9%) and in Group B twelve (28.5%) UTIs; P=0.02.

Discussion: Early removal of the ureteric stent tied with the urinary catheter is safe and in our experience was not associated with urinary leak. The obvious major benefit for the patients, of not needing a new admission for cystoscopic stent removal, is also associated with a reduced incidence of early and late UTIs.

P21

Economic cost and clinical benefit of iliac arterial assessment in a renal transplant population

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Introduction: Most UK renal transplant centres currently advocate preoperative imaging of the iliac arterial tree. A commonly used modality is ultrasound angiology (UA). It is postulated that this will enhance operative decision-making over and above simple clinical examination. However UA is costly and its clinical utility and economic cost are not known within this expanding patient group.

Methods: 385 renal transplant recipients were studied between January 2011 and December 2012. 355 of these patients had pre-operative UA. Data was collected on UA results, abnormality of the femoral pulse on clinical examination and any documented changes in the operative management plan such as a change in laterality of kidney implantation. We also recorded data on patient age, sex, BMI, smoking status; history of heart disease diabetes and dialysis states.

Results: Of the 355 patients with UA data, 46 had abnormal results suggestive of iliac arterial disease. This led to a change in laterality of kidney implantation in 7 patients. 4/7 had abnormalities of the femoral pulse documented on clinical examination. Postoperative arterial complication rates were similar in those with and without UA proven iliac arterial disease (2 v 3% $p>0.05$). Thus for every 1 clinically significant iliac lesion identified the number needed to scan was 64. At a unit cost of £120 the cost of identification of one surgically important lesion was £7680. The only associated risk factors for iliac arterial disease in this population was advancing age (47.2 v 52.7 $p=0.01$)

Discussion: Iliac arterial disease is present in only a minority of patients otherwise eligible for renal transplantation. Radiological assessment is costly and rarely changes the operative management plan over and above simple clinical examination. Except for advancing age traditional cardiovascular risk factors are not implicated in this population.

P22

TAP block vs No TAP block in patients undergoing living donor kidney transplant

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Introduction: Postoperative pain control in renal transplant surgery is challenging due to recipients pre morbid condition and altered pharmacokinetics of opioids resulting in undesirable side effects. The transversus abdominis plane (TAP) block provides additional analgesic benefit reducing opioid intake. In this study we aimed to test whether addition of TAP block to standard analgesic regime reduced post-operative opiate requirement.

Methods: 161 consecutive live related renal transplant recipients (76 TAP vs 85 no TAP) from 2009 to 2011 were included. Both groups received standard patient controlled fentanyl analgesia and paracetamol. Data was collected for fentanyl requirements, nausea, sedation and pain scores intraoperatively, in recovery and at 24 hours. The primary outcome was total fentanyl consumption in first 24 hours; other outcomes measured included pain scores, nausea, vomiting and sedation.

Results: Intra-operative (IO) Fentanyl use was significantly different between the two groups (Median (range) TAP: 277 mcg (100-600) vs. No-TAP: 329 mcg (100-800), p=0.003). However, this did not progress to statistical in terms of fentanyl requirement on the ward (p=0.57) and total fentanyl requirement in the first 24 hour period (p=0.181). The trend towards lesser Fentanyl use in recovery also did not reach statistical significance (TAP [279 mcg (0-2250) vs. No-TAP 390 mcg (0-2600), p=0.08). A subgroup analysis revealed no benefit of a bilateral TAP block over unilateral block. No difference was found between the two groups with regards to Nausea score (p=0.77) as well as Sedation score (p=0.54).

Conclusion: The addition of TAP block led to less fentanyl requirement intra-operatively as well as in the recovery room in our study. However this was a limited effect that did not extend beyond the immediate post-operative period.

P23

The role of micturating cystourethrogram (MCUG) in the evaluation of recurrent urinary tract infections following renal transplantation

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Introduction: Urinary tract infections (UTIs) are the most common infectious complication after kidney transplantation. Recurrent UTIs and transplant pyelonephritis (TxP) in particular can lead to morbidity and may be associated with graft loss and mortality. There appears to be insufficient data regarding the association between transplant vesicoureteric reflux (TxR), recurrent UTIs and TxP. We evaluate the impact of micturating cystourethrogram (MCUG) on the investigation scheme of renal transplant patients with recurrent UTIs and TxP.

Methods: We retrospectively reviewed kidney transplant patients with recurrent UTIs and TxP between January 2007 and October 2013 who were investigated with MCUG.

Results: 84 patients (75 women; 9 men) were assessed with MCUG (Mean age 42 years, range 19-78). Time from transplant surgery to MCUG ranged from 1 month to 32 years (median 5.5 yrs; mean 8yrs).
71 (84.5%) patients had TxR; of which at least 58% had Grade III to V reflux. 25 (30%) patients had reflux into the native ureters. 15 of 25 patients (40%) with native reflux had surgical intervention; 7 native nephrectomy, 6 subureteral injection of dextranomer/hyaluronic acid copolymer (Deflux); two native open approach ureteral ligation. The majority of the TxR patients (87%) are being managed conservatively with prophylactic antibiotics; 9 TxR patients had Deflux injection to the transplant ureter.

Conclusion: MCUG is an important investigation in the management of transplant patients with UTI and TxP. It identifies reflux into native and transplant ureters which can then be treated with various surgical strategies. This may potentially reduce the risk of graft dysfunction and patient morbidity.

Category: Pancreas and Intestinal 1

P24

Are we discarding transplantable pancreases? Correlation between donor demographics, surgical assessment and histopathology

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Introduction: Donor pancreases are frequently discarded due to concerns over quality, but the assessment process leading to discard is subjective. Here we investigate the correlation between donor demographics, surgical assessment and, for the first time, histological markers of pancreas gland quality.

Methods: Donor pancreases that were retrieved for transplantation, but subsequently declined, were assessed by an experienced surgeon for Fattiness (*None*, *Mild*, *Moderate* or *Severe*), Consistency (*Soft*, *Normal*, *Firm* or *Very Firm*) and quality of perfusion (*Poor*, *Borderline*, *Good* and *Excellent*). Digital analysis of H&E, EVG and Chromogranin A staining was used to quantify intraparenchymal fat, degree of fibrosis and islet cell content in the pancreatic head, body and tail. Vascular disease was assessed by quantification of arteriolar luminal stenosis.

Results: 38 pancreases were declined, due to concerns about gland quality on gross inspection (44.7%), damage (32.5%), prolonged cold ischaemia (13.2%), or for other reasons (9.6%). Donor BMI correlated, as expected, with Fattiness of the gland on gross inspection (p=0.004). However, there was no correlation between donor demographics (age, BMI, abdominal girth, smoking history or hypertension) and intraparenchymal fat, fibrosis, islet cell content or arteriolar luminal stenosis. While pancreases varied greatly in Fattiness and Consistency on gross inspection, this did not correlate with intraparenchymal fat or fibrosis on histopathological assessment. There was no statistically significant difference between pancreases declined due to damage (but otherwise transplantable) and gland quality, in intraparenchymal fat (19.2±9.7% vs. 19.0±10.8 %, p=0.973), fibrosis (82.9±15.0% vs. 69.9±23.3%, p=0.212) or islet cell content (2.1±1.8% vs. 2.8±2.1%, p=0.071).

Conclusion: Donor demographics and gross assessment are not predictive of histological markers of gland quality. Notably, donor BMI and gross assessment of fattiness do not correlate with intraparenchymal fat. Pancreatic characteristics that impact on transplant outcomes remain enigmatic but it may be possible to identify a subset of currently-declined pancreases that could be safely transplanted.

P25

Biopsy should be the standard of care in pancreas transplant recipients. Pancreas rejection is frequent in amylasaemia and has a high failure rate

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Introduction: It is well known that rejection in a pancreas transplant is associated with poor graft survival. We have shown previously that pancreas transplant biopsy has a high diagnostic yield. High amylase, deteriorating C peptide and deteriorating kidney function prompt a pancreas biopsy. The aim of this study was to investigate the risk factors for biopsy-proven rejection in pancreas transplants and its effect on outcomes including graft survival.

Methods: Between January 2008 and November 2013, 78 pancreas transplants were performed in a single transplant centre with ATG induction and no steroids. Forty-seven (47) percutaneous US-guided biopsies of pancreatic allografts were performed on 31 patients during this time period.

Results: The biopsies were performed a median of 4 months (range 1-18) post transplant. 17 biopsies were from recipients of SPK transplants, 8 from Pancreas After Kidney (PAK) and 6 from Pancreas Transplant Alone (PTA) recipients. Of the biopsies from SPK recipients, 10 had a concurrent renal biopsy. The indication for biopsy was high amylase in 33 (70%). 14 patients had a diagnosis of pancreas rejection (18% of the total). 19 (40%) biopsies showed ACR, 5 (11%) AMR [all patients were PAK or PTA], 1 (2%) a combination of ACR and AMR, 4 (9%) were indeterminate and 18 (38%) showed no rejection. Of the 10 cases where a concurrent renal biopsy was taken, 2 showed histological discordance. In all but 3 patients amylasaemia was transient but was associated with rejection in 77% of biopsies. 57% of those with rejection had positive DSA at the time of rejection compared to 40% in those without but this was not associated with the DSA level except in patients with AMR. Of the patients who had AMR rejection, 3 responded initially but only one of them kept his pancreas over a year.

Conclusion: Pancreas biopsy is the only reliable method to diagnose pancreas rejection. Amylasaemia patients after the initial discharge should always be investigated with pancreas biopsy. AMR is associated with very high failure rate in spite of aggressive treatment.

P26

Pregnancy following simultaneous pancreas kidney (SPK) transplantation - single unit experience

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Introduction: The number of pregnancies in women with simultaneous pancreas kidney (SPK) transplants is increasing; however knowledge of pregnancy outcomes is limited. Maternal and fetal outcomes of pregnancies following SPK transplantation since 1996 in a tertiary referral centre are reported.

Methods: Female patients who had become pregnant following pancreas transplant were identified from a local database. Medical and obstetric records were reviewed.

Results: There were 286 pancreas transplants between 1996 and 2013, including 6 women who had 8 pregnancies following SPK (3 bladder and 3 enteric drained). One pancreas graft had failed prior to conception. The median time between transplantation and delivery was 7 years (IQR 7). Median maternal age was 36 years (IQR 6). Live birth rate was 100%. Three deliveries were performed by emergency caesarean section (CS), 3 by elective CS, 1 by forceps and 1 was a preterm spontaneous vaginal delivery. One woman had a bladder injury during emergency CS that was repaired intra-operatively. Median gestational age at delivery was 33.5 weeks (IQR 7). Three infants (38%) were small for gestational age (<10th centile). Three infants were admitted to neonatal special care.

Three episodes of hydronephrosis in 3 pregnancies in two women occurred at 22, 28 and 32 weeks' gestation. Two required nephrostomy and stenting in one woman. The case at 32 weeks resolved spontaneously following delivery. Renal graft dysfunction was observed in all women with improvement following delivery. Pancreas graft function was unaffected by pregnancy.

Discussion: Successful pregnancies following SPK transplantation are possible but have high rates of maternal and fetal complications. Multidisciplinary antenatal care is required in specialist centres.

P27

Patient reported quality of life in pancreas transplant recipients: is it worth it?

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Patients and methods: 73 patients were interviewed using 2 instruments of measurement of QOL: SF36- a generic health questionnaire for chronic illness and EORTC health thermometer. Patients were interviewed at different time points, listing, 6 months and 12 months post transplant. Any patients having an infection, acute rejection or major event within 4 weeks of those time points were excluded. We present data of the first 20 patients.

Results: The scores in physical function improve marginally at 6 months compared to baseline from 50 to 60 (p=0.1) and return to baseline at 12 months post transplant, it was also dependent on recipient age (p=0.05), with a better score found in patients less than 40 but also on donor age (p=0.07). The emotional limitation improved significantly to 6 months (43 to 88, p=0.01) but there was a non-significant deterioration thereafter. The social function improved at 6 months (59 to 79, p=0.02) and remained stable at 12 months. The overall perceived general health improved significantly at 6 months (30 to 65, p=0.03) and that was independent of donor or recipient age. Health thermometer scores improved significantly at both 6 and 12 months (p=0.08 and 0.03) with younger patients scoring higher (87 vs. 67, p=0.013).Better scores at 6 months in the limitations due to physical health section were associated with younger recipient age (p=0.05) and weakly with donor age (p=0.1). The amount of pain the patient had at 6 months was not dependent on recipient or donor age, but at 12 months younger donor age translated to lower amounts of pain (p=0.07).

Conclusion: Pancreas transplant recipients have a good subjective QOL post transplantation as measured by both scoring systems. Their overall health improves significantly. The age of the recipient and the age of the donor both have an affect on physical dimensions of the scores. Patients perception of their overall health is also affected by their age with younger recipients doing better. Targeted approaches on both expectations and psychological support could achieve better overall outcomes

P28

Graft-versus-host disease after intestinal transplantation

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Introduction: Graft vs. host disease (GVHD) occurs when immunocompetent donor lymphoid cells damage recipient tissues after allogeneic transplantation. This complication is more anticipated after intestinal transplantation (ITx) because the large inoculum of lymphoid cells. There are no data on GVHD post vascularized skin transplantation.

Methods: We studied patients who received an intestinal transplant in our institution. Donors were of the same blood type with the exception of one recipient who was blood type B and received organs from a type O donor. The diagnosis of GVHD was based on clinical suspicion and confirmed by biopsy. Treatment consisted of an increase in baseline immunosuppression and steroids.

Results: From October 2008 to November 2013, 24 patients underwent ITx in our institute. Four patients received a Modified Multivisceral Transplant and 20 an Isolated Small Bowel Transplant. Mean age was 42±2.8 years (range 23- 73). M/F ratio 14/10. Median follow up 485 days (range 29- 1879) for surviving/ 85 days (range 28- 823) for non-surviving patients. All had Campath induction and Tacrolimus monotherapy. Ten patients received a vascularized skin component in addition to the ITx (8 Abdominal Wall Transplants and 2 Vascularized Sentinel Skin Grafts).

Median time to onset for GVHD was 52 days. Incidence 4/24 (17%). Mortality from GVHD 8% (2/24). Interestingly, 3/4 patients had a skin component. The skin graft in all these 3 patients was spared from the rash and helped in the early diagnostic process. Both patients that died were immunosuppressed pre transplantation.

Discussion: Patients on pre transplant immunosuppression may present with higher risk for acute GVHD after ITx, due to the possibility of immunosuppressing the recipient more than the graft. However, early signs (skin rash, pulmonary compromise and rising bilirubin), high index of suspicion accompanied by appropriate investigations (Chimeric studies, Recipient Specific Antibodies) may help in early treatment and reduction in mortality.

P29

Cardiopulmonary exercise testing in simultaneous pancreas and kidney transplantation

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Background: Outcome prediction in simultaneous pancreas and kidney transplantation (SPKT) remains challenging without validated objective investigations informing risk stratification. Cardiopulmonary Exercise Testing (CPET) identifies patients at increased peri-operative risk following major surgery. We aimed to establish CPET's utility in patients undergoing SPKT.

Methods: A prospective study of all patients undergoing CPET assessment with a view to SPKT was performed over 7 years (2005- 2012). CPET data, using established thresholds for major vascular surgery (anaerobic threshold (AT) <10.2ml/kg/min, peak O_2 <15ml/kg/min and ventilatory equivalents for CO_2 (VE/VCO_2) >34), were used as predictive comparators against outcome measures (one-year mortality, cardiac events, total inpatient length of stay (LOS) and Critical Care length of stay (CCLOS)). Univariate and multivariate regression analysis for outcome measures was modelled accounting for confounding factors.

Results: 56 patients (35 male, 21 female; mean age at CPET 41.8 (SD 7.8)) with mean AT 11.4ml/kg/min (SD 3.3), mean peak VO_2 17.7ml/kg/min (SD 3.8), mean VE/VCO_2 28.5 (SD 3.3) and mean % predicted peak VO_2 57.1% (SD14.9) were included. 17 patients had AT <10.2ml/kg/min and 17 had VO_2 <15ml/kg/min. An AT threshold of 10.2ml/kg/min demonstrated no differences in mean LOS and CCLOS (p= 0.54 and 0.79 respectively). Peak VO_2 threshold of 15ml/kg/min also demonstrated no difference in mean LOS and CCLOS (p= 0.56 and 0.78 respectively). No patients had VE/VCO_2 >34. 2 patients had cardiac events in the immediate post-operative period, both having AT >10.2ml/kg/min and VO_2 >15ml/kg/min. There was no mortality at 1 year.

Conclusion: Established CPET thresholds do not identify patients at increased risk of mortality and morbidity following SPKT. The use of the CPET data in the listing process limits the conclusions, but sub-optimal CPET should not currently preclude from listing for SPKT. Further evaluation in a larger cohort of patients is required to elicit potential benefits in SPKT.

Category: Infection

P30

The use of a standard surveillance programme for the detection of bk polyoma virus in kidney transplant recipients significantly reduces the time to diagnosis

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Introduction: Surveillance testing for BK Virus Nephropathy (BKVN) in kidney transplant recipients (KTRs) is recommended by the BTS/RA although the evidence remains relatively weak. Prior to the local introduction of a surveillance programme, we wished to compare the time to diagnosis of BKVN using an investigation strategy based on clinical indications alone with that achieved using a standard surveillance programme (testing for BKV by PCR at monthly intervals for the first six months and subsequently at months 9, 12, 18, 24 and 36).

Methods: Microbiological and histological databases were retrospectively searched to provide a cohort of KTRs with BKVN. Further patient data were collected from the electronic records system and the medical notes. For each patient, the point in time at which testing for BKVN became clinically indicated was retrospectively-determined from the records of renal function, proteinuria, and concomitant evidence of over-immunosuppression. The following were then determined: time from transplantation to diagnosis of BKVN; time from retrospectively-determined indication for testing for BKVN to the diagnosis of BKVN ('clinical lag time'); time from retrospectively-determined indication for testing for BKVN to the subsequent screening test ('screening lag time'); duration of follow up from diagnosis of BKVN.

Results: We identified 18 KTRs (17 kidney-alone and one SPK transplant) with BKVN. Fourteen (77.8%) patients were male. The mean age was 55 years (range 33-74). Eight (44%) received organs from live donors. The indications for testing for BKVN were: deteriorating renal function in 12 (66%); new or deteriorating proteinuria in 4 (22.2%); CMV viraemia in 1 (5.6%); other in 1 (5.6%). The diagnostic test was renal transplant biopsy in 9 (50%) patients, blood PCR in 8 (44.4%) patients and urinary PCR in 1 (5.6%) patient. The mean time from transplantation to diagnosis was 392 days (range 60 – 986 days). The mean duration of follow-up from time of diagnosis was 482 days (range 1-1732 days). The mean 'clinical lag time' was 123 days (range 2 – 422 days). The mean 'screening lag time' was 71 days. When the lower of the two lag times was taken for each patient (indicative of the time to diagnosis if both clinical judgement and a screening programme were used together), the mean time from retrospectively-determined clinical indication for testing to diagnosis of BKVN fell from 123 days to 47 days.

Conclusion: The switch to a surveillance programme for BKVN from testing on clinical judgement alone should reduce the mean time to diagnosis from 123 days to 47 days. It also dramatically reduces the number of patients waiting over 100 days for diagnosis (from 6 patients down to 1 patient in this study). At this centre, the cost of implementing the 3 year screening programme would be ≈ £750 per patient (although a lower cost is achievable in centres with in-house PCR testing).

P31

Kidney and pancreas transplantation form HBcAb positive donors carry very low and preventable risk of HBV transmission to the recipient

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Introduction: There is variation of practice amongst UK kidney and pancreas transplant units in implanting grafts from HBcAb +ve donors due to the perceived risk of transmission of hepatitis B (HBV). Centres transplanting such grafts have variable practice of antiviral prophylaxis with lamivudine ranging from no prophylaxis to life-long prophylaxis. The aim of this study was to assess the rate of HBV infection in HBsAg -ve recipients of renal and pancreas allografts receiving organs from HBcAb +ve, HBsAg –ve donors.

Methods: We surveyed the UK kidney and pancreas transplant units regarding their practices of accepting HBcAb +ve donor grafts and the subsequent use of antiviral prophylaxis. All patients receiving a kidney (KT) and or pancreas (PT) allograft from HBcAb +ve, HBsAg –ve donors between Jan 2002 and Dec 2011 were identified retrospectively from the UK Transplant Registry. Post transplant virology data were also collected. All patients had a minimum follow-up of 2 years.

Results: The survey was incomplete at the time of this analysis and hence is not presented. A total of 277 patients were identified who underwent KT (n=252) or PT (n=25) from HBcAb +ve donors. Of these 2 KT recipients were HBsAg +ve prior to transplantation and were excluded from the analysis. Of the remaining 275, seven recipients (6 KT, 1 PT) had documented evidence of HBV positive virology post transplant (2.5%). At the time of this analysis, 178 patients (159 KT, 19 PT) had documented negative virology (65%) and 98 (93 KT and 5 PT) were recorded as ‘not reported’ (35%). Of the 11 KT in our centre, no HBV transmission recorded. All received 100 day lamivudine prophylaxis

Conclusions: The risk of HBV transmission following kidney and pancreas transplantation from HBcAb +ve donors remains low. Use of antiviral prophylaxis can help reduce this risk further. We suggest 100-day post-transplant lamivudine prophylaxis in kidney and pancreas transplantation. There is a need for clear guidelines for the safe and effective use of HBcAb +ve grafts

P32

Immune dysregulation in adult renal transplant recipients with chronic high level EBV DNAemia

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Introduction: We previously investigated EBV DNAemia patterns over 1 year in 500 stable adult renal transplant recipients. DNAemia was detected in 46% of patients and chronic high viral loads (CHVL) in 7%. Risk factors for DNAemia included time from transplant and EBV recipient seronegative status, while mycophenolate was associated with low rates of DNAemia. We now report a nested case control study recruiting 60 patients from the original 500, matched for age and time from transplant and stratified by viral load into; group 1, undetectable (n=19), group 2 low (<75% samples >1000copies/ml) (n=20) and group 3 CHVL (≥75% samples >1000copies/ml or ≥3 samples over >6 months with ≥10,000 copies/ml) (n=21).

Methods: We analysed serology (EBV VCA and EBNA-1 antibodies), DNAemia in whole blood and plasma, lymphocyte subsets, ultrasound examination of cervical lymph node chains and immunosuppression burden.

Results: All participants were EBV seropositive (antibodies to VCA). VCA levels were significantly higher in those with a CHVL. 7 patients had DNA detectable in plasma as well as whole blood (6/7 were in Group 3). This small sub-group had lower CD4:8 ratios than those with DNA in whole blood only (p=0.041), with higher CD8 counts (p=0.09). Group 3 had more individuals with lymph node numbers ≥2 measuring >0.5mm than Group 1 (62% v 26%; OR 4.6; CI 1.2-17.5; p=0.03). A “heavy” immunosuppression burden was identified in 0% of Group 1 and 29% of Group 3 (p=0.012). No association between mycophenolate and lymphocyte subset counts was identified. PTLD has not been identified in any of the 3 patient groups to date.

Conclusion: Chronic immunosuppression and immune dysregulation may predispose to EBV DNAemia, with similarities to the HIV setting. There may be scope to optimise immunosuppression in the setting of high level EBV DNAemia. A planned 5 year follow-up of the study patients will provide outcome data in relation to immune function and lymph node findings.

P33

ABO-incompatible kidney transplantation is a novel risk factor for BK nephropathy

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Introduction: Recent work has introduced an association between ABO-incompatible kidney transplantation and risk for BK-virus allograft nephropathy (BKVAN). In a single-centre analysis at Johns Hopkins Hospital, 11 out of 62 ABO-incompatible kidney allograft recipients were diagnosed with BKVAN (incidence 17.7%). 6 of these 11 BKVAN cases had been diagnosed by indication biopsy (incidence 9.7%). This 17.7% incidence among ABO-incompatible recipients was higher than HLA-incompatible (5.9%) and compatible (3.0%) kidney recipients respectively. To date no corroborating evidence has been published and the aim of our study was to analyse incidence of BKVAN in our ABO-incompatible kidney allograft recipient cohort as a comparison to the published data.

Methods: We analysed all ABO-incompatible kidney allograft transplants performed at our centre since the program began in 2007. Our desensitisation protocol includes pre-transplantation immunoabsorption (IA), with number of sessions dependent upon starting titre. Rituximab was utilised as part of the desensitisation protocol but has been omitted since 2011. Standard immunosuppression includes basiliximab induction with maintenance tacrolimus, mycophenolate mofetil and corticosteroids. Indication biopsies were performed in the context of allograft dysfunction (creatinine >20% rise +/- new-onset proteinuria), with no protocol biopsy framework. BK virus screening was on clinical suspicion only.

Results: 59 ABO-incompatible kidney transplant procedures have been performed at our institution since 2007. Six cases of BKVAN have been diagnosed on indication biopsy (incidence 10.2%). Median time post-transplantation for BKVAN diagnosis was 7 months (range 3-11 months). ABOi/BKVAN+ recipients were more likely to be male compared to ABOi/BKVAN- recipients, but this failed to achieve statistical significance (83.3% versus 43.4% respectively, p=0.076). Significant difference was observed in the frequency of ABO blood group distribution comparing donors (ABOi/BKVAN+; A1=0.0%, A2=16.7%, B=50.0%, AB= 33.3%, O=0.0% versus ABOi/BKVAN-; A1=60.4%, A2=7.5%, B=26.4%, AB=3.8%, O=1.9%, p=0.016) and recipients (ABOi/BKVAN+; A=50.0%, B=16.7%, AB= 0.0%, O=33.3% versus ABOi/BKVAN-; A=7.5%, B=20.8%, AB=0.0%, O=71.7%, p=0.009). Mean starting ABO titre (22 versus 67, p=0.112) and number of IA sessions (1.6 versus 2.6, p=0.036) was lower for ABOi/BKVAN+ recipients versus ABOi/BKVAN- recipients respectively.

Conclusion: The incidence of BKVAN among our ABOi cohort based upon indication biopsies was identical to published data from Johns Hopkins Hospital (10.2% versus 9.7% respectively). We advise routine screening for BK viraemia for all ABO-incompatible allograft recipients, with or without protocol biopsies, in the first year post kidney transplantation. Further investigation of the pathophysiology of BKVAN in ABO-incompatible kidney transplantation is required to shed light on underlying mechanisms.

P34

Comparison of organisms causing urinary tract infection after renal transplantation with those identified in normal individuals

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Introduction: Urinary Tract Infection (UTI) is a common complication following renal transplantation. It is usual practice to administer antibiotics peri-operatively, and use co-trimoxazole as prophylaxis against PCP infection after solid-organ transplantation. The use of antibiotics and instrumentation of the urinary tract may alter the pathogens causing UTI in the early post-transplant period.

Methods: Over a two year period, we identified the first microbiologically confirmed UTI that occurred in the six weeks following renal transplantation. We compared the organisms identified and their antibiotic sensitivity profiles against a matched control group of 249 samples from the same laboratory.

Results: 40 post-transplant UTIs were identified from 117 patients. Use and/or duration of ureteric stent was not associated with UTI in transplant patients.

% of Isolates Resistant	Control	Post-Transpl
Amoxicillin	51	50
Trimethoprim	40	75
Co-Amoxiclav	11	31
Levofloxacin	9	24
Cephradine	8	32
Nitrofurantoin	3	8

% Frequency of Organism	Control	Post-Transpl
E. Coli	79	28
Coliform	9	15
Enterococcus	3	40
Proteus	2	0
Pseudomonas	1	5
Other	6	12

Discussion: A number of reasons exist for the observed differences between these groups, including the recent or current antibacterial exposure of transplant recipients, the instrumentation of the urinary tract and the historical exposure of renal patients to antibiotics and nosocomial pathogens. Different protocols for empirical first line antibiotics should be applied to these patients, based on local resistance patterns within this select group.

P35

What is the long-term effect of CMV infection after renal transplantation?

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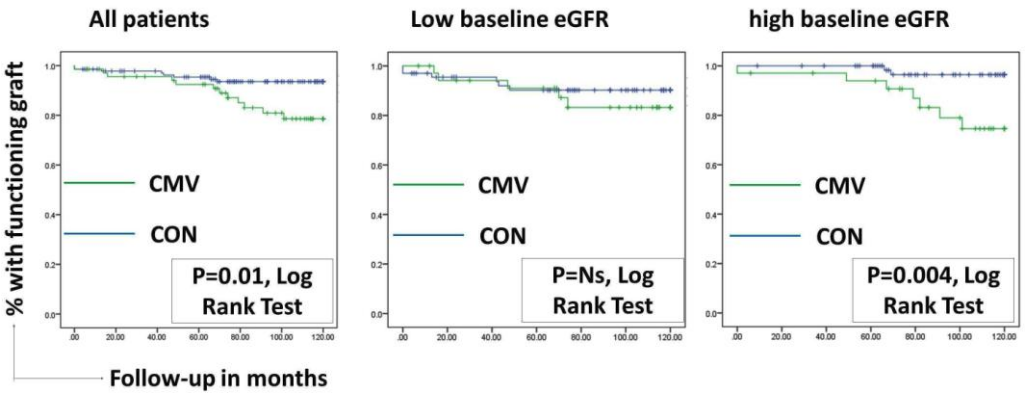
Introduction: Cytomegalovirus infection is a major cause of morbidity and mortality during the first post-transplant year. However with the current anti-viral prophylaxis the long-term effects of CMV are less likely to be significant. In this study we have retrospectively analysed the impact of a proven CMV viral infection on long-term graft outcomes.

Methods and results: A total of 70 renal transplant recipients with CMV infection were identified between 1988 and 2008. To match these patients 136 age, GFR and graft vintage matched controls (CON) were selected from our centre and the two groups were compared for graft survival, patient survival, new onset diabetes mellitus after transplantation (NODAT) and renal function as assessed by serial serum creatinine values and proteinuria. The median time to CMV infection was 3 months (IQR 0-7) with 94% of these occurring within the first post-transplant year. At 10 year follow-up there was no statistically significant difference in the patient survival and NODAT. However, patients with CMV had significantly worse death censored graft survival (P=0.01). Interestingly this difference in graft survival was only significant in patients with superior baseline renal function when compared to those with relatively poor baseline function (See figure below). Patients with CMV had significantly worse proteinuria (measured by urine Protein Creatinine Ratio) over a five year follow-up period when compared to the controls (1yr CMV 42, CON 25, P=0.26; 2yrs CMV 56.8, CON 21.4, P=0.07; 3yrs CMV 46.1, CON 29.9, P=0.2; 4yrs CMV 61.8, CON 31, P=0.04; 5yrs CMV 80.5, CON 28.4, 0.02) Serum creatinine was relatively higher in the CMV group (6 months CMV 176, CON 147, p=0.02; 1yr CMV 159, CON 156, P=Ns; 2yr CMV 171 CON 151, P=0.2; 3yr CMV 180, CON 146, P=0.02; 4yr CMV 183, CON 146, P=0.06; 5yr 160, CON 148, P=Ns). We have finally analysed the immediate effect of CMV on haemoglobin. By 1 year from the time of CMV infection, the haemoglobin levels were similar to those without CMV infection.

Conclusions: From this retrospective analysis we conclude that the main long-term impact of CMV infection is on allograft function. This was noticed to be more significant in patients with relatively superior baseline renal function.



P36

Introduction of routine surveillance culture to identify unsuspected microbial contamination of renal allografts during retrieval and transplantation

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Introduction: Contamination of an allograft at the time of retrieval can cause serious infection in the recipient and graft loss. Routine culture of preservation fluid and/or donor tissue may allow identification and preemptive treatment of potential infection. Following a serious graft-site fungal infection, we introduced this initiative and here present the results of this policy change.

Methods: Samples of preservation fluid and/or donor ureteric tissue were collected at the time of transplantation and cultured for bacterial and fungal pathogens. We defined a transmitted infection as later isolation of the same organism in the recipient from what would normally be a sterile site

Results: One or more organisms were cultured in 23 of 60 samples of preservation fluid and in 29 of 52 samples of ureteric tissue. In 12 samples (representing 10 donors and potentially affecting 17 renal allograft recipients) an organism was identified that was pathogenic, and 5 patients required additional treatment beyond our standard prophylaxis (intra-operative i.v. co-amoxiclav, then oral co-trimoxazole against PCP). One confirmed transmitted infection occurred within the first 6 weeks post-transplant (after a live-related kidney donation). All other cases of potentially significant innoculation occurred in DCD donations. There was no recognised bowel injury at time of retrieval in these donors and no association with any particular retrieval centre or NORS team.

Discussion: These findings reveal an unexpectedly high prevalence of microbial contamination of donated organs used for renal transplantation, particularly with respect to donation after cardiac death. Appropriate surveillance and early antibiotic therapy can prevent host infection in most cases. Transplant centres should consider routine screening for bacterial and fungal contamination of donated organs used for solid organ transplantation.

P37

Reducing CMV disease following kidney transplantation: a single centre audit

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Kidney transplantation improves quality and length of life for patients with End Stage Renal Disease. However, immunosuppression-related infections remain a challenge, especially that of late-onset cytomegalovirus (CMV) disease. In 2009, our centre updated its policy to extend CMV prophylaxis with oral valganciclovir (VGC) from 3 to 6 months in the donor positive (D+) / recipient negative (R-) setting and introduce the same in the D+/R+ and D-/R+ settings. The study aimed to determine whether this change in approach has improved CMV-related outcomes.

Data from patients receiving kidney / simultaneous kidney-pancreas transplants during April 2009–September 2012 (n=115; 43 D+/R-; 39 D+/R+; 33 D-/R+) was collected retrospectively and compared to our published data pertaining to January 2006–April 2009 (n=160; 61 D+/R-; 55 D+/R+; 44 D-/R+). Patients in receipt of organ grafts during the earlier and later periods were followed up for a minimum of 6 and 12 months respectively. Analysis was based on intention to treat.

Overall, CMV viraemia/disease was significantly reduced following the 2009 change in VGC prophylaxis (p=0.010) when analysed by a Kaplan-Meier Survival Curve. However, there was no significant difference in the D+/R- subgroup when analysed alone. Overall, graft failure and mortality was unaffected. Interestingly, 58% of patients in the post-2009 group did not complete the full course of prophylaxis.

These findings demonstrate that the updated policy has improved CMV-related outcomes. Whilst the lack of change in the D+/R- subgroup may suggest that there is no additional beneficial effect beyond 3 months of prophylaxis, it is more likely to reflect that the D+/R- group was the only setting in receipt of VGC prior to 2009.

Category: Ethics Law and Public Policy 1

P38

Challenges in the regulation of living organ donation

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Aims: Following the introduction of the Human Tissue Authority's (HTA) amended framework for the assessment of living organ donations, a commitment was made to review the first ten "complex" cases to be submitted in order to understand better the regulatory risks and challenges they posed, and whether these are increased from other cohorts of cases.

For the purposes of the HTA, complex cases are directed altruistic donations (these are living donations in which the donor and recipient did not have a relationship which pre-dated the need for transplant arising) and cases in which the donor is economically reliant on the recipient.

Methods: Primarily desk-based research. Review of the reports submitted by the Independent Assessors following their interviews with donor and recipient. Feed-in from the Board Members who assess such cases.

Results: Complex cases do not as a matter of course pose greater regulatory risk or challenge. The review highlighted that there are other factors which impact on the likelihood of a case requiring further scrutiny and posing greater challenge to the regulatory framework.

As yet, the HTA has not received a case where the donor and recipient met via a matching website, although these had been the cases about which there had been most concern within the transplant community and public more widely.

Conclusions: While some of the complex cases posed increased regulatory challenges, others posed none at all. We are entering a period in which the regulation of living organ donation is becoming increasing complex for a number of reasons, and many of these are not related to the relationship between donor and recipient.

P39

Substantial increases in deceased donor transplant rates could be achieved by altering the thresholds for accepting marginal donors

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Introduction: Expansion in donor numbers has not realised a proportional expansion in transplant numbers. Here we examine how alterations in the numbers and quality of cadaveric liver, pancreas and kidney offers between 2005 and 2012 have impacted upon transplant activity at a single UK centre.

Methods: A retrospective review of offers to our centre from April 2005 to March 2012 was performed. Donor characteristics, and numbers of kidney, liver and pancreas offers were recorded. As a marker for organ 'quality', the organ-specific 'donor risk index' (DRI) for organs offered and implanted was calculated.

Results: A total of 5628 organs were offered, with numbers increasing substantially, from 392 in 2005 to 1230 in 2012. This largely reflects an expansion in DCD offers; with the proportions of DCD kidney, liver and pancreas offers increasing from 19% to 77%, 6% to 64%, and 1%-62%, respectively. Transplant numbers for each organ have also increased, but more modestly (kidneys 68-127, livers 57-96, pancreases 4-22), with a significant increase in the mean DRI for each organ ($p<0.001$). Whilst in 2005 the mean DRI of organs offered was similar to those implanted, by 2012 the DRI for all organ types offered was significantly higher than that of those used. This is not solely due to changes in practice regarding DCD organ usage, because the DRI for kidneys implanted, which is not influenced by donor type, similarly increased during the study period. Despite the progressive use of more marginal organs, there was no observed difference in one-year graft survival from 2005 to 2011 [kidney (HR 0.42, 95% CI 0.8-2.25), liver (HR 1.07, 95%CI 0.43-2.65), pancreas (HR 1.47, 95% CI 0.1-2.18)].

Conclusions: Although we are transplanting more 'marginal' organs, there is an increasing discrepancy in the number and quality of organs offered to those used. Further increases in transplant numbers will likely require greater use of the large pool of marginal donors that are currently declined; the consistent survival times achieved for the organs implanted throughout the study period suggest that there may be potential to do so safely.

P40

Entrapment in living kidney donors

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Introduction: Feelings of entrapment in living kidney donors have not been researched in depth. Anecdotal evidence suggests that some donors may feel unable to discuss their concerns and doubts about donation with their recipient and may suffer any adverse psychological effects as a result. The aim of this study was to assess the extent of feelings of entrapment in living donors and the psychological consequences.

Methods: 100 living kidney donors were asked to complete a number of validated questionnaires 2-4 weeks before surgery. The questionnaire measured a variety of psychological factors including distress, stress, anxiety, personal wellbeing and social support. In addition, they were asked how easy it would be to discuss their concerns or doubts related to donation with their recipient, family, friends and the living donor team.

Results: 93 donors completed all components of the questionnaire. 33 (35.5%) would have found it difficult to discuss their doubts or concerns with their recipient. 30.5% of the sample found the same discussion with friends and family, and 16% with the living donor team, difficult. Those donors who would find communication with their recipient difficult scored worse on a range of psychological measures including personal wellbeing (30.1 vs. 27.6; p=0.038), distress (12.3 vs. 9.7; p=0.013), mood (0.94 vs. 0.35; p=0.006) and anxiety (12.4 vs. 10.3; p=0.02). Social support was also lower (65.9 vs. 71.1; p=0.005).

Discussion: A large proportion of living donors would find communication with their recipient difficult in the event of doubts or concerns about surgery and this may lead to feelings of entrapment. In many cases they would not be able to discuss this with the living donor team. The same donors suffer from increased distress, anxiety and lower mood and wellbeing. Living donor teams need to actively enquire about feelings of entrapment and attempt to elicit donor concerns or doubts prior to surgery.

P41

Final results on patients' views on the kidney allocation system in UK

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Introduction: The aim of this study was to assess patients' views and understanding on how kidneys are allocated on the deceased donor list in UK.

Methods: A two-part questionnaire was sent to all patients awaiting kidney transplantation at four transplant centres and three associated renal units in UK after research ethics approval (Ref 10/H083/61). Part-1 assessed patients' knowledge and priorities. Part-2 assessed patients' understanding and agreement after reading the UK kidney allocation guidelines.

Results: The response rate was 449/1332 (34%). Eighteen responded that they did not want to participate. The main issues patients think should be taken into consideration are the degree of tissue matching between recipient and kidney (86%), the time spent on the waiting list (78%), the likelihood the patient will die soon (76%), whether the patient will take their medication after transplantation (78%) and if they have a rare tissue type (71%).
The ability to pay (77%) and contribution to society (56%) were issues that most did not think should be part of the guidelines. 10% thought the ability to pay for a kidney should be part of the allocation system. Moreover, 53% thought that patient contribution to kidney failure should be part of the allocation system.
After reading the enclosed guidelines, there was an increase in understanding of the system from 39% to 84% saying that they mostly or completely understand the guidelines now. Finally, 74% said they mostly or completely agree with the current guidelines.

Conclusions: Patients were aware of some aspects of the current UK allocation system. When they are provided with the appropriate information the majority agree with the prioritization criteria. The majority also felt that the likelihood to die soon and compliance with medication should be part of the allocation system. Provision of more information and greater patient involvement should increase understanding of the system and help with management of expectations for patients on the transplant waiting list.

P42

Donation after cardiac death (DCD) renal transplantation in children in the United Kingdom

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Introduction: Renal transplantation using donations after cardiac death (DCD) donor kidneys account for around 42% of all deceased donor kidney transplants. NHSBT data shows that outcomes in adult patients following DCD renal transplantation were similar to those in adults receiving a kidney from a donation after brain death (DBD) donor, despite a higher incidence of delayed graft function. Although children listed for kidney transplantation should be considered as part of the new DCD donor kidney sharing scheme, there are limited data available on DCD kidneys transplanted into paediatric patients in the UK.

Methods: Data were obtained from the UK Transplant Registry on 28 paediatric kidney transplants performed in the UK using kidneys from DCD donor kidneys. Data were analysed in two cohorts; those performed before the year 2000 (n=15) and those performed between 2000 and 2012, inclusive (n=13). Paediatric recipients were defined as those aged less than 18 years at the time of transplant.

Results: In both eras, children that received a kidney from a DCD donor were predominately aged 10 to 18 years at the time of their transplant (73% and 62%, respectively), had waited in excess of one (46%) and two years (31%), were most commonly level 3 (53% and 54%) or level 4 (40% and 23%) HLA-mismatched, had a cold ischaemia time of less than 20 hours and experienced delayed graft function in 2 of 12 (17%) cases where the initial graft function had been reported.

The time to asystole was 6 to 35 (median 15) minutes and the functional warm ischaemia time (WIT) was 14 to 50 (median 24) minutes and the standard WIT was 8 to 22 (median 14) minutes. The donor serum creatinine in all 13 cases post-2000 was 22 to 103 (median 49)µmol/l. The recipient serum creatinine at three months post-transplant was 61 to 183 (median 90)µmol/l.

Discussion: In the post-2000 era, the limited evidence suggests that paediatric kidney transplants that utilise kidneys from DCD donors have excellent post-transplant graft survival with encouraging renal allograft function. The presented evidence suggests that kidneys from DCD donors should be used in paediatrics.

P43

Well-being in living kidney donors with primary carer status does not differ significantly from recipients on haemodialysis

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Introduction: Little is known about psychological well-being prior to living kidney donation, with the majority of studies using health-related quality of life instruments, such as the SF-12 or the SF-36. The aims of this study were to determine how pre-operative psychological well-being differed between living donors and recipients and to determine whether factors such as carer status were influential.

Methods: 151 donors and recipients awaiting surgery were recruited to a prospective study. They were asked to complete a number of validated questionnaires measuring personal well-being, mood, distress, stress, anxiety, life satisfaction and self-esteem.

Results: 101 living kidney donors and 50 living kidney recipients participated. Gender and age were equivalent (55.4% male vs. 52% male; $p>0.05$) (45 years (*sd* 12.89) vs. 43 years (*sd* 14.72); $p>0.05$). Recipients were found to have lower pre-operative wellbeing, mood, self-esteem, health related quality of life and life satisfaction and demonstrated higher stress and distress ($p<0.001$) than donors.

Donors who were primary carers of their recipient (43.6%) had lower wellbeing (31.2 vs. 27.1; $p<0.001$) and higher stress (5.5 vs. 3.9; $p=0.006$), anxiety (12.4 vs. 9.8; $p<0.001$) and distress (12.4 vs. 8.8; $p=0.001$) than their non-carer counterparts ($p\leq0.01$). A separate analysis comparing carers with recipients on dialysis (n=27) demonstrated that differences in personal well-being and stress that were no longer significant (27.2 vs. 24.7 and 5.5 vs. 5.9; $p>0.05$).

Discussion: This study has demonstrated that primary carer status in living kidney donors is associated with markedly inferior quality of life prior to surgery. Levels of personal well-being and stress in primary carer donors are not significantly different from patients on dialysis. Identification of primary carer status and interventions to improve psychological well-being may be useful.

P44

Increased circulatory death donation rates: which patients are benefiting?

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Introduction: DCD rates have increased substantially in the last 7 years, but it is not clear who receives and who benefits from DCD kidney transplants, particularly as the mean age of DCD donors continues to increase and DCD kidney allocation remains exempt from the national scheme. This study examines donor profile and outcomes according to age at listing for renal transplantation in one UK centre, where twice as many DCD as DBD kidney transplants are currently performed.

Methods: Outcomes of adult patients listed for renal transplantation between 1/8/2002 and 31/7/2012 were analysed, comparing elderly patients (age over 65) to a younger cohort (age under 45). Time of listing, death, de-listing and transplant details were recorded; DCD organs were allocated according to a local algorithm based on the national allocation scheme.

Results: Of patients listed for renal transplantation, 570 were aged under 45 and 139 over 65, with the proportion of elderly patients listed increasing annually (6% in 2002 cf 17% in 2012). Kaplan-Meier analysis confirmed that elderly patients were delisted at a faster rate than younger patients, with 46% vs 78% remaining active after 4 years. A significantly greater percentage of patients under 45 were transplanted (420 (74%) cf 73 (53%), >65). Median time to transplantation was not significantly different between the two groups (500 days, <45 cf 355 days, >65, $p=0.8$). Notably, whereas younger patients received an equivalent proportion of organs from DBD, DCD and living donors, elderly patients received predominantly DCD kidneys (64%, $p<0.001$), reflecting preferential national allocation of DBD organs to younger, HLA-matched, recipients. Graft survival was similar in the two groups and in both, transplantation conferred a survival benefit, although this did not reach significance in the elderly cohort (5-year survival: 82% in transplanted group vs 69% in non-transplanted group, $p=0.16$).

Conclusions: The time-frame for transplantation of elderly patients is limited. As numbers listed increase, greater use of elderly DCD donors may alleviate demand, yet still provide survival advantage.

P45

Three month psychological outcomes in living kidney donors and recipients - a lack of significant morbidity

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Introduction: Living donor studies reporting quality of life (QoL) data have previously demonstrated a decrease in QoL at 3 months. These studies have principally used generic health related QoL tools, such as the SF-36, which may not fully capture the psychological impact of donor surgery. The aims of this study were to conduct an in-depth analysis of living donor psychological outcomes at 3 months and to compare these with outcomes in recipients.

Methods: 150 living donors and their recipients were recruited to a prospective longitudinal study between Aug 2012-2013. They were asked to complete a range of validated psychological measures pre-operatively and 3 months after surgery. These included measures of wellbeing, stress, distress, mood, anxiety, life-satisfaction, self-esteem and physical health related quality of life.

Results: 81 donors and 37 recipients completed questionnaires at both time points. Pre-operative scores were significantly worse in the recipient group across each of the factors measured ($p \leq 0.01$). At 3 months there was no change in any of the psychological measures in the donor group ($p > 0.05$), except for a decrease in physical health related QoL (28.4 vs. 25.1; $p < 0.001$). Conversely, the recipient scores for all factors, except stress, improved significantly ($p < 0.05$). The pre-operative difference between donors and recipients in wellbeing, distress, stress, life-satisfaction and self-esteem were no longer significant ($p > 0.05$) and only a significant difference in mood (0.54 vs. 1.64; $p = 0.013$) and physical health related QoL (28.4 vs. 21.4; $p = 0.002$) persisted.

Discussion: This study has demonstrated understandable psychological differences between donors and recipients prior to surgery. By 3 months this difference is reduced, mainly due to improvements in the recipient group. There is no psychological benefit or morbidity in donors at 3 months; a finding which is contrary to findings from other studies. Due to the complexities of living donation, generic health related QoL tools may not be sufficient for use in living donors and future research should avoid using them in isolation.

Category: Clinical Immunosuppression 1

P46

CYP3A5/ABCB1 combined genotype has similar influence on pharmacokinetics of immediate and prolonged release tacrolimus in renal transplant recipients

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Background: Tacrolimus is available in twice daily immediate release formulations and as a once daily prolonged release preparation, Advagraf®. The oral bioavailability of tacrolimus varies greatly between individuals and depends largely on the activity of both the cytochrome P450 3A (CYP3A) subfamily of enzymes responsible for first-pass metabolism and the drug transporter P-glycoprotein (P-gp) encoded by the *ABCB1* gene. Expression of CYP3A decreases and expression of P-gp increases along the length of the gut. In this study, we assessed whether the well-defined influence of the *CYP3A5*3* and *ABCB1* genotypes on the pharmacokinetics of immediate release tacrolimus also applies for the prolonged release preparation.

Methods: A total of 43 patients receiving a stable dose of twice daily tacrolimus were changed to treatment of the same total daily dose of Advagraf® with 24 hour pharmacokinetic profiles before and two weeks after the change. *CYP3A5* / *ABCB1* genotypes were determined using a Roche Lightcycler®. Patients were allocated to 4 genotype categories based on expression of CYP3A5 (*1/*1 or *1/*3), CYP3A5 non-expressers (*3/*3), high expressers of P-gp (*3435C>T*: CC) or low expressers of P-gp (CT or TT). Tacrolimus blood concentrations were measured by liquid chromatography/tandem mass spectrometry and individual pharmacokinetic parameters were analysed using analysis of variance (ANOVA).

Results: Dose-adjusted $AUC_{0\text{-}24}$, dose-adjusted C_{max} and dose-adjusted trough concentration were significantly lower in *CYP3A5* expressers than in *CYP3A5* non-expressers for both preparations (Table). The influence of the *CYP3A5* and *ABCB1* genotype on tacrolimus exposure was the same for the prolonged release preparation Advagraf® as for the immediate release preparation, Prograf®.

Genotype			Twice daily tacrolimus			Advagraf®		
CYP3A5	ABCB1	n	$AUC_{0\text{-}24}$	C_{max}	C0	$AUC_{0\text{-}24}$	C_{max}	C0
Expresser	High	9	120.8	11.8	3.5	109	9.9	3.1
Expresser	Low	10	197.6	16.5	7.1	203	16.4	5.8
Non-expresser	High	2	452	29.3	16.0	329.2	23.8	9.7
Non-expresser	Low	22	327.5	24.9	11.4	305.4	21.3	9.6

Conclusions: CYP3A5 expression had a major influence and *ABCB1* genotype had a minor influence on tacrolimus exposure irrespective of preparation. Pharmacogenetic dosing strategies based on these genotypes are likely to be equally applicable to prescribing Advagraf® as to twice daily formulations.

P47

Non-compliance assessed by variability of blood calcineurin inhibitor (CNI) levels is associated with poor long-term graft survival in kidney transplant recipients (KTRs)

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Background: Non-compliance with treatment remains a major problem in clinical renal transplantation. There is an emerging interest in the development of objective markers of non-compliance. Variability of CNI drug levels is one such marker. However, there are no large scale studies that examined this marker. In this large single centre retrospective analysis, we examined the relationship between the overall graft outcomes and CNI variability.

Methods and results: A total of 10 plasma CNI levels were examined between the 2nd and 3rd post-transplant year for the analysis of variability for each of the 1235 consecutive KTRs. Variability was calculated as the percentage of the variance of these levels. Patients were divided into three tertiles based on their CNI $_{(2y-3y)}$ variability. Any patients with graft loss before the third transplant year were excluded from this analysis to exclude the effect of early CNI therapeutic modifications. Overall graft survival was examined over a 10 year follow-up period by Kaplan Meier analysis. The mean variability was significantly higher for younger KTRs (age lowest tertile (20yrs), 24.7 vs. middle tertile (40yrs), 21.9, vs. highest tertile (59yrs), 22.9; $P<0.05$, ANOVA). Overall, patients in the highest tertile group of CNI $_{(2y-3y)}$ variability had the worst overall graft survival when compared to the other tertiles. When the analysis was stratified by the age of the KTRs, patients with high variability in the lowest tertile group of age (i.e. youngest age group) had the worst outcomes. CNI $_{(2y-3y)}$ variability was not strongly associated with increased overall graft loss in older KTRs.

The utility of CNI level variability was re-examined in a validation set of 118 KTRs with allograft dysfunction. All these patients underwent an indication biopsy for either creeping creatinine or proteinuria. Low CNI level variability was associated with significantly improved post-biopsy graft survival in this selective group of patients with allograft dysfunction. However, there were no significant differences in the prevalence of DSA or CAMR in patients with high CNI variability.

Conclusions: To conclude, CNI drug level variability is a potential marker for predicting allograft outcomes. This has to be validated in further prospective studies.

P48

The impact of CYP3A5, CYP3A4*22 and ABCB1 polymorphisms on tacrolimus dosing and levels in Scottish renal transplant patients

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Introduction: Genetic polymorphisms (SNPs) of CYP3A5, CYP3A4 and ABCB1 (p-glycoprotein) have been shown to influence tacrolimus pharmacokinetics, in renal transplant patients. There have been no studies of the influence of these SNPs on tacrolimus in Scottish renal transplant patients to date.

Methods: Between January 2008 and August 2012, 185 renal transplant recipients were included in the study where stored DNA and access to clinical records were available. DNA samples were genotyped for SNPs of ABCB1 exon 26 (3435C>T), CYP3A5 (6986A>G) and CYP3A4 intron 6 (CYP3A4*22) using a Taqman® drug metabolism genotyping assay and real-time PCR technique. Tac dose/trough levels were evaluated at 14 time points in the first 12 months and correlated with clinical outcome data (acute rejection, creatinine, graft and patient survival).

Results: There were 126 (68.1%) males 59 (31.9%) females in the study with a mean age of 47.20±13.42 years. 149 (80.5%) patients did not express CYP3A5 (GG, *3/*3), 30 (16.2%) expressed one A allele (GA, *3/*1) and 6 (3.2%) two A alleles (AA, *1/*1). CYP3A5 expressers (*3/*1, *1/*1) were prescribed significantly higher doses of tacrolimus by the end of the 1st week post-transplant than non-expressers (*3/*3), 9.79±2.96 mg vs 7.44±2.51 mg. ($p<0.0001$). Trough tacrolimus levels were lower in CYP3A5 expressers immediately post-transplant (4.18±2.46 µg/L) than the non-expressers (8.60±4.94 µg/L), $p<0.0001$ and at every time point up to 2 months. The dose-corrected Tac level (level/dose) was significantly lower post-transplant in CYP3A5 expressers (0.68±0.39) compared with non-expressers (1.39±0.82), $p<0.0001$ and at every time point. ABCB1 and CYP3A4 SNPs did not significantly affect tacrolimus pharmacokinetics. Renal function, graft and patient survival and acute rejection were not influenced by variations of SNPs of CYP3A5, CYP3A4*22 or ABCB1.

Conclusion: Expression of CYP3A5 in renal transplant patients results in higher tac dose requirements, reduced tac levels immediately post-transplant and reduced dose corrected tac levels. This did not, however, affect clinical outcome.

P49

Conversion to mammalian target of rapamycin inhibitors and calcineurin inhibitor discontinuation in liver transplantation: a systematic review and meta-analysis of randomised controlled trials

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Introduction: Calcineurin inhibitor (CNI) nephrotoxicity represents a significant cause of morbidity following liver transplantation. Even though, mammalian target of rapamycin (mTOR) inhibitors are often used to circumvent this problem, the evidence base for this approach is not well defined.

Methods: We conducted a meta-analysis of all randomised controlled trials to test the hypothesis that, following liver transplantation, conversion to mTOR inhibitors (sirolimus or everolimus) compared to CNI continuation is associated with an improvement in renal function at 1 year. We searched all major databases and conference proceedings (April 2013) and contacted corresponding authors. We determined the pooled estimate of change in renal function (Glomerular Filtration Rate) and relative risk (RR) estimates of adverse events associated with mTOR based therapy at 1 year. Heterogeneity was assessed using the Q statistic and I^2; we accounted for timing of intervention and baseline renal function.

Results: Nine randomised control studies, with a total of 1,870 patients, met the final inclusion criteria. Use of an mTOR inhibitor was associated with a significant improvement in renal function of 6.1 mL/min [95% confidence interval (CI): 1.7-10.4, p=0.006] at 1 year. The risks of death (RR: 1.04, 95% CI: 0.62-1.75), graft loss (RR: 0.75, 95% CI: 0.34-1.66) or infection (RR: 1.18, 95% CI: 0.94-1.48) were not increased following conversion to an mTOR inhibitor. However, sirolimus or everolimus treatment increased the risk for acute rejection (RR: 1.99, 95% CI: 1.40-2.83), mouth ulcers (RR: 8.12, 95% CI: 2.80-23.52) and adverse event related treatment discontinuation (RR: 2.36, 95% CI: 1.29-4.29). Fewer patients on mTOR inhibitors needed renal replacement therapy (RR: 0.40, 95% CI: 0.19-0.84) after 1 year at the expense of higher proteinuria risk (RR: 2.71, 95% CI: 1.63-4.52), although reporting for these outcomes was incomplete.

Discussion: Use of mTOR inhibitors enables CNI discontinuation in liver transplant patients with a significant improvement in renal function after 1 year. This strategy needs to be balanced against an increased risk of adverse events.

P50

Adherence to immunosuppression treatment for kidney transplantation – a single centre experience

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Introduction: Non-adherence is a common problem and has been associated with higher risk of late acute rejection and allograft loss. We wanted to assess the scale of the problem in our transplant population and in particular to assess if there is a difference between once daily drugs and twice daily drugs.

Methods: Between January – June 2013 we invited all 194 renal transplant patients to take part in an interview to assess adherence status. We used the BAASIS interview questionnaire to assess taking and timing of immunosuppression drugs and whether patient's self-perception of adherence within the previous 4 weeks. We specifically looked at once daily medications (tacrolimus prolonged release [Advagraf}, sirolimus [Rapamune]; OD group) and twice daily medications (tacrolimus [Prograf], ciclosporin [Neoral]; BD group). We looked at whether there was a difference in adherence between once daily and twice daily medications. We also looked at whether there was a difference in adherence with regards to age, time since transplant, employment status and those who missed more than 2 appointments within the previous 1 year.

Results: We had 176 included in the study (52 on Neoral, 54 on Prograf, 60 on Advagraf, 10 on Rapamune 10). 36% were non-adherent, 13% missed 1 dose, 28% mis-timed their dose. Overall adherence rate was 59.4% for BD group vs 71.4% for OD group (p=0.071), taking dimension was 83.2% for BD group vs 92.9% for OD group (p=0.045), timing dimension was 69.8% for BD group vs 75.7% for OD group (p=0.248). Patient who were adherent scored themselves higher on average (96.3% vs 87%, p=<0.001).Younger patients (less than 40 years) were significantly more likely to be non-adherent (p=0.014).

Discussion: Patients taking once daily immunosuppression drugs were significantly less likely to miss a dose within the previous 4 weeks.

P51

The impact of CYP3A5, CYP3A4 and ABCB1 polymorphisms on renal transplant patients converted to once-daily tacrolimus (Advagraf®)

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Introduction: Genetic single nucleotide polymorphisms (SNPs) of CYP3A5, CYP3A4 and ABCB1 (p-glycoprotein) have been shown to influence tacrolimus pharmacokinetics, in renal transplant patients taking twice daily tacrolimus (Prograf®). The newer once-daily preparation of tacrolimus (Advagraf®) has different pharmacokinetics and is absorbed more distally in the gut. There is limited data on what effect these SNPs have on Advagraf® pharmacokinetics.

Methods: 43 patients who were converted to Advagraf® between September 2008 and December 2011 and where stored DNA was available were included in this study. DNA samples were genotyped for SNPs of ABCB1 exon 26 (3435C>T), CYP3A5 (6986A>G) and CYP3A4 intron 6 (CYP3A4*22) using a Taqman® drug metabolism genotyping assay and real-time PCR technique. Tac dose/trough levels were evaluated at the time of conversion and 1, 2, 3, 6 and 12 months and correlated with clinical outcome data (acute rejection, creatinine, adverse events).

Results: Patients were converted from Prograf® to Advagraf® at a median of 5 months (0-72 months) from transplantation. Expressers of CYP3A5 (*1/*3 or *1/*1 alleles) required significantly higher doses of Prograf® than non-expressers (*3/*3) 15.00±6.30 vs 5.85±2.91 mg, $p<0.0001$. The dose of Advagraf® was similarly higher at conversion (16.00±6.08 vs 6.17±3.62 mg, $p<0.0001$) and at every time point up to and including 12 months post conversion. There was no significant difference in the Tac levels between CYP3A5 expressers and non-expressers. The dose-corrected Tac level was significantly lower at every time point in CYP3A5 expressers. Creatinine did not differ between CYP3A5 expressers/non-expressers. There was no difference in acute rejection between CYP3A5 expressers/non-expressers. ABCB1 and CYP3A4 SNPs did not significantly affect tacrolimus pharmacokinetics of Advagraf® or clinical outcome.

Conclusion: Expression of CYP3A5 in renal transplant patients taking Advagraf® requires higher doses to achieve therapeutic tac levels with no impact on clinical outcome.

P52

5-Year outcomes of a randomized prospective trial of Alemtuzumab induction with Tacrolimus maintenance monotherapy compared to IL2R blockade with Tacrolimus/MMF maintenance in kidney transplantation (CamTac Trial)

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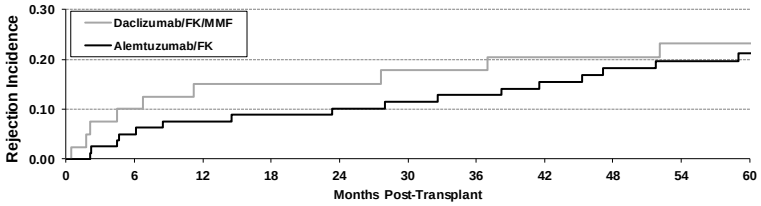
Introduction: We have undertaken medium-term (5 year) follow up of patients who took part in the CamTac trial comparing kidney transplant outcomes after Alemtuzumab induction with early (7 day) steroid cessation followed by Tacrolimus maintenance monotherapy (n=82) vs IL2R monoclonal (Daclizumab) induction with early steroid cessation and Tacrolimus/MMF combination maintenance. (Arms 'A' & 'D')

Results: Follow-up and outcome data were available on 98.5% of patients (2 in arm Alemtuzumab moved abroad). At 5 years, patient survival, death-censored graft survival, and survival with functioning graft were closely similar between the arms:

	Alemtuzumab-FK	IL2R-FK/MMF	
Patient survival	92.1%	94.7%	p=NS
Death-censored graft survival	88.8%	85.0%	p=NS
Survival with functioning graft	81.3%	80.5%	p=NS

The incidence of rejection, which showed a non-significant trend towards being higher in the IL2R arm at 1 and 3 years, had equalised at 5years:



Conclusions: The minimalist regimen of Alemtuzumab induction with 7-day steroid exposure and Tacrolimus maintenance monotherapy results in good graft and patient outcomes at 5 years, which are closely comparable to those produced by a more conventional immunosuppressive drug combination.

P53

Skin cancer and immunosuppression type in long-term renal transplant recipients: a case-controlled analysis

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Introduction: Renal transplant recipients are 3 times more likely to develop skin cancer (SC) when compared to age-matched general populations, and this is associated with increased morbidity and mortality. The reason underpinning the increased prevalence in this group most probably relates to treatment with immunosuppression (IS), however the association is not yet fully understood.

Objectives: To determine the prevalence of SC in our long-term kidney transplant recipients. To assess whether SC prevalence is related to the type of IS taken by this patient cohort.

Methods: We collected data from a retrospective cohort of all (n= 335) long-term (> 8 years) kidney recipients attending our annual review transplant clinic between 2010-2013. We documented the total number of SCs, time to development of first SC post transplantation and IS treatment. For the analysis of IS as risk factor, patients with SC were matched to an equal number of controls in age, total years from first transplant and skin type criteria. McNemar's test was used to test the effect of IS on risk of SC.

Results: 67 (21%) patients had at least one SC. In these a total of 281 basal cell carcinomas, 157 squamous cell carcinomas, 4 melanomas and 1 Kaposi's sarcoma were diagnosed. The average time to development of a SC was 13 years (range 2-32 years) after transplant. There were no statistically significant differences between case and control patients in the proportion of patients taking any of the IS drugs one year before the first SC. However the difference in the proportion of patients who developed SC after taking azathioprine, compared to controls, is borderline significant.

Drug	% SC Cases	% Matched Controls	McNemar's p-value
Prednisolone	62.7	62.7	1
Azathioprine	61.2	46.2	0.05
Cyclosporine	61.2	52.2	0.21
Tacrolimus	20.8	13.4	0.30
Mycophenolate Mofetil	26.8	31.3	0.66

Conclusion: We have identified a high prevalence of SC in our long-term kidney transplant patients. In our analysis we found that prevalence was not significantly related to the type of IS taken, although preliminary results point to azathioprine as a risk factor, and tacrolimus as protective. Further work to determine the relevance of cumulative IS dose is warranted.

Category: Marginal Transplantation 1

P54

Acceptable 1 year graft function following double kidney transplants from expanded criteria donors

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Introduction: Kidney transplantation is the optimal treatment for most patients with end-stage renal failure. In the UK, there are more than 6000 patients on the kidney transplant waiting list and organ shortage is a major challenge. One solution is to use both kidneys from a sub-optimal donor for a single recipient[1]. To date, there are limited follow-up data on this practice.

Aims: To analyse outcomes in double kidney transplants from expanded criteria donors at a single UK centre.

Methods: Donor and recipient demographic data was obtained on all double kidney transplant performed (n=26). Follow-up data (graft function, as indicated by 1 year creatinine, graft survival and patient survival) were obtained by manual search of the local transplant, biochemistry and pathology databases.

Results: 52 kidneys were obtained from 19 DCD and 7 DBD donors and implanted into 26 recipients. Biopsies were performed on all kidneys and scored by a histopathologist to guide allocation strategy. The mean Remuzzi score of double kidney transplants was 4.19 +/- 0.96). Median donor age was 73 years (range 49-79) and median recipient age 64 years (range 21-75). Delayed graft function occurred in 11/26 patients (42%). One patient required double graft nephrectomies at day 4 due to renal vein thrombosis. Three patients underwent removal of one of the two grafts within the first week post-transplant, but had reasonable residual function. There was one early death at day 10 (recipient aged 65 years) secondary to fulminant HSV hepatitis. 1 year creatinine was 143 +/- 40 µmol/l. 1 year transplant survival was 90% (47/52 kidneys) and patient survival was 96%.

Discussion: This study confirms acceptable outcomes from double kidney transplant, utilising kidneys from older donors that would otherwise have been discarded.

Reference: 1. Fernandez-Lorente L et al. *American Journal of Transplantation* 2012: 12; 2781–2788

P55

Delayed graft function: a syndrome or a diagnosis?

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Introduction: Delayed Graft Function (DGF) is an important prognostic indicator following renal transplantation. We hypothesised that different patterns of DGF reflect different pathological processes and may be associated with differing graft outcomes after transplant.

Methodology: Retrospective analysis of 762 consecutive renal transplants was performed. Serum creatinine of all patients with DGF was charted serially for the first 30 days following transplantation and patterns of DGF were identified. Measurements to describe the trends in serum creatinine were as follows: length of time on haemodialysis (t^{HD}); time to peak creatinine (t^{peak}); time for creatinine to half ($t^{½}$); time for creatinine to all within ten percent of baseline ($t^{10\%}$); maximum creatinine (Cr_{max}); best creatinine (Cr_{min}). These were correlated with serum creatinine at 1-year, 1-year graft and patient survival.

Results: 24.7% of patients developed DGF. There was no association between the pattern of DGF and 1 year graft or patient survival or serum creatinine at 1 year . $t^{½}$ greater than 15 days was associated with a higher serum creatinine at 1 year than patients with $t^{½}$ less than 5 days (300.6+/-54.3 vs. 211.3+/-26.0µmol/l; $p<0.01$). Patients with serum creatinine >180µmol/l at 1 year had longer t^{HD} and $t^{½}$ than those with serum creatinine at 1 year ≤180µmol/l (9.2+/1.3 vs. 7.0+/-0.7, $p=0.03$ and 11.6+/-1.7 vs. 6.0+/-0.4, $p<0.001$ respectively). $t^{½}$ of 6.5 days was best predictive of a serum creatinine ≤180µmol/l at 1 year (sensitivity 67.3%, specificity 79.4%, AUC 0.70).

Conclusions: DGF is not a single entity, rather the common presentation of a heterogenous variety of pathologies. The rate of resolution of renal function once the creatinine has begun to fall is predictive of long-term graft outcome.

P56

12 month outcomes of expanded criteria deceased donor kidney transplantation

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Introduction: Expanded criteria donors (ECDs) are those aged ≥60 or aged 50-59 with 2 of: hypertension, death from cerebrovascular cause or terminal serum creatinine >1.5mg/dL. They can be sub-divided into a junior group (under 70yrs, jECD) and a senior group (70yrs and over, sECD). Our use of these organs has recently increased and outcome data from such donors are limited.

Methods: We analysed results for all deceased donor (DD) kidney transplants performed at our centre in 2012. Variables included patient and graft survival, eGFR, biopsy rate and total length of all inpatient stays over 12 months (LOS).

Results: Of 114 DD transplants, 56 (49%) were from standard criteria donors (SCD) and 58 (51%) were from ECD. Of the ECDs, 39 were jECD and 19 were sECD. There were 3 deaths with a functioning graft, 1 SCD at day 59 and 2 ECDs at days 17 and 136 respectively. By 12 months, 3 recipients were lost to follow-up but all other recipients remain alive. All-cause graft loss rates at 12 months were 6 (11%) SCD, 8 (14%) ECD, 5 (13%) jECD and 3 (16%) sECD. The K-score was significantly different ($p<0.001$) between 37 SCD biopsies (mean 2.6, SD 1.4) and 39 ECD biopsies (mean 4, SD 1.6). Primary non-function rates were 1.8% for SCD, 6.9% for ECD, 5.1% for jECD and 10.5% for sECD. Delayed graft function rate was 32% in the SCD, 48% in ECD, 46% in jECD and 53% in sECD. Median MDRD eGFR was significantly higher in the SCD group than the ECD group at 3 months (48 vs 37; $p=0.001$), 6 months (49 vs 33; $p<0.001$) and 12 months (51 vs 34; $p<0.001$). There was no difference in GFR between jECD and sECD recipients. There was no significant difference in the number of biopsies or in median LOS (17.8 days SCD vs 20.2 days ECD; $p=0.498$) in the first 12 months.

Conclusions: These data show that ECD allografts do have higher rates of primary non-function, delayed graft function and lower eGFR at 3, 6 and 12 months. However, the lack of inferiority of the older ECDs compared with younger ECDs should encourage use of these organs.

P57

Renal transplantation in older patients: distinct survival advantage albeit with a higher infection risk

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Introduction: There is an annual increase in the number of elderly patients with end-stage renal failure (ESRF) requiring renal replacement (RRT) therapy. In this cohort, renal transplantation remains the optimal form of RRT with evidence for improved survival. However, clinician reticence persists in light of scarce resources and concerns regarding potential complications, especially due to immunosuppressive load. We aimed to compare survival and transplant risk in elderly patients post transplantation with a comparable group on the waiting list.

Methods: Retrospective analysis was performed of older patients (>60 years old), on dialysis for ESRF, who underwent kidney transplantation (n=164) and those remaining on the waiting list (n=400) as a comparable control (May 2007 - Nov 2012.) The primary endpoint was patient mortality. Potential confounding factors (co-morbidities, age, gender, time on dialysis and time on waiting list) were analysed. The incidence of opportunistic infections in the transplanted group was also analysed (CMV, BK/JC and EBV) as a secondary endpoint.

Results: Overall mortality in the transplant group was 4.3% (7/164) which was significantly lesser than the mortality in the waiting list group (10.5%; 42/400; p=0.02.) The 30-day and 1-year survival in the transplant group was 99.4% (163/164) and 96.8% (153/158) respectively, which was not significantly different from the waiting list group (100% and 97.8%). However, the 5-year survival was significantly better in the transplant group at 97% (27/30) vs 43.8% (32/73) in the waiting list group (p=0.0001). There was no difference in potential confounding factors. Opportunistic infection rate in the transplant group was 40.1% (CMV- 23%, BK/JC- 3.7%, EBV-3%, Recurrent UTI's- 11%).

Conclusions: Renal transplantation offers a significant survival advantage over dialysis in elderly patients with ESRF who are suitable for transplantation. However, the high rates of opportunistic infections in the elderly transplanted patients may suggest an element of over-immunosuppression in this cohort of patients necessitating consideration of a tailored regimen.

P58

Is the UKKDRI useful for predicting renal transplant graft survival in a single centre?

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Background: The varied spectrum of donor kidney quality has resulted in the development of donor risk indices to guide clinicians in predicting transplant outcome. Until recently, these indices were not specific for UK practice. However in 2012, *Watson et al* devised the UK Kidney donor risk index (UKKDRI) in order to predict transplant outcome. We addressed whether the UKKDRI would be applicable to our kidney transplant unit where the local demographic mix is highly heterogeneous and not reflective of the average UK population.

Methods: A retrospective single centre analysis of 335 renal transplants from deceased donors between 2005 and 2011. Patients were scored according to the UKKDRI, and correlated against known graft survival at year 1.

Results: At 1 year, 90% of patients with a UKKDRI score of ≤0.87 (n=60) and 91% with a score between 0.88-1.02 (n=43) continued to have a surviving kidney transplant. Patients with a UKKDRI score of 1.03-1.34 (n=93) and ≥1.35 (n=139) had a 1 year graft survival of 81.7% and 79.1%, respectively. This reached statistical significance ($\chi^2 = 8.52$, df = 3, $p = 0.04$).

Conclusion: These results concord that graft survival rates fall as the risk index increases. We conclude that the UKKDRI is applicable to our local population and can be used to predict renal transplant outcome at 1 year in an ethnically diverse recipient population. We suggest that it should be used as a decision-making tool in the allocation of deceased donor organs.

P59

A systematic review and meta-analysis of high-dose perioperative erythropoietin to improve graft function in deceased donor renal transplantation

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Background: The shortage of donor kidneys for transplantation has led to the increased use of organs from donation after circulatory death (DCD) and extended criteria donors (ECD). These are more susceptible to ischaemia reperfusion injury (IRI) with subsequent effects on graft function. There is much interest in methods of ameliorating IRI that may improve graft outcomes. This systematic review examined the effects of erythropoietin administration in deceased donor renal transplantation

Methods: A systematic review of randomized control trials (RCTs) was conducted to compare the effects of high-dose perioperative erythropoietin (EPO) with control on delayed graft function (DGF) in deceased donor renal transplantation using MEDLINE, Embase, Cochrane Library, the Transplant Library and trial registries. Meta-analysis was performed using a fixed effects model.

Results: From a total of 3033 publications, five RCTs published between 2010 and 2012 were identified and included, with a total of 397 patients. The total number of patients with DGF in the EPO group was 87 out of 195 (45%), compared with 101 out of 200 (51%) (odds ratio 0.76, 95% confidence interval 0.49 to 1.18, P=0.22). The incidence of thrombotic complications was 19 out of 195 (10%) in the EPO group, compared with 14 out of 200 (7%) in the control group (odds ratio 1.43, 0.70 to 2.92, P= 0.32).

Conclusion: This meta-analysis did not show a significant effect of erythropoietin on delayed graft function in deceased donor renal function. However, there was a numerical reduction in the rate of delayed graft function and studies were homogenous. A larger RCT, adequately powered, is required to give further information.

P60

Transplantation of liver and kidney from donors with malignancy: A 10 year experience from a single centre

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Introduction: Donor malignancy, once an absolute contraindication, is increasingly being considered for transplantation. Transplantation of such organs pose important clinical and ethical questions regarding informed consent, uncertainty of outcome, immunosuppression and follow up strategy. We review our experience of kidney and liver transplantation from donors with identified malignancy.

Method: Our institution's prospectively maintained database was complemented by the data obtained from NHSBT. All patients who received renal or liver transplants in the ten years between April 2003 and March 2013 were included.

Results: 71 recipients received 53 kidney and 18 liver transplants from donors with malignancy. These include 50 (70% overall, 34 kidney, 15 liver) CNS malignancy (Grade I-IV); 6 (8.4%) kidney; 3 (4.2%) lymphoma; 2 (2.8%) breast; 2 (2.8%) lung; 2 (2.8%) CIN; and one each (1.4%) of bowel, gallbladder, melanoma, atrial myxoma, papillary thyroid and liposarcoma. In 83% of recipients, the malignancy was known before transplantation. The remaining were identified when transplanting other organs (mostly kidney), donor autopsy, unsuspected biopsy or following occurrence of cancer in the recipient. Six kidneys, 3 ipsilateral and 3 contralateral with RCC were also transplanted.

Median ages of recipients were 48.5 for kidneys (range 3-71) and 53.5 for livers (range 21-62). One recipient developed donor-derived lung cancer in the transplant kidney (malignancy in donor unknown at time of transplant) after 2 years and subsequently died. One liver transplant recipient developed donor-transmitted lymphoma (known after transplant) and subsequently died. One liver transplant recipient with incidental donor GB cancer had a re-transplant and subsequently died. One kidney was removed on day 5 for diagnosis of renal cancer on implantation biopsy. Seven recipients developed donor un-related cancer; 3 skin, 2 lymphoma, 1 pancreas, 1 parotid, 1 nephroureteric TCC and 1 cholangiocarcinoma. No recipient developed cancer where donor had CNS or renal malignancy. The graft survival rate at 1,3 and 5 years was 97%, 89% and 76% for kidney and 88%, 75% and 66.6% for liver respectively. Patient survival at 1, 3 and 5 years was 92%, 79.4% and 65.5% for kidneys and 82.3%, 66.6% and 44.4% for livers. Median follow-up of 3.6 years.

Conclusions: Where donor malignancy is known, judicious use of kidney and liver transplant achieves satisfactory outcomes. Occasionally malignancy is diagnosed after implantation and the risk of transmission remains uncertain. The risk of transmission from donors with CNS and low-grade renal malignancy remain extremely low. When considering the risk of cancer transmission, the mortality on the waiting list should also be considered.

P61

Hypothermic machine perfusion during extended cold ischaemic times – an opportunity to improve pathways of care in cadaveric renal transplantation

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Introduction: The logistics of cadaveric renal transplantation are largely driven by Cold Ischaemic Time (CIT). However, to achieve successful outcomes in complex donor-recipient combinations, recipient and operative issues demand equal consideration. Extending CIT without detriment to graft function would therefore be of value. We have investigated the role of Hypothermic Machine Perfusion (HMP) as a tool by which such an extension of CIT might be obtained.

Methods: Cadaveric kidneys were allocated to a storage method depending on predicted time to theatre. Kidneys to be transplanted between 8am – 8pm in the dedicated transplant theatre remained in Static Cold Storage. If predicted operating time was out-of-hours, the kidney was transferred to HMP and transplanted at the earliest opportunity on the elective transplant list.

Results: 75 kidneys were transplanted from SCS; 68 from HMP. Median CIT was 24 hours in the HMP group compared to 13 hours in the SCS group ($p=<.0001$). 18 HMP kidneys suffered from DGF (26%) compared to 36 (48%) in the SCS group ($p=0.01$). There were no other significant differences in graft or post-operative complications.

Discussion: This study demonstrates that comparable outcomes can be achieved following longer CITs by utilising HMP storage rather than traditional SCS. This effect is likely to be multi-factorial; including improved recipient preparation, better peri-operative conditions and the inherent effects of HMP itself.

Category: Transplantation Medicine 1

P62

Twenty years with a functioning kidney transplant: what happens next?

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As a consequence of substantial advances in kidney transplantation, increasing numbers of recipients are entering their third decade with a functioning graft. Little is known about the clinical course of recipients after 20 years of graft function. This study aimed to address this.

Methods: All recipients of kidney transplants performed in Northern Ireland from 1968 to 1992 were included (n= 706). Clinical data on transplant and recipient outcomes is recorded prospectively. Factors associated with 20 years of graft survival were identified. Information on graft function and recipient co-morbidities at 20 years was collected and subsequent clinical events were recorded.

Results: There were 177 (25%) recipients with a functioning graft at 20 years. Younger recipient age, fewer HLA mismatches, and a living donor kidney were associated with 20 year survival. Twenty years after transplantation, the mean eGFR (MDRD) was 55 ml/min/1.73m^2. 58% of recipients were hypertensive; the mean number of anti-hypertensive agents prescribed per patient was 1.5. By 20 years after transplantation, 28% of recipients had a cancer diagnosis, 16% had a cardiovascular event, and 10% had new onset diabetes after transplantation (NODAT). The median graft and recipient survival in this group was 26 years. There were 23 cases of death-censored graft loss in this cohort; no recipient who had a graft biopsy received specific treatment. In the third and fourth decades of graft function, 35% of recipients had a *de novo* cancer diagnosis, 25% had a cardiovascular event and 6% developed NODAT. There were 56 deaths within the follow up period; the most common cause of death was cancer.

Conclusion: After 20 years of graft function, the greatest threat to both recipient and graft is the development of cancer and cardiovascular disease. Consideration should be given to minimisation of immunosuppression in this recipient cohort.

P63

Vitamin D deficiency is independently associated with adverse graft outcomes after renal transplantation

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Background: It is now established that vitamin D is functionally pleiotropic with diverse functions. Although there are studies that showed that vitamin D deficiency is highly prevalent in renal transplant recipients, its impact on long-term outcomes is not clear. In this study, we have analysed the independent impact of vitamin D deficiency on graft outcomes.

Methods and results: 504 renal transplant recipients had their vitamin D levels checked in 2008. Vitamin D deficiency was defined as a level <50nmol/L as per WHO guidelines. All patients were followed up for 5 years from the date of blood sampling. In this population, the prevalence of vitamin D deficiency was very high at 66.5% with a significantly higher prevalence in older (71.9% vs. 60.9%, P=0.006) and female recipients (male 62.1% vs. female 73.2%, P=0.006) and in relatively new transplants (recent transplants 72.3% vs. old transplants 60.6%, P=0.003). Not surprisingly mean PTH levels were significantly higher in patients with vitamin D deficiency and this was true in those with stable graft function (creatinine <130mmol/L) as well. Patients who were vitamin D deficient had significantly worse total (77% vs. 92%, P<0.001) and death censored graft survival (89% vs. 96%, P=0.009) when compared to those with normal levels. This was much significant in patients with relatively worse baseline renal function (67% vs. 89%, P=0.01). The analysis of the interaction between vitamin D and PTH levels and overall graft survival showed that patients with vitamin D deficiency had significantly worse outcomes even in the absence of secondary hyperparathyroidism. Vitamin D deficiency was associated with worse graft survival independent of recipient age, PTH levels, gender and time since transplantation in a multivariate Cox Proportional Hazards model (HR 2.7, 95% CI 1.5-4.9, P=0.001).

Conclusions: In conclusion, vitamin D deficiency which is highly prevalent in renal transplant recipients is associated with adverse graft outcomes. This study raises an important question about the need for a prospective study of vitamin D replacement in renal transplant recipients.

P64

Long term graft outcome following kidney transplantation in obese patients – a single centre experience

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Background: There is conflicting evidence regarding the outcome for obese patients following transplantation with few studies focussed on long term graft survival. The aim of this study was to compare the long term graft outcome for obese and non obese patients at our centre.

Methods: Consecutive patients with Body Mass Index (BMI) 15-40kg/m^2 who underwent a single organ renal transplant at Queen Elizabeth Hospital, Birmingham between Jan 2004 and July 2009 were included. Patients were divided into three groups depending on BMI (15-20kg/m^2, 20-30kg/m^2 or 30-40kg/m^2). Graft survival was calculated from date of transplant and censored at time of last follow up, or death with functioning graft.

Results: 573 patients were included in the study. There were 37(6.5%) BMI 15-20kg/m^2, 408 (71.2%) BMI 20-30kg/m^2 and 128 (22.3%) BMI 30-40kg/m^2. The underweight patients were significantly younger (mean age 32.0 $p<0.01$) and more likely to be female (62.2%, p0.002) compared to the other BMI groups. There was a significant difference in the outcomes for the different BMI groups with worst outcome in the BMI 30-40kg/m^2 group and best in the BMI 20-30kg/m^2 (log rank test $p=0.021$). Fig 1.

Conclusion: The graft survival for obese patients in this study was worse than for the non-obese group. This was largely due to a high early failure rate with problems such as vascular thrombosis. However the attrition rate after the first few weeks was similar to the non-obese cohort. Given the initial vulnerability of such grafts, careful management of obese recipients in the perioperative period is of paramount importance. Furthermore, comparable long term graft outcomes for obese recipients may be achievable with considered donor selection and optimisation of perioperative care.

P65

Long-term outcomes after haplo-identical living donor renal transplantation

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Introduction: '000' mismatch living donor renal transplant is presumed to be the gold-standard of living donor transplantation, however typing specificities vary, and greater accuracy is now possible. Tolerance-inducing or immunosuppression (IS) minimisation regimes are being trialled in such patients, as they represent a very low immune risk, however little data exists regarding the potential burden of IS in haplo-identical recipients.

Methods: Retrospective analysis of all patients (n=62) identified as receiving a '000' mismatch by NHSBT's definition in our unit between 2003-2011. Subequently, 6 patients were identified as having DSA (Cw, DP, DQ). 3 patients receiving an ABO-i transplant were excluded. 42 patients were identified as receiving a 5 x '0' mismatch from a sibling with 2 shared haplotypes transplanted (A, B, Cw, DR, DQ). Data was collected on outcomes including IS withdrawal, number of IS maintenance agents and post-transplant cardiovascular, infection & cancer morbidity.

Results: 42 patients transplanted with living donors with 2 shared haplotypes were identified. Mean follow up duration is 1400 days (range 435 – 3555). The majority of patients (69%) were receiving their first graft. Graft and patient survival were 100%. 31% of patients were identified as being on standard triple IS therapy; 21 patients (50%) were on 2 agents and 5% of patients were maintained on a single agent. Infections were the most common complication occurring in 50% of patients; new onset diabetes was reported in 12 patients (28%) while new cardiovascular morbidity was reported in 10 patients (24%). When analysed by IS regimes (number of agents), these complications were not statistically significant. One patient on 2 agents was treated for basal cell carcinoma.

Discussion: Patients with a true 00000 mismatch have excellent graft outcomes; however they are subject to complications of immunosuppression. While novel tolerance strategies are being pursued, more effort could be made to minimise current IS regimes.

P66

Survival of sensitised patients presenting for renal transplantation

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Introduction: For patients who are sensitised to HLA, the likelihood of a cross-match negative offer for transplantation via the deceased donor (DD) waiting list is low, and patients are likely to be sensitised against a possible living donor (LD). Options for such patients include waiting for a suitable DD offer, paired scheme entry or opting for antibody incompatible transplantation (AIT). We analysed survival for patients *without* a compatible living donor comparing paired scheme entry to AIT or remaining on the DD list.

Methods: Retrospective analysis of all kidney transplant candidates with a CRF of >20% at 1/1/2007, and all subsequently listed sensitised patients until 31/12/2012. Patients subsequently removed from the transplant waiting list were excluded from analysis (n= 12), as were patients with a compatible living donor outwith the paired scheme (n= 34). 4 groups were compared: 1. Untransplanted; 2. DD recipients; 3 Paired scheme matched recipients & 4: AIT recipients.

Results: Of the 247 sensitised candidates (mean follow up 1653ddays +/- 1261d), 151 (61%) patients remained untransplanted; 80(32%) received a deceased donor transplant and 11 (4.5%) an antibody incompatible (ABO-i or HLA-i) LD transplant. 20 patients were entered into the paired scheme, of whom 5 (25%) were matched through the scheme and included. 5yr survival for untransplanted patients was 82.1% v 92.5% for DD tx recipients v 100% paired scheme & 100% for the AIT group (log rank test p=0.003). Graft survival was comparable between groups. (2. 74%; 3. 80%; 4.82% p>0.05). Sex & ethnicity had no effect on transplantation status but previous transplantation and mean CRF between groups were significant factors (Mean CRF grp 1. 80.7%; grp 2 67%; grp 3 76.8%; grp 4 86.2% p = <0.05) .

Discussion: All attempts should be made to optimise chances of transplantation for sensitised patients at the time of listing. Patients with a high CRF who have been previously transplanted should be identified and counselled regarding their risk of death on the waiting list. Despite the presence of HLA antibody, transplant outcomes for sensitised patients are good. Novel strategies to transplant highly sensitised recipients with no LD should be considered.

P67

does the donor-recipient age gradient for renal transplants matter? a single centre experience

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Background: In renal transplantation it is established that donor age has an important impact on graft outcome. However, age mismatch between donor and recipient may also act as an important factor influencing graft function and this can be quantified by the Donor-Recipient Age Gradient (DRAG = donor age minus recipient age). We assessed the impact of DRAG on renal graft outcomes at a single UK transplantation centre.

Methods: A retrospective analysis of 303 patients with deceased donor kidney transplants between January 2005 and December 2011 was performed. Patients were allocated to 4 groups according to their DRAG. Group A ≤-21 years, Group B -20 to -1 years, Group C 0 to 20 years and Group D ≥21 years. Outcomes were renal function at 1 year and delayed graft function (DGF). Baseline data of donor and recipient age, number of HLA mismatches, cold ischaemic time (CIT) and donor type (DCD or DBD) were each analysed.

Results: Patient numbers were: Group A n=25, group B n=124, group C n=133 and group D n=21. HLA mismatch, CIT and donor type were not significantly different between the groups (HLA mismatch p=0.314, CIT p=0.330, donor type p=1.0). The renal function (and DGF) for the 4 groups was as follows: group A eGFR 62±17.0 (63.0%), group B 52.8±22.3 (49.6%), group C 47.1±18.6 (44.7%), group D 47.1±26.2 (58.35%). These results show that group A had a statistically higher eGFR relative to the other groups (p=0.002), yet a higher rate of DGF (χ^2 = 64.4, df = 3, p =0.0001). This is not due to an excess of DCD in group A relative to the other groups (p =1.0).

Conclusion: We have demonstrated that DRAG has an important influence on renal transplant function. When the donor is >20 years younger than the recipient there is an associated better graft function at 1 year. Although the higher rate of DGF cannot be fully explained, we are reassured by the good medium-term outcome for this group.

P68

Low incidence of cardiac death after renal transplantation in patients undergoing pre-emptive coronary angiography and revascularisation

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Because cardiovascular disease is one of the commonest and potentially treatable causes of death with a functioning renal allograft, all our high risk patients, including those > 50 years of age are offered pre transplant coronary angiography and revascularisation if flow-limiting disease is identified.

In this study we examine the outcomes of 572 transplant patients [m:f 368:204, mean age 56.7 ± 9.4 yrs, range 25 – 78] who underwent coronary angiography prior to renal transplantation. 133/572 [23.3%] had normal coronary angiograms, 296/572 [51.7%] had mild to moderate disease, 98/572 [17.1%] underwent intervention for significant disease [73 PCI, 25 CABG] and 45/572 [7.9%] with significant disease were managed medically. The mean follow up post transplant was 52 ± 28 months.

Only 9/572 [1.57%] of these patients died from cardiac causes. 87 other cardiac events occurred. 37/572 [6.5%] patients had NSTEMIs, 12/572 [2.1%] STEMIs and 38/572 [6.6%] had arrhythmias. Cardiac event-free survival at 1, 3 and 5 years was 94%, 90.4% and 87.8% for patients with normal coronary angiograms, 93.6%, 91.7% and 86.9% for patients with mild to moderate findings, 86.7%, 86.7%, 69% for patients with significant findings and 80.6%, 73.1%, 65.5% for patients who underwent intervention.

Cox-regression analysis showed that the presence of coronary artery disease requiring intervention increased the risk of subsequent cardiac events [Exp(B)=2.735, p=0.002]. History of pre-transplantation diabetes [Exp(B)=2.665, p=0.001] increased the risk for death.

This study, the largest of its kind, shows that patients managed in this way have a very low incidence of cardiac death after transplantation. Patients with normal or mild coronary disease have a very low incidence of subsequent cardiac events. However, patients with significant disease, despite intervention, continue to have cardiac events post transplant and this group of patients merit additional study and focus to reduce the burden of post transplant cardiac disease even further.

P69

The challenges and outcome of living donor kidney transplantation in paediatric and adolescent age group in a developing country: A critical analysis from a single centre of north India

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Introduction: Renal transplantation is the preferred treatment of choice for children with end-stage renal disease. The focus and priorities on pediatric renal transplantations are still inadequate in prospect of developing country like India; there is a paucity of data on their long-term outcome. This retrospective study is an attempt to evaluate the outcome and challenges for pediatric renal transplantation in Indian prospect

Methods: Seventy live related paediatric and adolescent transplantations were reviewed retrospectively. Variable analysed were; aetiology of ESRD, pre-transplant renal replacement modality, waiting period, Source of funding, donor relationship, surgical complications, rejection episodes, Compliance to immunosuppression(IS), graft survival and overall survival at one and five years.

Results: The cohort consisted of 13 (18%) female and 57 male (82%) recipients. Mean age was 14±1.4 years. The most common aetiology of ESRD were chronic glomerulonephritis (n=43). Mean waiting period was 4.3 ±1.6 years and financial issues (69.5 %) and donor issues (23%) were important contributing factors. Parent being the donor in 95% of transplantation and mother was the donor in 80% of cases. Total 14 acute rejection episodes were observed in six months and 6 had late acute rejection between 6 mo -1 yr. 34.5% recipients were poorly compliant to immunosuppression (Finances was major barrier). 15 post surgical complications (immediate and delayed) were noted in 13 patients. One yr, 3 yr and 5 yr graft survival rates were 94.3%, 89.2% and 66.8% respectively. Overall survival rates were 95.7%, 96.4% and 94.1 % for 1 yr, 3 yr and 5 yr respectively.

Conclusion: In our scenario the spectrum of aetiology of ESRD differs from west with Chronic glomerulonephritis being most common aetiology. The recipients are predominantly male with much older age. One year graft survival was encouraging but 5 year graft survival was clearly inferior as compared to the developed countries, which reflect the limitations and challenges we faced in related to financial constrain , lack of cadaveric donor and poor state of care in paediatric patients with renal failure.

Category: Surgical (inc Cardiothoracic)

P70

Bilateral lung transplantation (BLT) vs single lung transplantation (SLT) for end-stage chronic obstructive pulmonary disease (COPD) - impact on waiting times, early & mid-term survival

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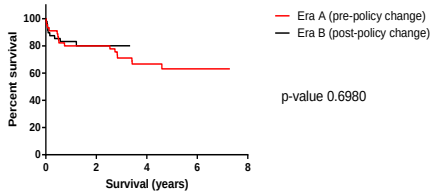
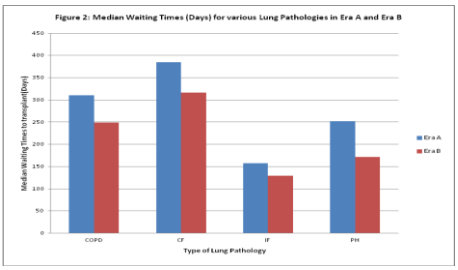
Introduction: Perceived improved outcomes after bilateral (BLT) rather than single (SLT) lung transplants for chronic obstructive pulmonary disease (COPD) prompted a policy change to perform BLT for COPD. We reviewed waiting times, early- & mid-term survival and function to see any impact on these patients and all other lung pathologies-Cystic Fibrosis (CF), Pulmonary Hypertension (PH), Idiopathic Fibrosis (IF).

Method: Database records of all patients who underwent lung transplantation from August 2006 till August 2013 were reviewed, divided into Era A (pre-policy change on 01/07/2010) and Era B (post-change).

Results: COPD patients in Era A and Era B were similar; Era A(23M:22F) age 53.4 +/-7.5 years, Era B(29M:19F) age 53.2+/-7.3 years; procedure was 20SLT:25BLT and 1SLT:47BLT respectively. 1 and 3 year survival was not significantly different, *p= 0.7325* (Figure 1). Mean FEV1, a measure of function, was significantly better in Era B at 6 months (2.59 v 2.04, *p=0.0111*), and 1 year (2.56 v2.04, *p =0.0216).* Waiting times for all lung pathologies, including COPD, decreased in Era B, reflecting a 45% increase in departmental activity (Figure 2). Waiting times for IF patients is decreased from median 147 days to 131.5 days which reflected better access to SLT's.

Figure 1: Survival Outcomes for Era A and Era B





Conclusions: Waiting times have shortened, rather than lengthened, for COPD patients, and have not worsened for any group. Increased activity has improved access for all pathologies, and IF patients may benefit from less competition for SLT. Although COPD survival has not improved, better early function may reduce late attrition**.**

P71

Blood transfusion after lung transplantation - impact on early function and survival

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Introduction: Blood Transfusion is associated with higher morbidity and mortality after general cardiothoracic surgery but impact within the transplant population is unclear. We investigated the profile of blood product transfusion in the bilateral lung transplant (BLT) population and impact on function and survival.

Method: 311 adult patients who underwent BLT between 2003 and 2013 were retrospectively reviewed. Patients were stratified according to pre-transplant diagnoses and amount of blood products transfused within 24 hours of transplant.

Results:174M:137Fpatients(mean age=41.4+/-14.0) underwent BLT, using cardiopulmonary bypass for cystic fibrosis(48.87%), fibrotic lung disease(12.21%), emphysema(27.01%), bronchiectasis(5.79%), pulmonary hypertension(1.29%) and others(4.50%). Median number of red blood cells(RBC) in the first 24 hours were 3(0-40)units, fresh frozen plasma(FFP)=2(0-26)units, platelets(PLTS)=1(0-7)units. Transfusion rates based on pre-transplant diagnosis were not significantly different. Survival was not influenced by whether patients were transfused with more or less than the median number of units of RBC(p-0.162) or FFP(p-0.298), but was adversely affected by PLTS(p-0.032). Mean FEV1 at 6 months was significantly better for patients transfused with more than median number of units of RBC, FFP and PLTS(p<0.0001).

Figure 1: Survival Outcomes for Groups stratified by median number of RBC transfused in the first 24 hours

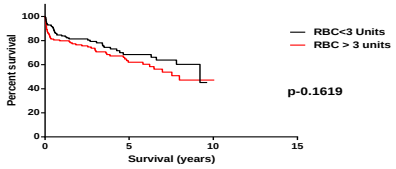
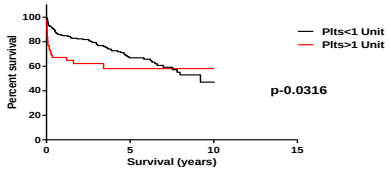


Figure 2: Survival Outcomes for Groups stratified by median number of Platelets transfused in the first 24 hours



Conclusions: Unlike general cardiothoracic surgery, blood transfusion has no effect on survival but administration of platelets has an adverse effect. Tranfusion rates are not significantly influenced by pre-transplant diagnoses. Interestingly, lung function at 6 months is significantly better for patients with more blood products transfusion.

P72

Donor CD4 T cell chimerism is common following lung transplantation, but the duration and the percentage of chimerism varies markedly between patients

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Introduction: Following solid organ transplantation, survival of passenger donor lymphocytes creates a chimeric state that is poorly understood, but may influence host auto- and allo-immune responses. Here we examine how donor CD4 T cell chimerism in lung transplant recipients is influenced by donor cell phenotype, the degree of donor / recipient HLA mismatch, and natural killer (NK) cell alloreactivity.

Methods: The presence and persistence of donor CD4 T cell chimerism following primary lung transplantation was determined by flow cytometric analysis of recipients' peripheral blood at set time-points after transplantation, with donor CD4 T cells identified on the basis of expression of mismatched donor HLA (n=21).

Results: Donor CD4 T cell chimerism was observed in all patients. The level of chimerism detected varied from 0.06% to 6% of the recipient CD4 T cell population. Donor CD4 T cells disappeared from the recipients' peripheral blood in three distinct patterns: early (within 6 weeks); intermediate (3 – 6 months); and late (> 11 months). All patients received poorly matched grafts; with 12 of 21 patients mismatched at more than >5 HLA antigens and recipient NK cell alloreactivity against donor cells expected in 10 of 21 recipient/donor pairs. There was, however, no correlation between the duration of donor CD4 T cell chimerism and either the degree of HLA mismatch or NK cell alloreactivity. Similarly, transcriptional analysis revealed similar phenotype and polarisation of the donor CD4 T cell population irrespective of whether purified from recipients with durable or transient chimerism.

Conclusions: Donor CD4 T cell chimerism following lung transplantation is common, but the duration of chimerism varies considerably between patients and the factors responsible for this variation are not immediately obvious.

P73

The efficacy of the primary extension technique in the prevention of dialysis access-associated steal syndrome (DASS)

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Background: DASS has been reported to affect 3-8% of haemodialysis patients. Its incidence is even higher in diabetic patients. Most studies have focused on the management of DASS and very few on its prevention. We report our experience with use of the Primary extension technique in the prevention of (DASS) in diabetic haemodialysis patients.

Methods: Between September 2001 and August 2012, the primary extension technique was used consecutively in diabetic patients requiring haemodialysis access. It entails the formation of a fistula between the median vein and the radial or ulnar arteries about 2-3 cm below the brachial artery bifurcation, thus preserving part of the blood supply to the hand. All patients were evaluated for patency, adequacy of needling and the absence of steal symptoms.

Results: There were 57 patients with Male: female 27:30, and age range 37-80. Only one patient developed DASS (1.7%). On investigation, he was found to have the fistula formed distal to the origin of a posterior branch with the bifurcation further distally. Symptoms improved with revision of the fistula. In 8 patients the cephalic vein became thrombosed (14%) but because the basilic vein was also well developed it was simply transposed instead of forming a new fistula. In 6 patients the cephalic vein was too deep to needle and required superficialisation (10.5%). 9 patients died during follow up (15.7%).

Conclusion: Our 11 year experience has demonstrated that the 'Primary extension technique' is a safe and effective procedure for prevention of DASS, with a patency rate comparable to that of brachio-cephalic fistula. Additional advantage of this technique is maturation of both cephalic and basilic veins.

P74

The effectiveness of the secondary extension technique in the management of dialysis access-associated steal syndrome - 12 year follow up

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Aims: To report the effectiveness of the secondary extension technique in the management of dialysis access-associated steal syndrome DASS

Methods: Between May 2001 and April 2013, 28 patients dialyzing through brachio-cephalic or brachio-basilic fistulas presented with steal syndrome. These patients were managed by using the 2ry extension technique. This entails closing the fistula and moving the anastomosis from the brachial artery to either the radial or the ulnar arteries 2-3 cm below the brachial bifurcation. In 13 patients a jump graft was needed. The procedure could not be performed in one patient due to marked calcification of the brachial artery and its bifurcation and the fistula had to be ligated. Male: female 15:11 with an age range of 29-78. 11 patients were diabetics. Out of the 28 patients 24 had a brachio-cephalic and 4 had a brachio-basilic fistula.

All patients were evaluated for resolution of symptoms, patency and adequacy of needling.

Results: There was a complete resolution of steal symptoms in 27 patients (96.2%). In one patient the fistula suddenly thrombosed 6 months after revision due to stenosis but was salvaged radiologically. Another patient developed needling difficulties and was found to have a stenosis which was managed radiologically. 3 patients had gangrenous changes and required digital amputation. In 3 patients the fistula thrombosed during follow up and could not be salvaged (11.1%). 3 patients were lost to follow up and 2 patients died.

Conclusion: Our 12 year experience demonstrates that the extension technique is an effective treatment for DASS.

P75

Implementation of a novel transplant-specific WHO surgical checklist

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Introduction: The WHO Safe Surgery Checklist was introduced to reinforce safety practices and foster better communication and teamwork between clinical disciplines. Transplantation presents specific challenges which are not covered by this checklist. An ABO blood group incompatible transplant, for example, is something the checklist is designed to prevent. In order to improve patient safety in the transplant population, our centre introduced a transplant-specific WHO checklist in order to cover the particular requirements of modern organ transplantation. We looked at the uptake and compliance with this checklist following its introduction in September 2013.

Method: All patients who received a transplant (including kidney and kidney-pancreas) at our centre following formal introduction of the new checklist were included. A retrospective analysis was made of patients' notes and the electronic patient record (EPR). The parameters were the presence of the new checklist in the notes and fullness of completion. For comparison, a similar analysis was made of the presence in the notes and completeness of documentation for the standard WHO safe surgery checklist.

Results: 27 patients were transplanted at our centre over 2 calendar months following introduction of the transplant-specific WHO checklist. The new checklist could be identified In 11 patients' records (41%). It was fully completed in 8 (30%), partially completed in 2 and not completed in 1. Documentation for the standard WHO safe surgery checklist was present in 23 (85%) of patients' notes and 20 of these (74%) were fully completed. There were no adverse events reported.

Conclusions: Although these figures are likely to be falsely low due to the loss of some documentation, we have found that the uptake of the new checklist has been sub-optimal. The challenge for our department will be to improve knowledge and availability of the checklist and stress its importance through education and training of the multi-disciplinary team. We believe it is an important step in improving patient safety in contemporary transplantation.

P76

Renal artery stenosis and calcification in potential donors for live donor nephrectomy: a national survey of transplant surgeons

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Introduction: In live donor nephrectomy (LDN), consideration must be given to donor kidney anatomy. Variations in renal anatomy are common and there remains some debate about donor suitability in the context of renal artery stenosis (RAS). However, very little is known about the implications of LDN in donors with non-flow-limiting renal artery calcification (RAC).

Methods: An online survey was distributed to 101 renal transplant surgeons from 23 institutions in the UK. Opinions were sought on donor suitability with unilateral or bilateral RAS or non-flow-limiting RAC, in the context of anti-hypertensive treatment (0,1,2 or 3+ agents) and presence or absence of other vascular disease.

Results: The survey response rate was 53.5%. Multiple variables were considered, for example, in potential donors with atherosclerotic RAS (on 0,1,2 or 3+ anti-hypertensive agents), the percentage of respondents who would consider LDN was: if unilateral: 86.5%, 76.9%, 39.2%, 4.2% (Fleiss' Kappa 0.368); if bilateral: 18.9%, 17.0%, 11.3%, 0% (Fleiss' Kappa 0.0337). In donors with non-flow-limiting RAC and no other vascular disease (on 0,1,2 or 3+ anti-hypertensive agents), the percentage of respondents who would consider LDN was: if unilateral: 97.9%, 91.9%, 38.0%, 2.0% (Fleiss' Kappa 0.628); if bilateral: 65.2%, 54.4%, 24.4%, 0% (Fleiss' Kappa 0.263). Similar comparisons were completed for patients with other anatomical considerations and comorbidities, showing variable levels of inter-observer agreement.

Discussion: RAC is highly associated with calcification in other vascular beds, independent of traditional risk factors. There is no evidence-based consensus on whether to accept donors with RAS or RAC and this national survey has demonstrated that there is a tendency for UK transplant surgeons not to consider unilateral non-flow limiting RAC as a contraindication to LDN, however consensus varies depending on the number of anti-hypertensive agents, comorbidities and whether both renal arteries are affected. Most respondents consider bilateral RAS a contraindication to LDN, irrespective of comorbidities. Further studies are required to investigate.

P77

Role of laparoscopic surgery in management of malfunctioning peritoneal catheter

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Background: Peritoneal catheter malfunction is a common complication of Peritoneal Dialysis (PD) with high failure rate with conservative management. Catheter replacement was historically, the standard surgical treatment of choice. Nowadays, laparoscopy has been introduced as alternative surgical modality to rescue the malfunctioning peritoneal catheter and also offers possibility of replacement if indicated. Therefore, in our study we compared outcomes of these two surgical modalities.

Methods: The medical records of consecutive patients who underwent a surgical treatment for malfunctioning PD catheters (between January 2010 and April 2013) were analyzed. The primary outcome included successful return to adequate PD. The secondary end-point was length of catheter patency and the cause of catheter failure.

Results: A total of 32 cases were identified of which 8 had open catheter replacement and 24 had a laparoscopic intervention. The overall median follow–up was 12.5 months. The success rate of laparoscopic surgery was 62.5% but was only 37.5% in open surgery. The median catheter patency after laparoscopic intervention was 14.7 months compared to only 12 months in open surgery group. The most common cause of catheter failure diagnosed during laparoscopic intervention was catheter migration (36.4%) followed by omental wrap (30.3%), catheter blockage and peritoneal adhesions. In contrast, open surgery doesn't have any diagnostic potential.

Conclusions: The laparoscopic intervention is the treatment of choice for malfunctioning PD. It's proven benefit includes simultaneous identification of the aetiological cause of malfunction together with direct correction of this problem therefore maximizing outcome. Secondly, it does allow rapid re-commencement of PD and avoidance of haemodialysis.

Category: Surgical 3

P78

Are we closer to neonatal kidney donation & transplantation? En bloc kidney transplantation from paediatric donors under 2 years of age in a single centre

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Introduction: The 2008 Department of Health initiative to increase deceased donation by 50% in 5 years has been met, albeit with a rise in DCD and ECD donation and an associated increase in organ discard rate. The potential for donation at the other extreme of age remains unexplored. Kidneys from paediatric donors under 5 years of age are offered and transplanted en bloc, usually into adult recipients. In the last decade, the utilization of kidneys from paediatric donors less than two years of age has been low at 1.5 transplants per year, with only a handful of donors under 1 year and no neonatal donors. We report a single centre experience of utilizing donors less than 2 years of age, including the youngest paediatric donor (5 weeks old) reported to date in the United Kingdom.

Methods: Donor and recipient characteristics as well as post-transplant recipient outcomes for all En bloc kidney transplants (EBKT) from donors less than two years of age performed at our institution were reviewed.

Results: Seven EBKT have been performed from majority DCD (86%) donors less than 2 years of age (mean 12months; range 5 weeks-24months). All were transplanted into adult or adolescent recipients with a mean age of 29 years (range 15-54 years). All kidneys had primary function with no graft loss during the mean follow up period of 32 months (3-64months), achieving mean serum creatinine of 74 (range 47-148) and GFR (MDRD) 111 ml/min/1.73m^2. Patient survival was 100% with 1,3 and 12-month creatinine (µmol/L) and GFR (ml/min/1.73m^2) of 119 (61), 93 (82) and 74 (91) respectively.

Conclusions: This is the largest single-centre UK experience of kidney transplantation from donors under 2 years of age with graft and patient outcomes comparable to adult deceased donor and living donor transplantation. Graft function continues to improve during and beyond first year achieving a GFR superior to living donor renal transplant. Successful transplant from the 5-week-old donor in this cohort supports utilizing neonatal donor kidneys for transplantation. We recommend organ donation to be a routine part of end of life care in all paediatric and neonatal patients.

P79

Organ transport fluid cultures: an analysis of outcomes

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Background: Following the potential contamination of organ preservation fluid in 2012, recommendations were that transport fluid be routinely cultured. This study aims to evaluate the impact of positive transport fluid cultures following deceased-donor kidney transplantation.

Methods/materials: A retrospective analysis over a 12-month period assessed 80 consecutive transport fluid cultures. Recipient demographics are as follows: median age 53.4 ± 14.2, inpatient-stay 5.7 ± 2 days, 55 DBD, 22 DCD, and 3 LD as part of kidney sharing scheme. All patients received prophylactic antibiotics as per institution protocol. Patients were followed-up for 90 days post-transplantation.

Results: 16 recipients had culture-positive perfusion fluid (CP) and 63 were negative (CN). There was no difference in white cell count, serum creatinine and eGFR at Day 7, 30 and 90. Patients in the CP group had a numerically higher rate of culture-proven infective episodes (urinary, wound or bacteraemia) compared to the CN group (13/16 vs 45/63, P 0.5). 1 patient in this group required graft nephrectomy for ongoing sepsis. Though this equates to only 5% of the study group, of these 13 infective episodes, 30% had similar organisms cultured to that of the transport fluid.

Conclusions: This study suggests that positive transport fluid cultures are associated with increased incidence of infections with the same cultured organism. This should prompt clinicians to be pro-active in ascertaining culture results and establishing appropriate treatment early in the post-transplant period.

P80

Transplantation after encapsulating peritoneal sclerosis: gold standard treatment

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Background: Formal surgical enterolysis in specialised centres offers distinct survival benefits for patients with encapsulating peritoneal sclerosis (EPS). However, overall mortality risk for these patients remains increased due to ongoing end-stage renal failure (ESRF). Subsequent transplantation therefore offers optimal ongoing treatment for these patients. However, clinician reticence persists due to complex previous surgical interventions causing misconceptions that successful transplantation may not be feasible in this cohort. We aimed to report our experiences of transplantation in EPS patients after successful surgery.

Methods: A review was performed of a contemporaneously maintained database to identify patients having transplantation after surgical intervention for EPS.

Results: 173 patients were identified (133 patients surgically treated, 12 patients with subsequent transplantation (8- Cadaveric kidney, 1- simultaneous pancreas and kidney (SPK), 3- live donor kidney). 7 further patients are on the waiting list and 5 are undergoing transplantation workup. 91.7% patients (11/12) had semi-elective enterolyis while 8.3% (1/12) had emergency surgery. 3 patients had previous transplants (1-kidney, 1-SPK, 1- two previous kidneys). Median age was 35 (24-73) years at enterolysis and 37 (27-74) years at transplantation with a median duration of 2 years between enterolysis and transplantation. 8.3% (1/12) patients had a stoma/intestinal fistula at the time of transplantation. Albumin was 32 (median, range 19-39) mg/dl at enterolysis and 42 (19-50) mg/dl pre-transplant (p=0.08). Median cold ischaemic time was 17 hours (1 hr 25 mins – 19 hrs 47mins). Median creatinine at 3-months and 2-years post- transplant was 109 µmol/l and 132 µmol/l respectively (p=0.9). Graft and patient survival was 100% at 2 years with no incidence of post-transplantation EPS recurrence.

Conclusions: Transplantation post-enterolysis for EPS is safe, feasible and also defines optimal treatment for suitable patients. However, given the rare and complex nature of the disease, transplantation is best performed in a centre with expertise in the management of patients with EPS.

P81

Successful superselective transcatheter embolisation of renal transplant arteriovenous fistulae

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Introduction: Arteriovenous fistulae are a recognised complication following percutaneous renal transplant biopsy; however their long-term clinical significance and appropriate management strategy are uncertain.

Methods: Consecutive patients identified with renal transplant arteriovenous fistulae (AVF) confirmed on magnetic resonance angiography (MRA) or computed tomography angiography (CTA) from October 2010 to October 2012 were identified. All patients who underwent subsequent radiological intervention were included for further analysis. A review of electronic records and the radiological database was performed and data collected on patient demographics, radiological intervention performed, complications and follow-up. Transplant function (serum Creatinine) was recorded pre-intervention and at two months post-procedure.

Results: Seventeen patients were identified with renal transplant arteriovenous fistulae on MRA or CTA. Four patients (23.5%) with confirmed high flow fistulae on formal angiography underwent radiological intervention. The mean age at intervention was 53 years (range, 40 – 73 years). A preceding percutaneous renal biopsy had been performed in all patients prior to identification of the arteriovenous fistula. The median time interval from transplantation to intervention was 30.5 months (range, 8 – 197 months). Superselective catheterisation of the fistula was achieved with a coaxial microcatheter and microcoils deployed to occlude the fistula in all patients. Definitive occlusion of the fistula was achieved consistently with a single procedure. This was confirmed on post-procedure duplex studies at one month and six month intervals. There was a significant improvement in serum Creatinine values obtained after fistula embolisation ($p=0.012$). The mean follow-up period was 25.5 months (range 12 - 36 months), with no reported post-procedural complications.

Discussion: Superselective transcatheter embolisation is a safe and effective treatment for renal allograft arteriovenous fistulae with significant improvement in renal function in the short-term.

P82

Enhanced recovery programme after kidney transplantation using TAP block

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Introduction: Enhanced recovery programme focused on a better pain control, patient education, physiotherapy and nutrition is proved to be effective in several surgical specialities. To achieve better pain control we introduced a protocol of transversus abdominis plane (TAP) block in the kidney transplant recipients. We assessed efficacy of this programme in patients undergoing renal transplantation.

Methods: 49 consecutive kidney transplant recipients during the period from May 2013 to November 2013 were treated following peri-operative protocol using TAP block for pain control. The catheter was placed to the muscle plane intra-operatively & levo-bupivacaine (chirocaine) 40 mg was administered TDS for 48 hours. The outcome regarding visual pain score and post-operative stay with a control group of 50 consecutive patients who were performed in the 6 months prior to use of the TAP with use patient controlled analgesia (PCA) only for pain control.

Results: The TAP and control group did not differ in the mean age (43 vs 44y) with ranges from 20-70 vs 19-64. The Female/Male in TAP were 15/34 vs 19/31in PCA group. Type of donors LD/DBD/DCD 23/17/9 in TAP vs 23/20/8). TAP was not used in 3 patients who needed early re-exploration due bleeding (1) or doubt about the kidney perfusion (2). 4 patients need addition of PCA to the TAP block due to insufficient pain control. The average pain score in the TAP group was 2 +- 2 in comparison to 6 +- 3 in the PCA group. The mean hospital stay in TAP block group was 8 +_ 4.5 days versus 10 +_ 3.2 days in the control group. Prolonged hospital stay in the TAP group was secondary to delayed graft function (DGF) (3) , rejection (2), wound complication (1) or graft loss 2ry to renal vein thrombosis (1). In the control group the causes were DGF (2), rejection (3), and wound complication (1). After exclusion of the patients who developed complication from the analysis, mean hospital stay was 6 +- 1.4 in TAP group versus 8 +- 3.1 in the PCA group.

Discussion: TAP block offered patients better pain control, earlier mobilisation and recovery and also allowed to significantly shorten hospital stay by average of 2 days in uncomplicated cases with no evidence of complication related to the TAP block.

P83

Laparoscopic donor nephrectomy training in the UK: results from an independent trainee survey

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Introduction: Laparoscopic donor nephrectomy (LDN) is an essential part of renal transplantation practice. No study has been done as yet to look at the LDN training of transplant trainees in the UK. Though training courses in donor nephrectomy are available, it is not clear if they materialize into training opportunities for transplant trainees. We aim to quantify the training of renal transplant trainees with a short survey.

Methods: An independent electronic survey consisting of ten questions was disseminated to surgical trainees via a web-based link (Survey monkey) placed on Carrel club forum and email/paper invitations to different transplant units across the UK.

Results: A total of 53 responses were received from across the UK. 70% and 22% transplant centres were reported to perform hand assisted LDN and “totally laparoscopic ” or hand assisted LDN respectively. 20% trainees were ST3-ST5, 22% ST6-ST8, 17% post CCT, 19% CF > 2 yr. transplant experience, 21% CF < 2 yr. transplant experience respectively. Majority of trainee responses were from England 58% followed by Scotland 15%, Wales 19% and Northern Ireland 9%. 96% trainees reported that they had performed < 10 laparoscopic donor nephrectomies as primary surgeon. 58% trainees had been first assistant in 11-25 donor nephrectomies and 24% had assisted in 26-50 donor nephrectomies. 40% trainees had been on a course for donor nephrectomy. There was no correlation in seniority in training grade compared to donor nephrectomies as primary surgeon ($p=0.9$). There was no correlation in donor nephrectomies as primary surgeon compared to trainees on rotation ($p=0.88$) and service post trainees ($p=0.82$). The likelihood of a trainee to perform >10 LDN in transplant training was < 1 in 25.

Conclusions: This study confirms poor training opportunities in LDN in UK. The trainers need to address this issue urgently. LDN fellowships can be a way forward.

P84

Complications following transperitoneal hand-assisted laparoscopic donor nephrectomy - experience of first 141 cases

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Background:The complications following transperitoneal hand-assisted laparoscopic donor nephrectomy (HALDN) in our centre is presented

Methods: Data was collected prospectively.

Results: The demography and the complications are shown on the table below:

Period of study	15/9/05 – 21/11/13
Number of HALDN	141
Age (median, range)	43 (21-73)
Sex Male: Female	62: 79
BMI (median, range)	27 (18-34)
Smokers	37 (26%)
Post-operative hospital stay (median, range) days	3 (1-8)
Operating time (knife to skin -arterial clamping)(minutes)	164 (107-307)
Chest infection	22 (15%)
Ileus	16 (11%)
Wound infection	9 (6%)
Retention of urine	6 (4%)
UTI	5 (3.5%)
Rectus sheath haematoma	3 (2%)
Deep vein thrombosis	3 (2%)
Lateral cutaneous nerve neuropraxia	2 (1.5%)

The donors developing chest infection had significantly higher BMI (28±2.7 vs. 26 ±3.3; $p<0.01$) and operating time (199±55 vs. 169±44 minutes; $p<0.05$) compared to those without. The incidence of ileus was not related to the operating time and BMI. The hospital stay was significantly prolonged in the presence of chest infection (4±1 vs. 3.3±1 days; $p<0.01$) and ileus (4.4±1.5 vs. 3.3±1 days; $p=0.01$). Conclusions: Chest infection and ileus were the two major complications following HALDN in our series causing morbidity, which prolonged the hospital stay.

P85

Does subtotal parathyroidectomy help preserve renal function in transplant patients?

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Introduction: Parathyroid hormone (PTH) appears to help preserve renal function in transplant recipients. Subtotal parathyroidectomy aims to leave a functional remnant in situ. We compared subtotal and total parathyroidectomy without autotransplantation to see if a difference exists.

Aim: To determine if subtotal parathyroidectomy preserves renal function when compared with total parathyroidectomy in renal transplant patients.

Method: A retrospective cohort study of all patients that received a parathyroidectomy after renal transplant at a single centre. Data extracted from a prospective database. Patients were excluded if their transplant had failed.

Outcome measures: Creatinine, eGFR, corrected Ca, PO4, ALP, PTH, use of calcium/Vit D supplementation. Recorded at days 0,1,7,14,30,180 & 360.

Results: There were 20 patients in total. 13 had a total parathyroidectomy, 7 had a subtotal parathyroidectomy. Similar results and trends were seen in both groups for all outcome measures. Renal function decreased in both groups. On average, the subtotal group took 233mg less alfacalcidol per day. There was one recurrence in the subtotal group (14%).

Conclusion: Subtotal parathyroidectomy does not appear to help preserve renal function or significantly reduce the requirement for oral supplements when compared with total parathyroidectomy. It does however increase the risk of recurrence.

P86

Multiple kidney re-transplantation in single recipients

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Background: Recurrent renal re-transplantation in a single recipient is under-reported. Kidney re-transplantation is a technically challenging procedure. This report presents our experience in recurrent kidney re-transplantation in two different recipients.

Methods and results: *Case 1:* Sixty years old male received the fourth kidney transplant (Deceased DBD, November 2011) in the right iliac fossa, where he had previous 2 kidneys, with the last failed kidney in the left iliac fossa. Operation was technically challenging with extensive adhesions down to the external iliac vessels, but was completed uneventfully with good kidney perfusion. Remnant of old transplant renal artery aneurysm was resected. Patient had initial delayed graft function (DGF), which required haemodialysis (once), and wound breakdown healed after 2 weeks. Two years post-transplant renal profile shows; Creatinine 74 mmol/L, Urea 9.8 mmol/L and eGFR >60 ml/min/1.73m^2.

Case 2: Forty-six years old female received the fifth transplant (live related, November 2013) in the left iliac fossa (LIF), which was the third in the same side. There were extensive adhesions. The peritoneum was breached and small remnant of old graft was identified and excised. The total operative time was 3 hours. There was high drain output (lymphocele) for 10 days. One month post-transplant renal profile shows; Creatinine 64 mmol/L, Urea 7 mmol/L and eGFR >60 ml/min/1.73m^2.

Conclusion: Recurrent kidney re-transplantation is a challenging procedure that requires expertise and care. However, the peri-operative surgical complications and long-term graft outcome are similar to those of de novo kidney transplants.

Category: Liver

P87

Delayed recovery of liver function tests after liver transplantation as predictive factor of postoperative complications

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Background: elevation of liver function tests is constant after every liver transplantation and posterior decrease of the transaminasas levels is expected. However the speed and the grade how this recovery takes place has not been properly investigated as well as its role as predictive factor of postoperative complications.

Methods: Reduction rate of transaminasas from day 1 after liver transplantation was estimated considering postoperative day 3 levels and postoperative day 5 levels. Early complications after liver transplantation as haemorrhage, portal vein thrombosis, hepatic artery thrombosis, bile leak, postoperative infection as well as postoperative mortality were analysed. Final uni/multivariate analysis with others well known risk factors such as ischemia time was completed.

Results: 1.299 patients that received a liver transplantation were analysed. AST reduction in the first 48 hours inferior to the 50% of the initial value was statistically significant ($p<0.001$) for the development of hepatic artery thrombosis, acute kidney injury, bile leak and postoperative mortality (OR and 95%CI of 0,429 (0,376-0,489); 0,884 (0,818-0,955); 0,860 (0,790-0,936) and 0,780 (0,684-0,889) respectively).

Conclusion: Initial elevation of transaminases followed by a slow reduction in its levels in the first 48 hours may predict the development of some postoperative complications.

P88

Liver transplantation form HBcAb positive donors carry minimal or no risk of hbv transmission to the recipient

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Introduction: There is variation of practice among UK liver transplant units in implanting livers from HBcAb +ve donors due to the perceived risk of transmission of hepatitis B (HBV) to the recipient. Centres transplanting such grafts have variable practice of antiviral prophylaxis with lamivudine ranging from no prophylaxis to life-long prophylaxis. The aim of this study was to assess the rate of HBV infection in HBsAg -ve recipients of liver allografts from HBcAb +ve, HBsAg –ve donors.

Methods: We conducted a survey of the UK liver transplant units regarding their practices of accepting HBcAb +ve donor grafts and the use of antiviral prophylaxis in the recipients of such grafts. All patients receiving a liver transplant (LT) from HBcAb +ve, HBsAg –ve donors between Jan 2002 and Dec 2011 were identified retrospectively from the UK Transplant Registry. Post operative virology data were also collected. All patients had a minimum follow-up of two years.

Results: The survey was not incomplete at the time of this analysis, hence the results are not presented. A total of 114 patients were identified who received liver grafts underwent from HBcAb +ve donors. Of these 27 were HBsAg +ve prior to transplantation and were excluded from the analysis. Of the remaining 87, none had evidence of HBV infection (HBcAb -ve). After liver transplantation only 21 patients (24.1%) had documented negative virology for HBV and 66 (75.9%) were recorded as ‘not reported’**.** Of the 14 LT in our centre, no HBV transmission was recorded. All had received life-long lamivudine prophylaxis

Conclusions: Risk of HBV transmission following LT from HBcAb +ve donors remains low. None of the recipients in our cohort had a documented HBV transmission after receiving a liver graft from HBcAb +ve donor. Use of antiviral prophylaxis can help reduce this risk further. We suggest 100-day post-transplant lamivudine prophylaxis in LT from HBcAb +ve donors. There is a need for clear guidelines for safe and effective use of liver grafts from HBcAb +ve donors.

P89

Predictive indices for primary graft non-function within 48 hours of liver transplantation.

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Introduction: Primary graft non-function (PNF) in liver transplantation is a catastrophic complication which is invariably fatal without urgent re-transplantation. Operative risk and organ shortage preclude re-transplantation before diagnosis is certain. However, delaying re-transplant in favour of diagnostic certainty increases morbidity and mortality. There are no reliable diagnostic models or scoring systems for the early diagnosis of PNF that use routinely available clinical data. We aimed to identify factors associated with the diagnosis of PNF within 48 hours of transplantation from routinely collected clinical data.

Methods: 16 PNF cases and 48 randomly selected controls were identified retrospectively from patients who had undergone orthotopic liver transplantation. Requirements for organ support and results of routine blood tests within 48 hours of initial transplantation were assessed in the two groups.

Results: Alanine aminotransferase, fibrinogen, lactate, prothrombin time, and bilirubin were found to be significantly different between PNF cases and controls at 24 hours after transplantation ($p < .05$). Requirement for vasopressors, high-strength dextrose, and continued ventilation up to 48 hours, were also found to be significantly different between PNF cases and controls ($p < .05$).

Conclusions: PNF may be identifiable from routine clinical data within 24 hours of liver transplantation. These observations may assist in developing a diagnostic model which would allow these critically-ill patients to be re-listed for transplantation as early as possible.

P90

Characteristics and outcomes of patients with incidental hepatocellular carcinoma after liver transplantation

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Introduction: Despite pre-operative cross-sectional imaging, incidental hepatocellular carcinoma (iHCC) is sometimes diagnosed upon histological examination of the liver explant following transplantation for another indication. Whilst liver transplantation is the treatment of choice for HCC fulfilling the Milan criteria, those out-with the criteria have poor outcomes. Here we describe the characteristics and outcomes of patients diagnosed with iHCC at our centre.

Methods: Over the five year period from January 2008 to December 2012, patients in whom iHCC was diagnosed were identified and data collected from a prospectively maintained transplant database and hospital records.

Results: 329 patients underwent liver transplantation, of which 62 (18.8%) were transplanted for HCC. iHCC was diagnosed in 12 further patients transplanted for other indications (3.6%). The mean age of these patients at listing was 57 years, and the mean UKELD at time of transplant was 56.5. Regarding pre-operative investigation, the median α-fetoprotein level of these patients at the time of listing was 3kU/l (range <2-61); the mean interval from pre-operative CT scan to transplantation was 152 days, and ultrasound scan was 62 days. Mean interval from placement on the waiting list to transplantation was 132 days. The mean size of the iHCC's was 16.2mm (range, 8.7-30). Of the 12 patients with iHCC, two did not fulfil the Milan criteria for liver transplantation: one had 5 small tumours (20, 15, 12, 9 and 5 mm) and 1 had small calibre vascular invasion. Median follow-up of these patients is 29 months (range 12-62). There has been no recurrence of HCC or mortality during the study period. In comparison, there have been 4 recurrences (6.5%) in those transplanted for HCC, 3 of which were found to be out-with the Milan criteria on explant analysis.

Discussion: Despite the incidence of iHCC in patients awaiting liver transplantation, outcomes of such patients appear equivalent to those in whom iHCC did not develop. These results do not support a requirement for more frequent imaging of patients whilst on the transplantation waiting list.

P91

Post-op platelet count as predictor of early graft loss post liver transplantation

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Background and aims: Platelets are essential for haemostasis. Recent studies have shown that platelets affect liver regeneration post liver resection. Post-operative platelets count of less than 60 on day 5 (60-5 Criteria) have been demonstrated to be indicative of adverse outcome including graft loss and death in liver transplant (LT) patients. In present study we try to validate these findings.

Methods: Adult patients who had LT at our institute between 2009 and 2013 were included in the study. Data collected from prospectively managed database. Donor and recipient characteristic, intra-operative transfusion requirements, platelet count pre- and post-LT (days 0-7), immunosuppression, infections, in hospital stay and episodes of rejection were recorded as parameters associated with 30-day mortality or retransplantation.

Results: 296 consecutive patients were included in the study. The mean age was 50±12.1 years. Mean follow up being 2.3 years. Main parameters associated with outcome in univariate analysis were cold ischemia time (OR 1.003; p=0.014), reperfusion time (OR 1.015; p=0.089), Platelet count on day 3 and 4 post-LT (OR 0.969; p=0.044, and OR 0.942; p=0.007, respectively). In the multivariate analysis, parameters included in the final model were reperfusion time (OR 1.031; p=0.026), platelet count on day 4 post-LT of 71 (OR 0.923; p=0.009) and episodes of rejection post-LT (OR 1.044; p=0.008). Platelet count of less than 60 on day 5 post-LT was not associated with adverse outcome in our study.

Conclusions: Our study did not confirm the utility of the previously proposed 60-5 criterion for early post-LT graft loss. However, in our cohort, lower platelet count on day 4 post-LT did predict 30-day mortality/ retransplantation with very good discriminative accuracy, as did longer reperfusion time, higher intra-operative transfusion requirements, and post-LT episodes of rejection. A more composite score to quantify the best discriminant platelet count may be needed

P92

De novo use of tacrolimus (Sandoz) in liver transplantation – a single centre experience with 1 year follow up

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Background: Use of generic formulations of tacrolimus in liver transplantation (LT) could result in significant cost savings associated with immunosuppression (IS). Generic formulations of tacrolimus have been shown to be bioequivalent to innovator tacrolimus in healthy volunteers, and in renal transplant patients. However, there are limited data on the safety, efficacy and costs associated with the *de novo* use of generic tacrolimus in liver transplanted patients.

The aims of this study were to determine if the *de novo* use of generic taacrolimus (Adoport, Sandoz,UK) was associated with any differences in important clinical outcomes, safety and cost compared to innovator tacrolimus (Prograf, Astellas, Japan) in LT.

Methods: Consecutive patients undergoing LT at a single centre were studied before and after a planned change from *de novo* IS with Prograf to Adoport. There were no other changes to the IS protocol. Baseline demographics, disease severity, post transplant outcomes (death, rejection, sepsis, acute kidney injury, CMV viraemia), tacrolimus levels, dose adjusted levels and costs were compared between Adoport and Prograf patients for the first 14 days post transplant. Tacrolimus doses and levels were analysed at 30 days and 1 year. Renal function between groups (serum creatinine and eGFR) was compared at 1 year .

Results: 94 (66% male) patients were studied, 46 patients received baseline IS with Prograf and 48 received Adoport. There were no significant differences in the aetiology of liver disease between groups. Adoport patients were significantly younger than Prograf patients but there were no significant differences in disease severity (MELD & UKELD) or renal function (eGFR) between the groups at time of LT. Use of a second agent such as azathioprine (AZA) or mycophenolate mofetil (MMF) was common (84%). All patients received steroids. Adoport patients received significantly less tacrolimus on day 1 and day 5, and were more frequently given basiliximab as part of a renal sparing regimen, despite no significant differences in renal function at baseline or following transplantation. Initial tacrolimus costs were significantly reduced with the *de novo* use of Adoport; however, overall costs were similar due to the increased use of basiliximab. At day 14, dose normalised levels showed significantly greater variation in Adoport treated patients compared to Prograf. At the day 30 and 1 year there were no significant differences in the dose or levels of tacrolimus between groups. At 1year eGFR was similar with although Prograf treated patients had a significantly higher serum creatinine.

There were no significant differences in the rates of biopsy proven rejection, CMV viraemia, episodes of acute kidney injury, sepsis or graft loss between groups.

Conclusions: Adoport is safe and effective compared to Prograf when used *de novo* in LT patients. Increased use of MMF and basiliximab in the Adoport treated patients occurred despite no observed increase in acute kidney injury, suggesting that the use of a new formulation of tacrolimus altered physician behavior. Tacrolimus costs were significantly reduced by the use of Adoport. The finding of wider variation in dose adjusted levels between Adoport and Prograf treated patients suggests greater inter-patient variability using this formulation and may have implications for switching stable patients from innovator to generic tacrolimus.

P93

Diagnostic indices of primary non-function in a large cohort after orthotopic liver transplantation

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Introduction: Primary graft non-function (PNF) in liver transplantation is a catastrophic complication which is invariably fatal without urgent re-transplantation. Previous studies have assessed donor and recipient risk factors associated with PNF. However, most grafts with risk factors (donor age, steatosis, cold ischaemic time) function adequately. Diagnostic certainty in PNF is therefore extremely difficult, however, early diagnosis and re-transplantation is the only way to reduce morbidity and mortality. We aimed to derive the most reliable diagnostic indices of PNF in a large cohort of liver transplant patients from routine data.

Methods: Routine laboratory data and clinical indices were collected retrospectively from 180 patients, of which 9 had received the diagnosis of PNF after liver transplantation. Logistic regression was used to determine those variables which had the strongest predictive relationship with PNF.

Results: Pre-operative factors (donor age and sex, recipient age and sex, donation after brain stem death or circulatory death, graft appearance and steatosis) were assessed. Sub-optimal appearance, as assessed by the retrieval team or by the implanting team, and cold ischaemic time were associated with PNF. Post-operative associations with PNF changed over time between 0 hours and 24 hours after transplant. At 24 hours, noradrenaline requirement, prothrombin time, bilirubin level, change in bilirubin, lactate level and fibrinogen level, but not creatinine or ALT, were significantly associated with PNF ($p<0.05$).

Conclusions: This study identified a small number of indices predictive of PNF. Outcomes from logistic regression imply a mathematical relationship between clinical data and the risk of PNF. These results may allow the construction of a model to derive the risk of PNF for individual patients after liver transplantation, supporting early diagnosis and appropriate management.

P94

Role of initial transaminase levels in early outcomes of liver transplantation

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Background: Initial elevation of transaminases after liver transplant has been commonly related to the preservation injury of the graft however its role as prognosis factor in the development of early complication has not been clearly reported.

Methods: Postoperative course after liver transplantation and early complications such as haemorrhage, hepatic artery thrombosis, portal vein thrombosis, bile leak, postoperative infection and postoperative mortality were analysed considering the levels of Alkaline Phosphate, AST and ALT on day 1, 3, 5 and 7 postransplant as risk factors for these complications in the context of univariate and multivariate analysis.

Results: 1.299 patients that received a liver transplantation were analysed. Day 1 transaminasas levels represent a predictive factor for postoperative mortality ($p<0.001$) while day 1 peak did not show any statistical significance for others postoperative complications. High levels of AST on day 3 are showed statistical significance with prolonged ITU stay and requirements of respiratory support.

Conclusion: Initial elevation of transaminases may represent a good registry of the ischemic injury of the graft and also can be consider a predictive factor of postoperative mortality.

P95

The end point of trials in liver transplantation: can we adopt the ICH-GCP system used for pharmaceutical trials?

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Introduction: Improvements over time have led to excellent patient and graft survival in patients undergoing liver transplantation. Because of this, the assessment of benefit of new treatment options requires trials with an unfeasibly large sample size. We proposed that the system for determining complication in pharmaceutical trials (International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use – Good Clinical Practice (ICH – GCP) definition) could be modified for use to determine the effects of new intervention in liver transplantation.

Methods: The association between significant complications as assessed by ICH-GCP (serious adverse events other than death or graft failure) and outcome were assessed in a consecutive series of adult liver transplant recipients at a single centre between 1999 and 2008 with a minimum follow-up of one year.

Results: Overall mortality at 3 months was 9%. Significant complications (as determined by ICH-GCP) occurred in 67%of 551 transplants (526 patients) within 3 months. At 3 months, the outcomes were significantly worse in patients with complications ($p < 0.01$): graft failure (4.4% versus 15.7%); mortality (2.2% versus 11.6%); hospital stay (21 days versus 33 days); intensive care unit stay (2 days versus 3 days); inability to work (10.6% versus 34.4%); and limitation of normal activities at 3 months (5% versus 19.7%). Similar differences in outcomes were noted at 12 months.

Discussion: Significant complications as defined by ICH-GCP correlate well with important liver transplant outcomes and should be validated with another transplant database and then in randomised clinical trials.

P96

Assessing donor livers for degree of steatosis: a comparison of three different methods. Initial report

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Introduction: An increased demand on donated human livers has had many consequences on the selection and allocation of harvested livers; one of these effects is increased utilisation of steatotic livers. Liver steatotis has been linked to liver dysfunction and poorer outcome in patients receiving fatty livers. Consequently, it would be essential to use an accurate and objective method for assessing steatotic livers. We compared 3 different methods to assess steatosis in rejected human livers; clinical assessment by the retrieval team, pathologist scoring of steatosis under light microscopy, and measurement of fat surface area using digital image analysis.

Methods: Wedge biopsy samples were collected from rejected human livers, a total of 80 biopsies (4 per liver) were paraffinised and stained with H&E stain. A pathologist assessed the slides under light microscopy, followed by measurement of fat proportionate areas using image analysis software. The assessors were blinded to the original samples in both methods. The results were compared to initial assessment by retrieving surgeons.

Results: Disagreement between the 3 methods was shown, were image analysis yielded lower fat percentage values than both light microscopy and surgical assessment. This discrepancy increased by increasing the level of steatosis.

Conclusions: Our results agree with other studies that suggested a discrepancy between measured and estimated steatosis done by image analysis and light microscopy, respectively. We further showed that this disagreement involves assessment by retrieval teams. As each of the systems above has its inherent faults, a more objective method needs to be employed. We are currently investigating other diagnostic options.

Category: Biomarkers and Immunology

P97

A pre-transplant microRNA signature correlates with adverse post-transplant allograft function.

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Pre-transplant prediction of post-transplant renal function and outcome is extremely challenging, particularly when applied to older and marginal donor organs. We have sought to demonstrate that parameters associated with post-transplant allograft function, including DGF, BPAR, and eGFR can be determined by assessment of miRNA expression levels in pre-transplant allograft biopsies.

Blind screening of the human microtranscriptome was undertaken in pre-implantation allograft biopsies and candidate miRNAs showing significant expression changes with clinical parameters were validated in the expanded cohort of 114 biopsies. Data were further analysed in relation to the clinico-pathological and functional parameters of renal allografts post-transplant.

We have identified pre-transplant allograft miRNA signatures that correlate with the occurrence of adverse post-transplant characteristics (DGF, BPAR and poor eGFR). These signatures also relate directly to cellular bio-ageing and stress responses and highlight the role of key pathways in maintenance of healthy organ function, including mTOR, PI3K-AKT and Sirtuin regulation. We have successfully used these miRNA signatures to develop simple scoring systems to predict, pre-transplant, potential problems that are likely to occur post-transplant with high sensitivity and specificity. These scoring systems can supplement and enhance currently utilised methodology including the Kidney Donor Risk Index (KDRI). These data are being replicated in a second, independent cohort.

Our data demonstrate a close relationship between specific pre-transplant microRNA expression levels and post-transplant outcomes for renal allografts. Furthermore, these data illustrate the key role played by bio-age and cellular stress in post-transplant renal allograft function. These findings present significant potential for the development of novel diagnostic and therapeutic modalities which may enhance current techniques and ultimately improve renal transplant success and extend the usable window of renal allografts.

P98

Neutrophil-gelatinase associated lipocalin (N-GAL) to assess perioperative acute kidney injury in hand-assisted laparoscopic donor nephrectomy: a pilot study

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Introduction: Perioperative insults, including hypotension, hypovolaemia and pneumoperitoneum, which may occur during live donor nephrectomy can have deleterious effects to both donor and recipient. The aim of this study was to evaluate acute kidney injury (AKI) in the donor using a novel biomarker (NGAL).

Methodology: A pilot study of 20 patients undergoing hand-assisted live donor nephrectomy was undertaken. eGFR and serum NGAL measurements (Triage CardioRenal Panel, Alere) were obtained pre-operatively, immediately post-operatively, day 1 and 6 weeks post-operatively. Data on perioperative fluid balance was also collected. Results are presented as mean+/-S.D.

Results: Mean age: 40.6+/-11.1. Mean pre-operative eGFR: 105.6+/-10.1ml/min/1.73m^2. Mean day 1 post-op eGFR: 65.7+/10.4 ml/min/1.73m^2 (37.7+/-9.2% reduction from baseline). Mean eGFR 6 weeks post-operatively was 74.1+/-8.6ml/min/1.73m^2 (29.4+/-8.8% reduction from baseline). Mean pre-operative intravenous fluid volume: 2250+/-1106.2ml in the 12 hours prior to surgery. Mean intra-operative intravenous fluid volume: 1175+/-466.6ml. Mean pre-operative N-GAL was 72.2+/-14.0ng/ml (normal: <153ng/ml) on the evening prior to surgery (day-1). Serum N-GAL increased by 34.1+/-16.7% following an overnight fast pre-operatively (day 0) (ΔNGAL 45.1+/-36.0ng/ml), by a further 14.9+/-7.2% following surgery (post-op) and a further 3.1+/-1.2% by post-operative day 1. The largest ΔNGAL was observed during the pre-operative fasting period.

ΔN-GAL [day -1 to day 0] and [day -1 to post-op] were found to correlate inversely with eGFR at 6 weeks ($p<0.05$, $r^2=0.47$ and $p<0.001$, $r^2=0.52$ respectively). No association was seen between fluid balance and ΔN-GAL.

Conclusion: AKI occurs following live donor nephrectomy. This can be difficult to quantify using standard biochemistry due to the overwhelming effect which nephrectomy itself has on eGFR. AKI is associated with poorer donor eGFR at 6 weeks. Pre-operative hypovolaemia plays a significant role in AKI. Optimisation of perioperative fluid management is likely to have a protective role.

P99

A patient-centred approach to biomarkers of tolerance

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Research is underway to develop a biomarker test that will identify kidney transplant patients who may be tolerant to their graft and therefore require little or no immunosuppressant (anti-rejection) medication. Biomarkers that define the immunological fingerprint of tolerance in kidney transplant patients have the potential to benefit both individual patients and society as a whole. For example, patients accurately identified as tolerant would benefit from a better quality of life, the avoidance of late graft loss (due to chronic rejection) and longer term survival. Society would benefit from maximising the use of donated kidneys, currently in scarce supply. However, biomarker tests are not 100% accurate and the benefits of minimizing immunosuppressant medication must be weighed against the risk of precipitating acute graft rejection.

This paper describes and discusses recent work by a multi-disciplinary team to incorporate 'patient-preference' into the formulation and categorisation of biomarkers of tolerance. A mixed method study involving 100 kidney transplant patients is in progress with the aim of producing a novel method by which the risk associated with 'biomarker-led care' can be adjusted to individual patient's circumstances. The research uses a modified Standard Gamble task to assess the level of risk that patients may be prepared to take, accompanied by an adjusted self-assessed quality-of-life and symptom burden Questionnaire to educe whether attitude to risk is associated with low quality of life and high symptom burden. This quantitative approach is augmented by a qualitative approach where 30 of the 100 participants are interviewed to elicit their attitude to risk and uncertainty and the range of influences that may affect their decision-making and choice in relation to biomarker tests of tolerance and biomarker-led care.

Early findings indicate that although patient preference for biomarker-led care and acceptance of risk may be associated with low quality-of-life and high symptom burden scores, individual patient choice will vary depending on singular and contextual criteria. Despite recognised advances in the treatment of kidney disease brought about by 'personalised medicine', analysis of these findings indicates that further benefit would be achieved by integrating a patient-centred approach into research at an early stage; incorporating a 'sensitive' rather than 'blunt' comprehension of patient choice. This in turn would facilitate the translation of biomarkers of tolerance into the clinic and into practice.

P100

DNA methylation: a biomarker in kidney transplantation?

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Death with a functioning graft remains a major cause of graft loss after kidney transplantation with much of the increased mortality in this population attributable to cardiovascular disease and cancer. Whole blood DNA methylation has been associated with both cardiovascular disease and cancer in the general population. This study aimed to investigate the association between DNA methylation and recipient survival following kidney transplantation.

Methods: DNA was acquired prior to transplantation from all recipients of 1st deceased donor, kidney transplants performed in Northern Ireland from 1986 to 2005. Data on clinical outcomes is recorded prospectively. DNA methylation was analysed at 485,577 CpG sites using the Infinium HumanMethylation 450K Beadchip (Illumina) for 432 recipients who had a functioning graft at 12 months. Standard quality control was performed and beta values were calculated. Cox regression analysis was undertaken, with adjustment for clinical covariates, to identify association with recipient survival. Biological pathway analysis was performed. Sanger sequencing was undertaken for the top ranked CpGs to identify single nucleotide polymorphisms (SNPs) and fine map CpG sites (pre/post bisulphite treatment).

Results: DNA methylation was associated with recipient survival at 64 CpGs ($P<10^{-5}$). There was no evidence of SNPs near the top 20 CpGs. The top ranked CpGs were associated with genes which have been implicated in cancer and cardiovascular disease. The top-ranked biological pathway was carcinogenic.

Conclusion: Whole blood DNA methylation prior to kidney transplantation is associated with recipient survival. The top ranked CpGs are implicated in cardiovascular disease and cancer. DNA methylation may prove to be a useful biomarker to identify recipients at increased risk of cardiovascular disease and cancer and to facilitate personalised tailoring of immunosuppression for these individuals.

P101

Transcriptomic signatures in human kidney biopsies at 30 minutes and 3 months post-transplantation

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Introduction: Renal allograft survival is improved in 1 year, but falls dramatically in 10 years. The transcriptomic signatures in human transplant kidney biopsies were investigated in order to identify novel biomarkers.

Methods: The renal biopsies from living donors (LD) and cadaveric donors (CAD) paired at 30 min and 3 months (M) post-transplantation (n = 5-6) were used for whole-genome profiling and ingenuity pathway analysis. Additional 33 biopsies (n = 6-13) unpaired at two time points were used for further validation and identifying potential biomarkers by qPCR. Differentially expressed genes were also correlated with fibrosis score and serum creatinine at 3, 6, 12 and 24 M.

Results: The overall gene profiles were clearly different in 30-min and 3-M biopsies regardless of donor type. There were 466 differentially expressed genes at 30 min between two donor types ($p<0.05$, fold change>1.5), which might be mainly due to significantly prolonged cold ischemic time in CAD, while differentially expressed genes were reduced to 149 at 3 M, with 25 genes in common between 2 time points. Many acute response genes (SERPINA3 27 fold, CAD vs. LD) were up-regulated at 30 min. More interestingly, the genes involved in immune responses, inflammation and proliferation were up (3 M vs. 30 min: SERPINA3 in LD; VCAN and TIMP1 in CAD) or down-regulated (FOS in both; and FGA in CAD). 120 differentially expressed genes including COL3A1, LCN2 and MMM9 were closed correlated with fibrosis score and serum creatinine at not only 3 M, but also 6, 12 and 24 M. Among them extra 10 genes were selected for further validation, with FTCD, TASPN7, SERPINA 3 and CBF confirmed to be up-regulated (CAD vs. LD) at 30 min and only FTCD at 3 M.

Conclusions: Transcriptomic signatures were shifted from acute responses to tissue damage and remodelling by post-transplant time with divergent profiles in LD and CAD, which might be linked to initial donor injury and adaptive immunity. Certain validated genes such as SERPINA3, VCAN, FOS and TIMP1, especially FTCD at both time points might be potential new biomarkers for timely assessment as well as intervention.

P102

Release of donor-specific soluble HLA Class I antigen in renal transplant recipients with HLA incompatible kidney transplantation and its impact

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Background: Presence of soluble HLA (sHLA) derived from a transplanted organ has been suggested to modulate immune response, but previous studies were limited by the lack of sensitive and specific assays to detect sHLA. The aim of this study was to measure total and donor specific sHLA in serum, and to examine the significance of sHLA in a preliminary cohort of patients who had HLA-incompatible kidney transplantation.

Method: sHLA was measured using an ELISA sandwich assay, utilising W6/32 and BB7.2 to measure total sHLA and sHLA-A2 respectively. Eighty five healthy controls were studied for total sHLA. Twelve patients where neither the donor nor recipient expressed HLA-A2 were used to derive negative threshold for the assay. Twelve cases whose transplanted kidney expressed HLA-A2 and where the recipient had antibodies to HLA-A2 were studied. Pre-transplant, day 3, 6, 10 & 30 post transplant serum were tested for sHLA-A2.

Results: We found the median concentration of sHLA class I in healthy people is 1.6µg/ml ranging from 0.4-6.3. sHLA concentrations in transplant recipients at every time point post-transplant was significantly lower than healthy controls. Further, sHLA concentration slowly decreased after transplant from 1.3µg/ml on day 3 to 0.7µg/ml on day 30. Donor specific sHLA was observed in 58% cases, at mean day 13 post transplantation (range 6-27). Donor derived sHLA-A2 was found frequently in cases with acute antibody mediated rejection (6\7 cases with sHLA had acute AMR, 3/5 cases with no sHLA had acute AMR ($p = 0.52$).

Conclusion: Soluble HLA was found at appreciable levels in transplant recipients as well as healthy individuals. In transplant recipients, sHLA concentration decreased over time to a level that is approximately 2x less than normal. Also, we show donor specific sHLA in patient sera can be measured using a sensitive and specific assay. The level of donor-derived sHLA was associated with acute AMR in the cases studied, although it did not reach statistical significance. Further analysis with cases that received B7 expressed kidney is in progress.

P103

A multiplatform biomarker signature of acute rejection in renal allograft recipients

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Background: Acute rejection (AR) remains a problem in renal transplantation, despite improved immunosuppressive strategies. Currently, AR is diagnosed after onset of renal dysfunction, by raised blood creatinine and confirmation by transplant biopsy. Novel molecular/cellular biomarkers may be able to predict AR before onset, allowing earlier diagnosis and management. The aim of this study was to identify a multiplatform cellular/mRNA biomarker signature enabling reliable, non-invasive and rapid diagnosis of AR in renal allograft recipients.

Methods: Peripheral blood samples were collected from adult renal transplant patients during the first year post-transplant in the KALIBRE study. Samples were collected at 26 time points and also immediately pre-biopsy in patients with suspected AR. Peripheral blood was collected in EDTA tubes for flow cytometry of peripheral blood mononuclear cells and Tempus™ tubes for mRNA extraction. A 10-colour flow cytometry platform and a unique lyoplate-based flow cytometry platform (LFP) were used to determine cytokine production and transcription factor expression in different Tcell subsets. Whole blood-derived mRNA was analysed using real time PCR. Gene expression was normalised to the control gene HPRT and analysed using the comparative CT method. Preliminary assignment of patient groups was carried out by identifying patients with a biopsy-proven AR episode Banff Category 4 (BPAR, n = 36) who were matched to patients with stable function for the 1st year post-transplant (STA, n=38).

Results: This paper will present and discuss preliminary bioinformatics analysis that will combine the information from RT-PCR and flow cytometry to predict BPAR. Using the combined information a number of statistical tools such as multivariate prediction models and ROC curves to evaluate performance will be used.

Conclusion: We believe the multiplatform approach may increase the diagnostic capabilities of each technique on their own.

P104

Steroid withdrawal normalises the proportion of transitional B cells but does not significantly change gene expression in renal transplant recipients

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Introduction: Long-term graft survival in renal transplantation relies on continuous immunosuppression with drugs associated with high mortality and morbidity. A set of biomarkers of tolerance has been previously defined and will form the basis for a test for safe immunosuppression minimization or withdrawal. We aimed to study the effect of immunosuppressants on the expression of this signature of tolerance. An available clinical model was used to focus on the effect of steroids, whereby we analysed the results from a set of patients undergoing steroid withdrawal. We aimed to demonstrate that steroid withdrawal would not alter the expression of the signature of tolerance.

Methods: 42 renal transplant recipients from the GAMBIT study (REC no: 09/H0713/12) were studied prospectively on a programme of steroid withdrawal. Flow Cytometry was used to assess lymphocyte populations and RT-PCR was used to assess the gene expression associated with the tolerant state in isolated PBMCs from a limited number of patients.

Results: Percentages of Transitional B cells in peripheral blood were significantly increased in patients who successfully underwent steroid withdrawal. However, only 1 out of 12 of the genes included in the signature of tolerance was significantly different in a group of the same patients.

Conclusion: This is the first evidence that levels of steroid dose uniquely affect transitional B cells and also α-1, 2 mannosidase gene expression, both important biomarkers in the characterisation of tolerance. Therefore it can be concluded that for the full clinical utility of the biomarkers of tolerance to be realised, and translation to the clinic achieved, patients might need to be stratified according to their steroid dose. Therefore, a larger study, including more patients should be conducted in which patients are categorised according to their steroid dose, and standardised in regard to the other immunosuppressants they are receiving, to cement the findings in this study.

P105

Defunctioning polymorphism in the inhibitory receptor FcγRIIB does not impact on kidney allograft survival

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Introduction: There is an increasing appreciation of the deleterious effects of antibody and B cells on acute and chronic transplant outcomes. Many effector functions of antibody are mediated by a family of receptors (Fc□Rs) that are expressed on the majority of immune cells, including neutrophils, natural killer (NK) cells and B cells. Most Fc□Rs are activating, and controlled by a single inhibitory receptor, Fc□RIIB (CD32B), which also regulates some aspects of B cell activation and antibody production. Fc□RIIB-deficient mice develop severe chronic arteriopathy in a murine cardiac allograft model. A single nucleotide polymorphism (SNP) in human Fc□RIIB (rs1050501) results in profound receptor dysfunction and is associated with systemic lupus erythematosus (SLE). The frequency of this Fc□RIIB-I/T232 polymorphism also shows significant racial variation.

Methods: In the present study, we sought to determine whether the Fc□RIIB-I/T232 SNP rs1050501 affected susceptibility to renal allograft rejection or loss, and transplant recipient survival. Fc□RIIB-I/T232 genotype was determined in 2851 Caucasian and 570 Afro-Caribbean renal transplant recipients, and in 236 transplant recipients with a primary diagnosis of SLE, all of whom were enrolled into the Collaborative Transplant Study.

Results: We found no significant difference in acute rejection at 1-year nor in 10-year transplant or patient survival in individuals with differing *FCGR2B* genotype. The proportion of patients with pre-transplant PRA of >10% was highest in the Fc□RIIB-T/T232 group (31.1%) versus 24.2% and 23.9% in the subjects with the Fc□RIIB-T/I232 and Fc□RIIB-I/I232 genotypes respectively, but this did not reach statistical significance

Conclusions: This negative result is surprising, given the importance of this receptor in modulating antibody effector function. Of note, NK cells express only activating Fc□R. Therefore, a defunctioning *FCGR2B* SNP would not influence the deleterious effects of alloantibody–mediated NK cell activation on the allograft.

P106

The role for helminths in achieving immunological tolerance

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Background: Helminth worms currently infect more than one quarter of the world's population and their success as parasites owes much to their active immunomodulation of the host immune response. Whilst this primarily secures on-going survival of the parasites, helminth-induced immunomodulation also results in significantly lower prevalence of allergic and autoimmune conditions in helminth-infected populations.

Hypothesis: Helminth infection reduces the immune response to allograft transplantation and this may be therapeutically tractable.

Methods: Under Home Office licence C57BL/6 mice were implanted with a subcutaneous minipump delivering a continuous infusion of secreted products from the model mouse intestinal parasite, *Heligmosomoides polygyrus*. Simultaneously, fully allogeneic skin grafts were performed from BALBc donors. Seven days later, lymphocytes were isolated from allograft draining lymph nodes and analysed by flow cytometry.

Results: Flow cytometric analysis reveals a 41.7% increase in the mean percentage of $CD4^+CD25^+Foxp3^+$ regulatory T cells (of total $CD4^+$ cells) in treated vs. untreated mice ($p=0.0085$). Treatment with parasite products also increased mean expression of the regulatory cell surface receptor PD-1, specifically in the effector CD4+ T cell population, by 62.2% ($p=0.03$).

Conclusions: Our results demonstrate that helminth-derived products can powerfully induce regulatory immunological mechanisms in the presence of a fully-allogeneic transplant. This was achieved with physiological concentrations, similar to those experienced by millions of (largely asymptomatic) patients with chronic helminth infection. Identification of the specific mechanisms involved in suppression of allograft rejection by helminth parasites may lead towards development of safe and effective novel therapeutic strategies.

Category: Surgical 4

P107

Audit on bleeding post kidney only transplantation - incidence and risk factors and can we reduce the rates?

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Background: The aim of this study was to identify the incidence and risk factors for bleeding in the first 30 days post kidney only transplantation.

Method: Kidney only transplants performed from January 2011 to December 2012 in a single centre were analysed retrospectively. Bleeding was identified as presence of haematoma diagnosed on imaging or during surgical re-exploration. It was classified into minor or major (requiring surgical re-exploration or blood transfusion). Intra-operative oozing, haematuria, minor wound bleeding, gastrointestinal bleeds, non-transplant related bleeds and bleeding post-transplant biopsy were not included as bleeding episodes related to the transplant surgery.

Results: 33 (18%) of the total 183 transplants included had a graft-related bleed post-operatively. 14 (7.7%) had minor and 19 (10.4%) major bleeding. Bleeding occurred within the first 48 hours after surgery in 19 patients (58%). 12 (6.6%) patients needed surgical re-exploration. One patient lost the allograft. Recipient age, gender, preoperative use of aspirin, donor type (DBD/DCD), HLA/ABO incompatible transplantation were not associated with increased bleeding risk. Preoperative use of warfarin and/or post-operative therapeutic heparinisation and delayed graft function were associated with increased risk of bleeding. The timing of initiation of therapeutic heparinisation post-transplantation and the use of heparin on dialysis in those with delayed graft function varied hugely between patients as there was no centre protocol for perioperative management of anticoagulation at the time of the study. Only one patient was on clopidogrel in the preoperative period and did not have any bleeding complication.

Conclusions: The majority of the bleeds occurred in the first 48 hours after surgery and was probably related to varied in-centre practice in perioperative anti-coagulation. A unit protocol for management of anticoagulation in the post-transplant period based on venous thromboembolic risk and indications for warfarin has now been implemented. Further re-auditing is planned to examine if this strategy has reduced bleeding risk post-transplantation.

P108

Salvage of a live related kidney transplant using an interposition polytetrafluoroethylene (PTFE) graft

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Introduction: We report an unusual case of arterial renal vessel reconstruction in live related kidney transplantation (LRKT) using polytetrafluoroethylene (PTFE) vascular graft.

Methods: A 20-year old female patient underwent a LRKT from her mother. The intraoperative dissection of the external iliac artery was challenging, because the vessels were fragile, thin, weak and easily damaged during dissection. At first, the usual end-to-side renal arterial anastomosis to the external iliac artery was fashioned, but the kidney was not reperfused adequately. It was then decided to redo the arterial anastomosis using the internal iliac artery in an end-to-end fashion. Kidney perfusion was significantly improved. CT angiogram on the following morning showed a tight stenosis at the arterial anastomosis site and poor, patchy perfusion of the transplant kidney. Patient was returned to theatres for re-exploration and attempted redo primary anastomosis, which was extremely difficult, due to the short length of both renal and internal iliac arteries, after two previous unsuccessful arterial anastomoses. It was then decided to interpose a 4 cm PTFE graft (6mm diameter) between the renal and the internal iliac artery with interrupted 6.0 Prolene sutures.

Results: PTFE graft interposition proved to be very successful with immediate reperfusion of the kidney. Both intra- and post-operative ultrasound scans demonstrated good global perfusion of the transplant graft. Repeat CT angiogram on the following morning showed a patent graft and good opacification of the distal renal arteries. Ultrasound scans performed daily thereafter showed an adequately perfused and unobstructed transplant kidney. Delayed graft function persisted for 2 weeks. Creatinine levels started to decline on day 16, kidney graft function improved and the patient became dialysis independent.

Discussion: There are only few reports in the literature regarding the use of PTFE grafts in kidney transplantation, with good long term results. This is the first report, to our knowledge, of a successful arterial anastomosis in kidney transplantation using an interposition PTFE graft to the internal iliac artery.

P109

Dual surveillance system of haemodialysis access

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Objectives: To report the efficacy of a dual surveillance system for arterio-venous fistulas. Early detection of stenosis and improved access patency.

Materials and methods: Between April 2012 and April 2013, all arteriovenous fistulas in two dialysis units were regularly monitored using transonic flow measurements and Sonosite imaging. Fistulas with drop of access flow on two consecutive occasions were imaged by dialysis nurses with Sonosite and were then reviewed in a weekly surveillance clinic run by the vascular surgeon and held on the dialysis unit. Fistulas with inconclusive imaging results were investigated further using duplex scanning in the vascular lab. Subsequently early decisions were made regarding fistulography/Fistuloplasty.

Results: 71 fistulas were investigated. 44 fistulas required radiological intervention with successful outcome. Only one fistula was lost. 3 fistulas required frequent interventions over a short period of time and were labelled as failing fistulas. Back-up fistulas were created in the contra-lateral arms while the original fistulas were kept functioning to prevent interruption of dialysis and to avoid the use of central access. There was only one false negative result on fistulogram.

Conclusions: The dual monitoring system has been found to be effective in early detection of fistula problems with improvement of access patency. It ensures that endovascular intervention is reserved for only those fistulas with genuine problems and minimises unnecessary interventions. Implementation of such a system is highly dependent on good teamwork between the dialysis staff, surgeons and the radiology department.

P110

Implementing an enhanced recovery programme for renal transplant recipients

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Aims: In 2011 Halawa et al. implemented the first UK enhanced recovery programme (ERP) for renal transplant recipients at Sheffield Teaching Hospitals. This produced a reduced length of stay, which would benefit patients and reduce costs. We have therefore started implementation of a similar programme at our hospital.

Methods: A retrospective audit was performed looking at 75 consecutive transplant recipients at our Trust over a ten month period. Average length of stay was determined for live donor and cadaveric transplants, and note was made of the causes for prolonged stays. This information was then used to assist development of an ERP protocol and documentation.

Results: The mean length of stay was 10 days, with a median of 8 days (range 5-34). This compared favourably with national figures, but fell short of Sheffield's results after ERP implementation (mean 6 days, median 5 days). The majority of transplant recipients had an uncomplicated course and would benefit from an ERP. A small number of patients required an inpatient stay of more than two weeks, but in these cases there were clear reasons for the prolonged stay.

Conclusions: Although some patients will need prolonged admission due to complications of surgery, the majority should benefit from an enhanced recovery programme. We have therefore developed an ERP protocol and are in the process of integrating it with current documentation and practices.

P111

Surgical management of persistent hyperparathyroidism following renal transplant: an audit against national standards

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Introduction: In a minority of cases hyperparathyroidism (HPT) persists despite successful renal transplant. Left untreated HPT can lead to significant bone and cardiovascular complications. Therefore, early appropriate referral for parathyroidectomy (PTX), following renal transplant, is essential. The NKF KDOQI has produced evidence-based biochemistry monitoring guidelines for all renal transplant patients. They recommend specific timings for calcium, phosphorus and parathyroid hormone (PTH) for one-year post renal transplant.

Methods: This was a retrospective clinical audit conducted at a regional renal transplant centre. All adult renal transplants carried out between 1 January 2010 and 5 October 2011 were included, with a minimum of one year follow up. Paediatric transplants and those patients who moved out of region were excluded. Calcium and parathyroid hormone (PTH) values were recorded for one year post transplant using the national renal 'Proton' system. Clinical notes were reviewed for any patients that progressed to PTX.

Results: A total of 110 patients were included. Overall 5 % (6/110) of patients underwent PTX. The average time from transplant to referral was 11 months and from referral to PTX was 6 months. Indications for PTX referral were high parathyroid hormone (PTH) (50%) and hypercalcaemia (50%). For those that progressed to PTX calcium was monitored as per NKF KDOQI guidance in 97 % of cases. Measurement of PTH was only completed in according to guidance in 39 % of cases in first 3 months and 33 % from 4 months to one year.

Conclusions:

- Our data suggests that we are not adhering to NKF KDOQI biochemistry guidelines following renal transplant. In particular we are not recording PTH appropriately.
- A delay has been highlighted between referral for PTX and surgery. We need to analyse our own internal structures to minimise this delay.

P112

Spiral laminar flow, an earliest predictor for maturation of arteriovenous fistula for hemodialysis access

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Introduction and objective: Arterio-venous fistula (AVF) is the gold standard vascular access for hemodialysis (HD). A thrill or murmur immediately after creation of AVF is often attributed to as a predictive sign of success. However, this does not ensure final maturation for successful HD. Our objective was to determine different patterns of flow on duplex within AVF to predict maturation at the earliest and subsequent successful HD.

Methods: A prospective observational study was conducted on 187 patients, who had AVF formation from July 2012 to May 2013. Following surgery all patients had DU at day 0 and 7. Duplex parameters noted in outflow vein were: thrill or murmur, broadening of spectral waveform with increased peak systolic velocity (PSV) and the spiral laminar flow (SLF). Patients, with at least one positive parameter at day 0, were followed up serially and underwent repeat duplex imaging at day 7. Patients with absence of all three parameters at day 0 were excluded from the study. Endpoint was maturation of AVF i.e. successful HD. Statistical analysis was performed with SPSS version 20, binary logistic regression. We tried to find out the strongest and earliest predictor for maturation of AVF.

Results: SLF and broadening of spectral waveform with increased PSV were found to have significant association with maturation ($p = 0.000$). Presence of SLF at day 0, most strongly predicted the maturation. Presence of thrill or murmur could not predict the maturation.

Conclusions: SLF pattern in AVF is the most important and the earliest predictor of maturation

P113

Routine ultrasonography after urinary catheter removal in post-operative renal transplant recipients is not clinically necessary

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Introduction: Current national guidelines do not address routine post-operative USS of renal transplants. We surveyed 24 UK transplant centres. Marked variation exists in the use and timing of post-operative USS: ~⅓rd of units undertake no routine imaging; ~⅓rd scan all patients on day 1; and the remaining ~⅓rd is split between units that scan immediately and those that typically scan beyond 24 hours. There is also in-centre variation in practice for live and deceased donors. One centre performs post-catheter removal USS and one performs post-stent removal USS. One centre uses MAG3 in preference to USS. Three units did not respond.

Methods: This variation in results prompted a retrospective analysis of post-catheter removal USSs (performed in addition to a day 0/1 scan) to exclude bladder outflow problems in 89 consecutive recipients.

Results: An USS after catheter removal was performed in 60 (67.4%) patients. 41 (68.3%) were normal. The 19 abnormal scan results comprised: 3 mild hydronephrosis or pelvicalyceal dilatation; 5 collections; 4 graft perfusion or vascular flow abnormalities; 5 abnormal RIs; and, 2 AV fistulae after transplant biopsy. No patients had post-micturition residuals. The USS findings did not directly lead to intervention in any patients although surveillance imaging was commenced in one patient. In 2 of the 19 patients there were concomitant indications for the scan aside from catheter removal. Further investigations were judged to have been performed as a direct result of the abnormal post-catheter removal USSs in 6 (31.6%) of the 19 patients with abnormal post-catheter ultrasound scans and no other indication to scan. None of the 29 patients who did not undergo routine post-catheter ultrasonography subsequently developed hydronephrosis.

Conclusions: Considerable variation in post-operative USS use exists between centres. Routine USS after catheter removal is clinically unnecessary and results in further investigations. It should be reserved for high risk patient groups (eg older, previously anuric males) or those with a history of obstructive nephropathy. A pre-transplant 'bladder outflow' questionnaire may help to identify high risk patients.

P114

Ureteric reconstruction for the management of ureteric stricture following renal transplant: a single centre experience

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Introduction: This study aims to review the outcomes of patients with ureteric strictures and reconstruction following renal transplantation in a single centre**.**

Methods: All patients who developed ureteric stricture and subsequently underwent ureteric reconstruction between December 2003 and November 2013 were included in this study.

Results: 1560 renal transplants were performed during the study period**.** 42 ureteric reconstructions were performed in this period. Two reconstructions were performed at the time of transplant for high ureteric injury, the remaining 40 for ureteric stricture, giving an incidence of 2.5%. There were 25 male and 15 female recipients with a median age of 48 (range 14–78). Of these, 18 (45%) received a DBD, 12 (30%) received a DCD (including one dual transplant) and 10 (25%) received a living donor (LD) graft. 5 were re-transplant (2^{nd} or 3^{rd}). The median time to stricture was 78 days (range 41–1016 days) from transplant. The median cold and warm ischaemic times were 14:38hr (32m–24:30hr) and 33 minutes (20m –42m) respectively. 7 kidneys had multiple arteries, 3 with a lower polar artery that was anastomosed. The majority of patients underwent nephrostomy insertion and antegrade stenting prior to surgical repair. 19 patients were reconstructed by re-implantation to the bladder, 18 utilized a Boari flap, 2 used an ileal conduit and 1 an anastomosis to a native ureter. All ureteric anastomosis were stented. In one patient reconstruction was deemed impossible and was subsequently managed with an extra-anatomic stent. Two patients (5%) required re-operation for re-stricture and kinking. Median serum creatinine at 12 months following surgery was 148 (84–508) µmol/l. There was no 90 day mortality and 11 grafts were lost with a median time of 323 days (27–3103 days) after reconstruction.

Discussion: The incidence of ureteric stricture following renal transplant in our centre is low. Reconstruction of the transplant ureter is successful in the majority of the patients with low risk of recurrence.

P115

Role of pre-operative duplex ultrasonographic parameters to predict functional maturation of wrist radio-cephalic arterio-venous fistula for hemodialysis access

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Introduction: Radio-cephalic arterio-venous fistula (RCAVF) is the first choice for native AVF. Pre-operative vessel assessment with ultrasonography has been reported to enhance the outcome of autogenous AVF but data regarding its predictive value for functional maturation of RCAVF is scanty. We aimed to determine the role of preoperative duplex ultrasonography for prediction of functional maturity of radio-cephalic fistula in wrist.

Materials and methods: The data from 173 patients were analysed.The estimated Duplex variable included size, patency and continuity of cephalic vein and size, peak-systolic velocity and wall calcifications in radial artery at wrist .The subjects underwent RCAVF creation and were reviewed 6-8 weeks post -procedure for adequacy of maturation. Doppler variables between successful and failed maturation groups were compared.

Results: Successful functional fistula maturation was noted in 138 (80.9%) patients. The cut-off values for radial artery diameter, cephalic vein diameter and peak systolic velocity for maximal chance of successful maturation of RCAVF were 2.3 mm, 2.2 mm and 32.8cm/s respectively. Vascular calcifications were detected pre-operatively in 15 diabetic patients and 9(60%) had fistula failure.

Conclusion: Pre-operative Duplex USG can provide a good prediction on functional maturation of RCAVF. Vascular calcifications were associated with high risk of maturation failure in diabetics

Category: Surgical 2

P116

Early graft loss after kidney transplantation: risk factors and consequences

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Introduction: The increasing use of kidneys from marginal donors may be associated with a higher risk of early graft loss, which is a potentially catastrophic outcome. However, the risk factors and consequences of early graft loss after kidney transplantation have not previously been examined among different donor types.

Methods: Recipients of kidney-only transplants between January 2002 and April 2012 in our centre who suffered graft loss within 30 days were identified from a prospectively-maintained database. Factors associated with early graft loss were determined by multivariate analysis.

Results: 1090 patients received a kidney-only transplant: 435 (39.9%) received grafts from donors after circulatory death (DCD), 366 (33.6%) from donors after brain death (DBD) and 289 (26.5%) from living donor grafts. Early graft loss occurred in 52 (4.8%) recipients. Causes included acute vascular occlusion (19; 1.7%), primary non-function (19; 1.7%), haemorrhage (7; 0.6%) and rejection (3; 0.3%). Only DCD donor type was a significant risk factor for early graft loss ($p=0.006$), although one-year graft survival after DCD and DBD transplantation was similar (89.9% vs 93.2%; $p=0.089$). Patients with early graft loss had 8.5 times increased risk of death ($p<0.001$); their one-year patient survival was less than those on the waiting list (76.9% vs 88.8%), but 5-year patient survival in the early graft loss group was better (69.3% vs 51.4%; log–rank test: $p=0.030$). Re-transplantation after early graft loss was associated with a good outcome with a one-year graft survival of 86.7%.

Discussion: Early kidney graft loss, irrespective of donor type, is a major risk factor for patient mortality. However, long-term patient survival after early kidney graft loss is still superior to the survival of those who remain on the waiting list.

P117

Vascular complication in live related renal transplant: An experience of 2500 cases.

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Introduction and objective: Among the surgical complications in renal transplantation, the vascular complications are probably most dreaded, dramatic, and likely to cause sudden loss of renal allograft. We present our experience and analysis of the outcome of such complications in a series of 2500 live related renal transplants.

Materials and methods: Two thousand and five hundred consecutive live related renal transplants were evaluated retrospectively for vascular complications. Complications were recorded and analyzed for frequency, time of presentation, clinical presentation, and their management.

Results: The age of patients ranged from 6 to 56 years (mean = 42). Vascular complications were found in 28 patients (1.12%). Most common among these was transplant renal artery stenosis found in 13 (0.52%), followed by transplant renal artery thrombosis in 10 (0.4%), renal vein thrombosis in 3 (0.12%), and aneurysm formation at arterial anastmosis in 2 (0.04%) patient. The time of presentation also varied amongst complications. All cases of arterial thrombosis had sudden onset anuria with minimal or no abdominal discomfort, while venous thrombosis presented as severe oliguria associated with intense graft site pain and tenderness. Management of cases with vascular thrombosis was done by immediate surgical exploration. Two patients of renal artery stenosis were managed with angioplasty and stent placement.

Conclusions: Major vascular complications are relatively uncommon after renal transplantation but still constitute an important cause of graft loss in early postoperative period. Aneurysm and vessel thrombosis usually require graft nephrectomy. Transplant renal artery stenosis is amenable to correction by endovascular techniques

P118

Is there still a role for the Whitaker test in patients with renal allograft hydronephrosis?

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Introduction: Ureteric stenosis and bladder outflow obstruction are significant urological complications after renal transplantation. The Whitaker test is an antegrade pressure-flow investigation designed to delineate renal obstruction. In the 6 studies detailing its use in renal allografts, there are advocates and critics of the test. Our aim was to identify outcomes and indications for the technique.

Methods: A prospectively collated database of all patients undergoing video urodynamics for the 10 year period 2003 - 2013 was searched to identify 8 patients with renal allografts who underwent a Whitaker test. All tests were performed using a pre-inserted nephrostomy. Filling rate was 10ml/min in all with subtracted bladder and nephrostomy pressure lines. Antegrade pyelography and Video cystometrogram was also performed. Pressure rises were characterised as; normal <15cmH_20, equivocal 15-25cmH_20 and obstructed >25cm H_20.

Results: Patient mean age was 54 with 9:1 male:female ratio. 3 had live related and 5 cadeveric renal grafts. Patients had nephrostomy insertion for graft hydronephrosis and elevated creatinine (Cr). Overall 3/8 demonstrated obstruction and 5/8 normal flow. The test significantly impacted patient management in 6/8 patients. In 3 patients bladder outflow obstruction (BOO) was identified rather than ureteric stenosis. In one patient normal ureteral flow was observed whilst supine, but obstructed flow at the PUJ whilst sitting, which guided reconstructive options. In 2 patients with equivocal antegrade pyelography and minimal Cr improvement with nephrostomy, demonstration of normal flow allowed successful nephrostomy removal. 2 patients with significant Cr reduction after nephrostomy, demonstrated obstructed flow which was merely confirmatory before stenting and reimplantation.

Discussion: In our experience the Whitaker test can be a useful tool which changes patient management, when used selectively in diagnostic dilemmas. It should be particularly considered in patients with potential bladder problems (e.g. BOO, neuropathic) and equivocal antegrade pyelography or creatinine changes post nephrostomy. Combination with vCMG provides additional information.

P119

Retroperitoneoscopic donor nephrectomy (RDN) in donors with circum-aortic or retro-aortic left renal vein: First Reported series from a European Center

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Introduction: Total Retroperitoneoscopic donor nephrectomy (TRDN) provides posterior approach to kidney which has its own advantages in dealing with anomalous vasculature of the kidney. We established the safety of TRDN in donors with normal renal vasculature in our consecutive case series since 2011. However, the suitability of this technique for donors with anomalous vasculature was circumspect. We compared the donor and recipient outcome data of 05 patients with circumaortic or retroaortic left renal vein operated by TRDN technique. This is the first reported case series from a European Centre.

Materials and methods: Of 49 patients undergoing laparoscopic donor nephrectomy at our institution from June 2011 to October 2013, 05 (10.2%) had either a circum-aortic (3/49; 06%) or retro-aortic (2/49;04%) left renal vein. Demographic and perioperative parameters of these donors and their recipients were retrospectively analysed.

Results: All laparoscopic procedures were completed successfully without open conversion. Median age of donors and recipients was 31 yr. and 57 yr. respectively; median operative time was 145 min; median blood loss was 125 cc and the median hospital stay was 2.1 days. Median warm ischemia time was 2.1 min. Median recipient serum creatinine was 180 µmol/L-Week 1; 165 µmol/L - 12 weeks and 146 µmol/L - 24 weeks

Conclusions: Due to posterior approach of TRDN, it is plain sailing to deal with circumaortic/retroaortic left renal vein with excellent results in donors and recipients. TRDN is highly recommended in these venous anomalies.

P120

Post renal transplant lymphatic complications: A paradigm shift

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Introduction and objectives: With refinement in surgical technique of kidney transplant including harvesting and grafting, surgical outcome has improved over time. Similarly,better understanding of basic patho-physiology and risk factors related to post transplant lymphatic complications, has made positive impact on its incidence, management protocol and ultimately outcome.We have evaluated the changing trend of post transplant lymphatic complications including incidence of lymphocele, significant lymphorrhea and their predisposing factors, prevention as well management.

Materials and methods: Between 1989 to 2001, 735(Group I, predominantly Open donor nephrectomy period) and since 2002 to 2012, 1360(Group 2, predominantly laparoscopic donor nephrectomy period) live related transplantations were performed. Group I was evaluated retrospectively where as group II evaluated prospectively. For significant lymphorrhea (> 100 ml lymph fluid through drain beyond 5^{th} POD) patients were randomized in two groups (Group A received early betadine 0.2% and Group B,no /late betadine instillations) on basis of management. Fisher exact test or chi square test used for categorical data, where as descriptive statistics and t test was used for continuous data. Absolute risk reduction and NNT with CI was calculated to estimate effect of Betadine instillation for treatment of Lymphorrhea

Results: In group I, 5.3% had lymphocele (2% symptomatic & 3.2% asymtomatic).BMI(p=0.01),External iliac arterial (EIA) anastomoses(p=0.04) ,multiple arterial anastomoses(MA)(p=0.008),acute graft dysfunction(AGD)(0.0001) and renal biopsy(Bx)(0.0001) were significantly associated with lymphocele formations on univariate analysis. On multivariate analysis only MA, AGD and Bx were found to be significant.

In group II , total lymphatic complications was seen in 186(13.8%) patients which include Asymptomatic lymphocele(3.9%),symptomatic lymphocele(1.1%),lymphorrhea (8.8%). BMI,EIA,MA,open donor nephrectomy,AGD,Bx were significantly associated with lymphatic complications. But On multivariate analysis only AGD and Bx were significant predictors.Betadine instillations significantly reduced lymphorrhaea(95% vs 39%,Group A Vs GroupB) with absolute risk reduction of 34.37%. On subgroup analysis, the lymphorrea found to be a significant risk factor for lymphocele formation (p=0.0001) and betadine instillation has significantly reduced the risk.

Conclusion: Symptomatic lymphocele has decreased in minimal invasive era but lymphorrhea remained an important cause of morbidity. AGD and Bx were significant risk factors for lymphatic complications.Treatment of lymphorrhea with betadine may prevent symptomatic lymphocele formation

P121

Morbidity after hand assisted laparoscopic live donor nephrectomy (HALDN): a single centre experience

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Aim: To analyse the morbidity rates after HALDN

Methods: A retrospective analysis of all HALDNs performed at our centre between Jan 2012 and Sep 2013 was undertaken. The complications categorised as major and minor were recorded during in hospital stay, post discharge, at 6 weeks follow up and at 1 year follow up. Major complication is defined as return to theatre. We compared the complications recorded historically for open nephrectomy performed at our centre between 2000 & 2009 with this cohort of HALDN and also with published literature.

Results: A total of 174 consecutive patients underwent HALDN during the study period. 84 (48.3%) were males and 90 (51.7%) were females. The mean age was 47.2 years. Parents were the largest group of donors at 27% and in the decreasing order of frequency, the others were siblings 18.4%, spouses 17.8%, other relatives 11.5%, and altruistic donors 10.3%. The major complication rate was 3.5% with 2 patients with small bowel obstruction and relaparotomy, 2 patients with colonic perforations and 4 patients with port site hernias. The commonest minor complication was constipation at 25.3% and pain 14.9%, wound problems 14.9%. There were no mortalities. When compared with the open technique, there was a significant higher rate of pain, wound infections and other complications. This may be explained in part by the longer follow up of HALDN patients.

Complications	**HALDN (%) n = 174**	**Open (%) n = 140**	**p Value**	**Literature %**
Major	8 (4.6)	-	-	4.5
Constipation	44 (25.3)	-	-	-
N+V	13 (7.47)	0	-	-
Fever	12 (6.89)	-	-	-
Consolidation / Atelectasis	11 (6.32)	15 (10.7)	0.216	-
Pain	26 (14.94)	7 (5)	***0.005***	-
Ileus	6 (3.45)	0	-	-
Wound infections	26 (14.94)	10 (7.14)	***0.033***	1.3
UTI	8 (4.6)	6 (4.3)	1	-
Incisional hernia	4 (2.3)	6 (4.3)	0.35	-
High BP	9 (5.17)	-	-	-
Others	34 (19.54)	7 (5)	***0.0002***	10.3

Conclusions: HALDN is a safe procedure with minimal major complication rate. Our major complication rate is similar to that reported in literature. As the surgeons' experience and technology improve, so will the complications in donors.

P122

Dual kidney transplantation through a midline infraumbilical extraperitoneal incision

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Background: Dual kidney transplantation of organs from extended criteria donors improves organ utilisation and is a good option for older patients who may not survive long waiting times. Techniques used in dual transplantation include, single incision unilateral extraperitoneal iliac fossa placement, bilateral extraperitoneal placement through separate incisions in both iliac fossae and intraperitoneal placement of both kidneys. We describe a novel, less invasive technique of dual transplantation through a midline infra-umbilical extraperitoneal incision.

Case report: A 64-year-old female on haemodialysis for end-stage renal failure due to diabetes mellitus received a dual kidney transplant from a 75-year-old female donor after cardiac death (DCD) due to intracranial haemorrhage. The donor had a long standing history of hypertension requiring multiple antihypertensives but had normal renal function with a preterminal creatinine of 69 µmol/l. A lower abdominal infra-umbilical midline incision was made down to the pubic symphysis. The operating surgeon was stood on the opposite side of implantation for better view of the operative field. Upon reaching the peritoneum, sharp and blunt dissection of the extraperitoneal space was carried out bilaterally until the iliac vessels were exposed. The inferior epigastric artery was not divided as it did not interfere with the operative field. A self-retaining (omnitract) retractor was placed to retract the peritoneum medially and expose the iliac vessels for safe implantation. Dual transplantation was performed by placing one kidney in each iliac fossa. Total ischaemic time for the right kidney was 15 hours and for the left kidney was 18 hours. The patient required 2 sessions of dialysis post-operatively for delayed graft function but was discharged home 12 days later with a creatinine of 112 µmol/l.

Discussion: To our knowledge, this is the first report of the use of a totally infraumbilical midline extraperitoneal approach for dual kidney transplantation in the UK. Advantages potentially include lesser pain, early mobility, lesser incidence of neuralgia and incisional hernia. Limitations are with access in obese patients.

P123

The fate of the fistula following renal transplantation

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Introduction: The fate of arteriovenous fistulae (AVF) following renal transplantation is poorly described. There is no consensus as to optimal management of the AVF following transplantation. We describe our units experience.

Methods: Retrospective review of all patients (n=1074) undergoing renal transplantation from January 2001 to date was undertaken. Data was collected on dialysis modality/ access at time of transplantation; date of AVF thrombosis/ ligation (and reasons for ligation) and AVF patency at time of graft failure.

Results: Data was available for 947 patients (88.2%). Mean age: 47.2+/-13.4 years. At time of transplantation 794 patients (73.9%) were on haemodialysis. Of these 458 (57.7%) used AVF; 36 (4.5%) used AVG and 300 (37.8%) used tunnelled central venous catheters (TCVCs). Follow-up data was available on 398 of the AVF (86.9%); mean follow-up 5.2+/-1.3 years. 25 AVF (6.3%) clotted in the early post-transplant period (<7 days). 320 AVF (80.4%) remained patent at 1-year following transplantation. 52 AVF (13.1%) were ligated (42 for cosmesis; 7 for arm swelling with central vein stenosis; 2 for rupture; 1 for high output cardiac failure). 98 patients (24.6%) had graft loss during the follow-up period. Of these 65 (66.3%) had a functioning AVF at the time of graft loss. A further 4 patients (4.1%) underwent mechanical thrombectomy to restore patency of a thrombosed AVF. Of the 29 others, only 3 (10.3%) had a de novo AVF at the time of re-commencing haemodialysis

Conclusion: The majority of AVF continued to function without complication following transplantation, with most patients opting to maintain their AVF. Two-thirds of patients with graft loss re-commenced haemodialysis through their original AVF, however of those who had lost their AVF the overwhelming majority needed TCVC. AVF should be preserved wherever possible following transplantation and, in those who loose their AVF, further vascular access should be considered early in the process of graft loss.

P124

Persistent serous leak: An unusual complication of a synthetic graft used as an arterio-venous shunt for dialysis access

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Aim: To present an unusual case of serous leak from a polytetrafluoroethylene (PTFE) graft used for haemodialysis access.

Materials and methods: A single case report of perigraft seroma that occurred in a patient who had a PTFE graft in the arm, is described. Valid consent was obtained from the patient to use all the details pertaining to the case. A detailed histological & electron microscopic analysis of the explanted graft was performed by the manufacturing company Vascutek Ltd. A literature search was performed and similar case reports were reviewed.

Results: The leaking graft had to be ultimately replaced by a gelatine coated PTFE graft. The explanted PTFE graft showed no physical defects with electron microscopy. Histological examination revealed medium term implantation with no evidence of inflammation or infection. Literature search showed the incidence of seroma formation in PTFE grafts to be 1.7%.

Conclusion: Perigraft leak & seroma formation after a PTFE graft for dialysis is a rare complication. Important causative factors seem to be location – in the arm, intra operative technique, and development of a fibroblast inhibitor. It is therefore suggested that they are preferably placed in the forearm with meticulous operative technique. Leaking grafts may be salvageable with a bypass of the affected segment. Replacement of the graft with a different material often gives the best cure rate.

Category: Pancreas and Intestinal 2

P125

Post transplantation lymphoproliferative disorder after intestinal transplantation

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Introduction: Post-transplantation lymphoproliferative disorder (PTLD) is the second most common malignancy in adults who receive solid organ transplants. Intestinal transplant (ITx) recipients show an incidence of 10% to 45%, often early within the first year post transplant. Despite a growing understanding of the pathogenesis of EBV infection and EBV-associated diseases in transplant recipients there remains uncertainty regarding the best clinical management of these patients.

Methods: We identified all patients who received an Tx in our institution and developed PTLD.

Results: From October 2008 to November 2013, 24 patients underwent ITx. Mean age 42 years (range 23- 73). M/F ratio 14/10. Median follow up 485 days (range 29- 1879) for surviving/ 85 days (range 28- 823) for non-surviving patients. All patients received Campath 30mg IV at induction and at 24 hours later. Maintenance immunosuppression was Tacrolimus (trough levels 8- 12ng/ml). All patients were EBV IgG + (100%) pre transplantation. 16/24 developed EBV viremia (67%). 6 with EBV PCR> 10^4 (25%).

PTLD was diagnosed in 3 patients (12.5%) at 2, 6 and 9 months respectively (median 5.5 months). Two patients on routine histology and one patient had a mass in the stoma, All patients had received an Isolated Small Bowel graft. Two patients had a PET FDG positive and were treated with Rituximab. One patient was PET negative and had a decrease in immunosuppression (5- 7ng/ml). He remains under surveillance. Full remission was observed in all patients. There were no deaths attributed to PTLD.

Discussion: In compliance with literature all EBV episodes happened before the 1st year. Our cohort shows low incidence for PTLD. PET positive patients were treated with Rituximab and showed full remission.

P126

Subcutaneous alemtuzumab (campath) induction in pancreas transplantation: a safe alternative to intravenous administration

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Introduction: Alemtuzumab is usually administered intravenously. Such administration is associated with a high incidence of a first-dose cytokine release reaction. This is a review of a single centre experience of subcutaneous administration in pancreas transplantation.

Method: Since 2004 all patients undergoing pancreas transplantation received induction with subcutaneous alemtuzumab. The records of these patients were reviewed with respect to survival and occurrence of rejection, infection and cancer.

Results: 153 combined kidney and pancreas, and 3 solitary pancreas transplant recipients received alemtuzumab. Mean follow-up time was 4 years. Following subcutaneous alemtuzumab, no systemic adverse reactions were noted. 2 patients were inadvertently given the second dose of alemtuzumab intravenously; both developed a reaction, characterised by hypotension, fevers and rigors. One year patient, pancreas and kidney survivals were 99%, 93% and 99% respectively. Overall, biopsy-proven rejection was observed in 38 (24%) of patients, with 31 (20%) patients having at least 1 episode of rejection in the first year. T cell-mediated rejection (TCMR) occurred in 34/156 patients, three of which went on to develop antibody-mediated rejection (AMR) at a later date. Three patients had AMR and two of these subsequently developed TCMR. Two patients had both TCMR and AMR. 43 (28%) of patients were admitted with a total of 74 episodes of infection. Of the viral infections encountered, 31 patients (20%) developed CMV, 6 (4%) VZV and 24 (15%) BK viraemia. 3 (2%) patients developed a non-skin malignancy. 2 (1%) patients developed *de novo* autoimmune disease and recurrent type 1 diabetes was seen in 5 patients (3%).

Conclusion: Subcutaneous alemtuzumab is an effective induction agent with good short and long-term results.

P127

Outcome of pancreas allograft salvage following segmental ischaemia: a single centre experience

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Introduction: Segmental pancreatic allograft ischaemia in the peri-operative period has traditionally resulted in organ explant, due to concerns over immediate viability and potential morbidity. We aimed to establish outcomes following attempted salvage in this cohort.

Methods: A retrospective analysis of all pancreas transplants performed at a single centre over 12 years (2001- 2013, n=300) identified patients undergoing segmental resection for partial ischaemia (duodenum +/- head or isolated tail). Primary endpoints were graft and patient survival and length of stay (LOS).

Results: 10 patients (3.3%) underwent salvage resection (5 male, 5 female; mean age 42.5 (SD 10.5), BMI 25.2 (2.6) and CIT 868mins (SD 240)). Median LOS was 32.5 days (14- 205 days) with 70% (7/10) and 37.5% (3/8) graft survival at 1 month and 1 year respectively. There was no one year mortality and no differences in recipient and donor confounding factors. Three patients had isolated duodenal resection (all SPK; mean age 42.3 (SD 13.1), BMI 27.6 (SD 1.4), CIT 868mins (SD 240) and LOS 28.3days (SD 6.5)). Three patients underwent allograft head and duodenal resection (1 PAK, 2 SPK; mean age 42.3 (SD 13.1), BMI 22.7 (SD 2.6), CIT 795mins (SD 183) and LOS 30 days (SD 14.5)). Four patients had distal pancreas resection (all SPK; mean age 42.8 (SD 10.2), BMI 25.3 (SD 1.5) and CIT 874mins (242), and median LOS 113 days (14- 205)). All developed peri-pancreatic collections related to ductal leak, treated with antibiotics and either radiological or surgical drainage. One month graft survivals for these subgroups were 66.6% (2/3), 66.6% (2/3) and 75% (3/4) respectively and one year graft survivals were 66.6% (2/3), 0% (0/2) and 33.3% (1/3) respectively.

Conclusion: Approaches utilising limited resection with unconventional drainage techniques provide viable salvage options and increased graft utilisation. However, distal pancreas resections potentially lead to higher morbidity.

P128

Identifying factors related to graft failure after pancreas transplantation: proposal for a novel follow-up protocol

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Introduction: Over 200 pancreatic transplants (SPK, PAK, PTA, pancreas after SPK) are performed annually in the UK. Pancreatic graft loss is a combination of early (acute rejection, surgical complications) and late (chronic rejection, auto-/allo-immunity) events that lead to a modest pancreatic allograft survival rate of 70% at 5 years. Surveillance pancreas biopsies may be useful in detecting rejection in the early post-transplant period but also carry a non-negligible risk of complications. Furthermore, rejection may be missed in the time interval between biopsies and the rate of subclinical rejection episodes is very high in some series, particularly for PTA patients. These clearly indicate the need for a better post-transplant follow-up protocol able to guide the clinician to recognize and treat rejection episodes as early as possible.

Methods and results: We present a novel follow-up protocol for pancreatic grafts based on metabolic, immunologic and histopathologic parameters. The baseline pre-transplant metabolic profile includes HbA1c, continuous glucose monitoring (CGM) and diabetes autoantibodies (glutamic acid dehydrogenase – GAD Abs, pancreatic islet cell Abs). The baseline immunologic profile includes panel reactive antibody (PRA) assay, HLA typing and T-cell subtypes. These are repeated at three months post-transplant with the addition of a mixed meal test and a surveillance protocol biopsy of the graft. A renal graft biopsy is taken for SPK or PAK recipients. Additionally, routine post-transplant serum studies at three-month intervals thereafter include HbA1c, glucose levels, C-peptide levels (for calculation of the SUITO index) and diabetes autoantibodies. In cases with HbA1c >6.0% or a HbA1c rise >0.5% from the baseline post-transplant level, a pancreatic graft angiogram and biopsy are performed. The transplant and diabetic teams jointly follow all patients.

Conclusion: We implement a novel surveillance protocol for all pancreatic graft recipients. We aim to improve graft survival by earlier detection and treatment of rejection episodes and this remains to be prospectively evaluated.

P129

Salvage of thrombosed pancreas graft after successful splenic artery thrombectomy

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Introduction: Pancreas graft venous thrombosis is not uncommon after pancreas allotransplantation, which often results in very early graft failure requiring graft pancreatectomy. However arterial thrombosis of the allograft should not be overlooked. We identified poor perfusion of a transplanted pancreas due to a thrombus occluding the splenic artery of the graft. Prompt intervention by surgical thrombectomy of the splenic artery thrombus resulted in salvage of the graft.

Methods and results: A 40 year old female with a previous Simultaneous Pancreas and Kidney Transplant received a Pancreas Transplant following the failure of her previous graft. In view of the previous graft pancreatectomy on the right side, the new pancreas was implanted on the left sided iliac vessels by an end to side anastamosis. Good reperfusion of the graft was observed and the duodenum was enterically drained. Post-operatively blood glucose (BM) was down to five mmoles/lit and the patient was stable. However six days post-transplant the patient became unwell and hyperglycaemic with a raised amylase. A CT angiogram identified poor perfusion of the graft and a thrombus occluding in the splenic artery of the graft. Urgent exploration showed poor perfusion of pancreas and thrombosed splenic artery. A thrombectomy of the splenic artery was done with a Fogarty catheter resulting in excellent reperfusion of the pancreas. The patient was given intraveonous heparin infusion (300- 500 units per hour) post operatively. During this period the BM's slowly improved and the patient was discharged home 12 days later with excellent blood sugars and a well perfused graft.

Discussion: Early identification of pancreatic graft arterial thrombus by CT angiogram and timely surgical intervention by surgical thrombectomy allowed us to rescue the graft perfusion and its associated complications. As far as we know this is the first case to be reported in the literature.

P130

Pancreatic machine organ perfusion - experimental models compared to kidney machine perfusion

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Background: Advantages of hypothermic machine perfusion (HMP) over cold-storage for organ preservation include facilitating thorough vasculature washouts; delivery of oxygen/nutrients, removal of toxic metabolites, and opportunities for real-time viability assessment and pharmacological intervention. The majority of research into HMP has been conducted in kidney preservation; experimental studies into HMP for whole organ pancreatic preservation are lacking, and may be related to fundamental differences in their flow characteristics. The pancreas is physiologically a low-flow organ, thus attempts to establish pancreatic perfusion models are challenging. Here we compare models of stable HMP of porcine pancreases to a higher-flow and pressure model of renal HMP.

Methods: Nine kidneys (warm ischaemia (WI)=10mins) and seven pancreases (WI=30mins) were retrieved from landrace-pigs. Organs were benched and underwent HMP using UW solution on a Waters Medical RM3 perfusion machine for 5 hours. Perfusion consisted of a priming phase (2h) followed by stable perfusion(3h). Perfusion dynamics, graft weight gain were recorded, and the perfusion flow index (PFI) calculated for each organ.

Results: Target stable perfusion pressures in kidneys was 40mmHg (40Group), in 4 pancreases 30mmHg (30Group), and in 3 pancreases <20mmHg (20Group) $p<0.05$. Overall flow rates were similar in 40Group and 30Group, and lower in 20Group (32.5, 26.8 and 18.6 ml/min/100g $p<0.05$). PFI were statistically similar between all three groups (0.80 [40Group], 0.91 [30Group], and 1.26 [20Group]) but trended higher as perfusion pressures decreased. Weight gain was highest (56.7%) in 30Group Pancreases, 34.4% in Kidneys and least in 20Group Pancreases (15.3%, $p<0.05$). Statistics employed included ANOVA and Student's T-Test, $p<0.05$ is considered indicative of significance.

Conclusions: Preliminary data has demonstrated that optimum systolic perfusion requirements and flow rates for pancreatic HMP are significantly lower than those used in renal HMP. Determination of viable flow using perfusion calculations shows that use of very low perfusion pressures (<20mmHg) produces improving PFI profiles. The pancreas is susceptible to oedema but with low perfusion pressures demonstrates minimal weight gain. It is important to consider these observations in the development of further protocols for pancreatic HMP of pancreatic grafts for either preservation, viability assessment, or for pharmacological delivery and pre-conditioning.

Category: Ethics Law and Public Policy 2

P131

The HTA's code of practice on the human transplantation (Wales) act 2013

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Aims: To provide Congress with an overview of the responses to the HTA's consultation on the Code of Practice to support the Human Transplantation (Wales) Act 2013. To pull out key themes and concerns, and the steps taken to address these in the redrafted Code of Practice.

Methods: A twelve week public consultation was held during October, November and December 2013 during which stakeholders and members of the public were invited to respond to the consultation questions. Two stakeholder events were held; one in Cardiff and one in London. Three public events were held in Wales.

Results: As yet the consultation has not closed so we do not have all responses. However, key themes include the role of the family, who can object and how and the ordinarily resident test.

Conclusions: As yet we cannot reach conclusions. However, the level of engagement has been high and we expect a comprehensive range of responses.

P132

Assessment on the incidence of missed potential for ABO - incompatible kidney transplantation in the west of Scotland

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Introduction: ABO incompatibility had previously been considered a contra-indication to living donor kidney transplantation but in recent years, ABO incompatible kidney transplantation (ABOi KT) has been increasingly performed in the UK with good results. In the West of Scotland, an ABOi KT program commenced in 2011, utilising a protocol based on Rituximab, plasma exchange and conventional triple-drug immunosuppressive. We wished to investigate the potential that ABOi donors who had previously not been worked up may now still be suitable options for their respective recipients.

Methods: Patients on the deceased donor waiting list were identified from the Strathclyde Electronic Renal Patient Record (SERPR, updated in July 2013) and patients' address were collected from the NHSGGC Portal system. An up-to-date transplant status (active or suspended) was obtained from the NHS Blood and Transplant (updated Sept. 2013). Every patient was filtered and investigated to correct for any discrepancy in transplant status found between the two systems. A total of 398 patients were identified and categorized into two groups: active (293, 73.6%) and suspended (105, 26.4%). 398 patients were informed through a letter about the ABOi KT and requested to respond with a phone call to 1) investigate any history of an ABOi donor and 2) ascertain contact details. Blood groups incompatibility and HLA crossmatch results were confirmed using MANZEN database. 242 patients responded and underwent telephone interview.

Results: 5 patients of 242 patients interviewed (2.07%: 4 active, 1 suspended) were categorized as missed potential for ABO-incompatible kidney transplantation

Conclusion: Patients who might now benefit from transplantation via an ABOi donor and who represent previous missed potential are a relatively small group. This suggests most of such patients have achieved transplantation via an alternative pathway. Some such patients may have died or been removed from the waiting list in the interim.

P133

A survey of experience and attitudes to assessment of altruistic live kidney donors in the UK

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Introduction: The Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006 provide a legal framework for organ and tissue donation in the UK. The rules set out by the Human Tissue Authority (HTA) have enabled non-directed altruistic organ donation, which has the potential to increase live kidney donation further. However concerns have been raised regarding donation in the very old and very young. The aim of this survey was to assess the experience and variation in practice in altruistic live kidney donation across the UK.

Methodology: An identical electronic and paper survey was distributed at the 2013 British Transplant Society (BTS) Annual Congress and emailed to all BTS members via newsletter. Questions were asked regarding assessment of altruistic donors, numbers performed per unit, psychology input, age limits and unit policy.

Results: 38 responses were received from 10 Transplant centres and referring nephrology units (32% surgeons, 43% nephrologist, 13% coordinators). 83% responders discussed potential altruistic donors at MDT and 75% of units had access to psychological or psychiatric input. 82 % of units had assessed altruistic donors. 71% of units had performed between 10 - 70 live donor nephrectomies last year, however the number of altruistic donation procedures ranged between 0-15 per year. 9 % of the units had agreed age limits for altruistic live kidney donation. Those specified age over 18, with one exception (lower age limit of 30 years). When asked for a personal view regarding age in altruistic donors, the majority of respondents wished for a discussion on a case-by-case basis. Specifically when considering the assessment of an 18 year old potential donor, 35% of respondents would proceed, 6.5% would refuse at their centre, 32% would refer for a second opinion and 38% would ask the donor to wait for a period of time.

Conclusion: This survey has highlighted significant variations in practice and attitudes towards altruistic donation. It is important to share experience of the assessment process and outcome of this increasing donor population in order to provide a consistent approach throughout the UK.

P134

Acceptance and perception of digital medical photography (DMP) by patients in renal transplant setting: a quality assessment survey

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Introduction: Rare and uncommon anatomical variations, difficult surgical steps in transplant surgery can at times be of extreme importance for research and educational purposes. Digital medical photography (DMP) can be resource to revisit the clinical situation. DMP requires fine balance between technological possibility and acceptance by the patients. Patient perception is paramount in developing a healthy doctor-patient relationship and thus avoiding unnecessary medico-legal situations. We conducted a survey to determine the acceptance and perception of patients to medical photography in renal transplant setting pre-operatively .

Methods: A 6 point questionnaire was given to patients going for transplant surgery pre-operatively between Sept 2012 –July 2013 . The questionnaire aimed to assess patients' acceptability of the use of identifiable and non-identifiable photography for teaching, presentation; publication purposes. Patient preferences on who should view their images and equipment used were also recorded. N= 77 completed questionnaires were analysed and statistically assessed.

Results: The acceptability to the use of personal cameras (09%) and phones (05%) was low compared to hospital camera (78% $p<0.001$). The use of non-identifiable photographs was more acceptable for all purposes (88% $p<0.001$). Patients consenting for DMP reported to have their photographs used by treating doctors (91%), other doctors (76%), for student teaching (88%) or patient education (85%).

Conclusion: Medical photography was acceptable to most of the transplant patients. Pre operative consenting for DMP may be done for all transplant patients. Patient confidentiality is of extreme importance to avoid legal-ethical mishaps.

P135

Social media and online exposure as an early measure of the impact of transplant research

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Introduction: Traditional measures of the impact of published research such as citation counts are open to manipulation and take time to accrue. The use of social media, social bookmarking, expert recommendations and news mentions as alternative measures of research impact is gaining popularity and used by leading medical journals such as Nature and PLOS Medicine.

Methods: We searched MEDLINE (Pubmed) for articles with subject headings relating to solid organ transplantation over a one year period between 1/8/11 and 31/7/12. MEDLINE data was extracted into a database. Citation data were retrieved from SCOPUS, and data regarding mentions in social media (Twitter, Facebook, Blogs, Reddit, Pinterest), social bookmarking sites (Mendeley, CiteULike), news outlets and expert recommendation sites (Faculty of 1000) were retrieved from the data at www.altmetric.com. Data were analysed for associations between alternative metric data and citation rate and also article characteristics, using the statistical package R.

Results: The MEDLINE search retrieved 6,981 publications from 1,165 different journals. Median number of SCOPUS citations per article was 1 (range 0-399), with 4,604 (66.0%) having at least one citation. 1,346 (19.3%) articles had mentions in social media, 915 (13.1%) had social bookmarks, 63 (0.9%) had expert recommendations and 8 were picked up by online news outlets. Likelihood of later citation was significantly associated with mention in social media (OR 1.91, $p<0.001$), expert recommendation (OR 6.05, $p<0.001$), social bookmarking (OR 3.12, $p<0.001$), publication in English language (OR 7.34, $p<0.001$) and for articles identified as meta-analyses, multicentre studies, reviews or clinical trials. The mean time between listing on Pubmed and the last recorded mention in social media was 122±177 days.

Discussion: Social media mentions and online exposure acts as an early predictor of the impact of transplant research as measured by later citation rate. Expert recommendation, in particular, is associated with higher citation rates.

P136

ABO incompatible kidney transplantation (ABOiKTx) – beginning to assess the patient experience

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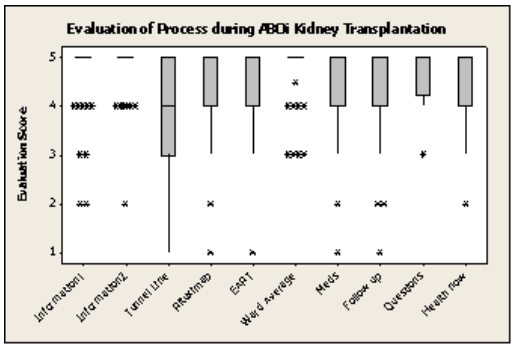
Introduction and background: ABO incompatible live donor kidney transplantation affords timely transplantation with acceptable short term and long term outcomes. We surveyed ABOiKTx recipients at our centre to assess their experience of the process of preparation and follow-up.

Methods: There were 10 domains for feedback related to each process during ABOiKTx These were quantified using a simple linear scale a 'satisfaction score'. We received replies from 37 patients who received an ABOiKTx. In addition, questionnaires were sent to patients who were treated with antibody removal, but did not proceed to transplantation. These results were compared for patients treated before and after appointment of an antibody incompatible specialist nurse (AISN).

Results: Median response for each satisfaction score is shown in the figure. Line insertion scored lower than other variables ($p<0.01$), identifying this as an area to concentrate counselling and preparation. 51.4% (19/37) were pre-emptive recipients who had not previously required vascular access insertion). AISN was associated with improved reported understanding of medications ($p=0.04$). The experience reported by 4 patients who did not proceed to transplantation was not significantly different to the others although the numbers are small.



Conclusions - Patient experience was very good for all stages of procedures, other than line insertion. The process of line insertion is now specifically discussed at the initial assessment for ABOi transplantation. AISN seems to improve patient reported perceptions of understanding of transplant medications.

P137

Renal transplant consent: has practice improved since the 2011 BTS guidance?

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Introduction: This study was performed to assess the quality of consent taken at the time of renal transplantation in a single centre. Consent practice was assessed following the introduction of NHS BT and BTS guidelines 2011. Findings were compared to practice prior to the introduction of these guidelines.

Methods: 118 transplants were performed from April 2011 and March 2012. The consent forms at the time of surgery were assessed according to the NHS BT and BTS 'Guidelines for consent for solid organ transplantation in adults 2011'. Consent forms were assessed for proposed procedure, organ, doctor obtaining consent, and documentation of 15 key risks:- surgical; bleeding, delayed function, non-function/failure, technical problems, nephrectomy, VTE, and medical; acute rejection, biopsies, infection, malignancy, drug side effects, weight gain, NODAT, disease recurrence, CV risk. Actual complications occurring were also examined.

Results: 15 paediatric recipients were removed from analysis. 2 sets of notes had no consent form filed. 97 consent forms were accessible. All had been dated and signed by consenter and patient. 65% had no documentation of type of graft. No single consent form listed all 15 key risks. The number of consented risks ranged from 0-10. The mean number of risks listed was 6. Medical risks were the least commonly documented. 10% consent forms were completed by surgical SpRs. There was no significant difference between number of risks consented for by consultants and SpRs (Chi2 p=0.795). Overall there had been an increase in the number of risks consented for compared to findings from 2002. Overall actual complications were uncommon, but consent was rarely taken for three of the most frequently occurring complications: drug side effects, NODAT and biopsies.

Discussion: Overall consent was more detailed in 2011 compared to 2002. The significant variability in the amount of detail on consent forms lends weight to the call for the use of procedure specific forms. Uniformity and consensus are needed. Medical complications were particularly poorly documented. This leads us to question whether separate medical and surgical consent forms are required.

P138

The wishes and best interests of the individual in controlled donation after circulatory death

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Introduction: In controlled donation after circulatory death (DCD) adjustments to the clinical management of the patient can significantly increase the chances of successful transplantation. These pre-mortem interventions involve individuals who have no legal capacity and therefore fall under the Mental Capacity Act 2005. Pre-mortem interventions continue to raise ethical and legal challenges however, they are lawful where it is established that they are in the best interests of the individual. This determination presupposes, first of all, that organ donation is in the best interests of the individual. This decision is a balancing exercise and involves taking into consideration a number of factors, including the wishes and beliefs of the individual as well as the views of the family and those interested in the welfare of the person.

Aims and objectives: This paper focuses on the wishes of the individual regarding organ donation in the following situations: 1) where there is evidence of an explicit wish to donate; and 2) where there is no evidence of a wish to donate. The aim is to examine how the wishes of the individual and of third parties are taken into account when determining whether organ donation is in the best interests of the person.

Conclusion: It is argued that where decisions have implications for end of life management the degree of confidence with which we can establish the wishes of the individual is crucial. This paper critiques the current legal framework on the grounds that it fails to uphold the individual's wish to donate, when such wish plainly exists, and it allows donation to proceed, where there is no evidence of a wish to donate, on the basis of inferences made by third parties.

P139

The road to repatriation: from rhetoric to reality

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Introduction: The number of patients in Wales receiving kidney transplants is increasing. Redesigning post-transplant services is an opportunity to meet increasing service demand, create quality improvement and significantly reduce escalating costs by enabling the managed switch of drug brands for the long-term.

Methods: Reallocation of primary care drug expenditure has allowed secondary care provision of immunosuppressants at significantly lower acquisition costs. Our Renal Medicines Service was established to co-ordinate all aspects of this new service provision: prescribing, supply, monitoring & review. These enablers allowed for the repatriation from primary care and the managed switch of branded drugs. Significant reductions in drug acquisition costs were delivered by national procurement contracts. By engaging with our patient groups and primary care colleagues we redesigned our service to meet their needs & expectations.

Results: New service provision enabled:

- The repatriation of all kidney transplant recipients from primary care
- A safe, managed switch of branded tacrolimus and mycophenolate mofetil
- Significant & demonstrable reductions in all drug acquisition costs
- The prevention of inadvertent brand switching in primary care
- Improved patient monitoring and access to specialist services
- Improved quality, greater productivity and efficiency

Discussion and conclusion: Reconfiguration has enabled the transplant service to prescribe and supply immunosuppressants in place of the GP. Better medicines management and strategic changes have delivered demonstrable cost reductions by developing new models of drug provision that ensure clinical and cost-efficiency. Our medicines co-ordination service focuses on quality to deliver better patient care, improved communication and better patient access. This work highlights a model of sustaining and self-funding an improved post-transplant service. Savings made against drug acquisition costs underpins ongoing revenue needs and releases additional savings for the healthcare economy.

Category: Clinical Immunosuppression 2

P140

Effect of amiloride on tacrolimus-induced hypomagnesaemia

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Introduction: Hypomagnesaemia happens in more than 50% of Tacrolimus treated patients. There is growing evidence that supplementing Mg in those patients has very little effect if any. Amiloride was used successfully in treating amphotericin B-induced hypomagnesaemia and in Gitleman's syndrome. It is hypothesised that Amiloride stimulates magnesium reabsorption within the distal tubule through sensoring Ca2+/Mg+2 receptors. This study aim is to assess the effect of Amiloride on refractory hypomagnesaemia in Tacrolimus-treated kidney transplant patients.

Methods: Prospective audit on 13 patients with low Mg secondary to Tacrolimus.

Results: No significant correlation was noticed between follow up mg level and Amiloride dose, duration of treatment, Mg dose or Creatinine. Paired T Test shows no significant change in Mg mean (mg1= 0.48±0.07, mg2= 0.50±0.07, p= 0.17). However, significant rise in potassium was observed (K1= 4.26±0.67, K2=5.08±0.61, p<0.0001).

	Minimum	Maximum	Mean	SD
Mg1(mmol/l)	0.38	0.59	0.48	0.07
Mg2 (mmol/l)	0.40	0.61	0.50	0.07
K1 (mmol/l)	2.9	5.2	4.26	0.67
K2 (mmol/l)	3.6	5.9	5.08	0.61
Amiloride dose (mg/day)	2.5	5.0	3.46	1.26
Mg supplement (mmol/day)	0	40	11.69	12.16
F/u Duration (week)	2	5	3.23	1
Creatinine mmol/l	70	420	193	91

Conclusion: Amiloride failed to increase Mg levels using a dose of 2.5 to 5 mg daily over short period follow up. Audit was stopped early due to Mg no- effect results and significant rise in potassium levels.

P141

Impact of CYP3A5 and ABCB1 genotype on the pharmacokinetics of prednisolone in renal transplant recipients

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[1]William Harvey Research Institute, Barts and The London, Queen Mary University of London, London, UK, [2]Analytical Services International, St. George's, University of London, London, UK, [3]Division of Clinical Sciences-Renal Medicine, St. George's, University of London, London, UK

Background: Prednisolone is widely used in solid organ transplantation with standard doses given to all patients without therapeutic drug monitoring. Prednisolone is metabolised by enzymes in the cytochrome P4503A family (CYP3A4/CYP3A5) and is transported by the drug transporter P-glycoprotein encoded by the *ABCB1* gene. The aim of this study was to investigate the relationship between genetically determined variation in CYP3A and P-gp expression and prednisolone pharmacokinetic in adult renal transplantation recipients.

Methods: Forty-three renal transplant recipients receiving 5mg prednisolone once daily enrolled in the study after providing written informed consent. Patients were genotyped for *CYP3A5*3* (*1/*1 or *1/*3 are functional CYP3A5 expressers, *3/*3 are non-expressers) and *ABCB1 3435C>T* (Wild-type CC have more P-gp expression than CT or TT). Plasma prednisolone concentrations were measured by liquid chromatography/tandem mass spectrometry and individual pharmacokinetic parameters were analysed using analysis of variance (ANOVA).

Results: There were no significant differences in prednisolone pharmacokinetics between the *CYP3A5**1/*1, *1/*3 and *3/*3 genotypes. In addition, no statistically significant differences in prednisolone pharmacokinetics were observed between the *ABCB1* CC, CT and TT heterozygotes. The mean Prednisolone AUC_{0-24} for *CYP3A5**1/*1, *1/*3 and *3/*3genotype were 1177 ± 420 hng/mL, 1238.1 ± 258 hng/mL and 1013.4 ± 233 hng/mL, respectively and for *ABCB1* CC, CT and TT heterozygotes were 1181 ± 364 hng/mL, 1084.3 ± 279 hng/mL and 1107.3 ± 273.6 hng/mL, respectively. The mean Prednisolone C_{max} for *CYP3A5**1/*1, *1/*3 and *3/*3 genotype were 175.3 ± 43.1 ng/mL, 161.3 ± 37.1 ng/mL and 151.6 ± 32.3 ng/mL, respectively and for *ABCB1* CC, CT and TT heterozygotes were 162.3 ± 43.3 ng/mL, 169 ± 40.4 ng/mL and 149.0 ± 25.9 ng/mL, respectively.

Conclusions: Neither the *CYP3A5* nor *ABCB1* genotype was associated with prednisolone exposure. Genotyping at these loci is unlikely to allow individualisation of prednisolone dose.

P142

Allograft failure after alemtuzumab induction in renal transplantation

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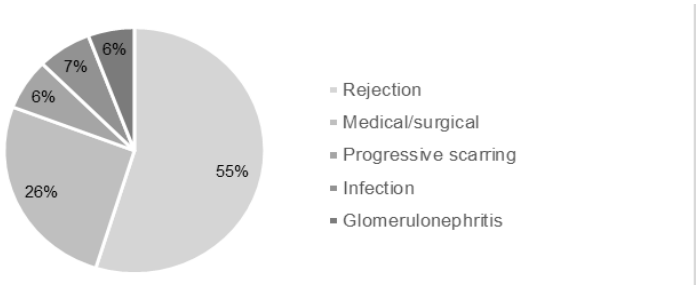
Alemtuzumab [AZ] is a potent lymphodepleting anti CD-52 monoclonal antibody, which is used as an induction agent in renal transplantation. Early observations suggested that this agent might induce “Prope Tolerance” and reduce graft loss from rejection. The aim of this study was to describe the medium to long-term outcomes of a large cohort of renal transplant recipients following AZ induction. We retrospectively studied 927 patients [610(65.8%) male, 446(48.1%) living donor, 426(46.0%) Caucasian] who received a renal transplant with AZ induction, a tacrolimus based and steroid sparing immunosuppressive regime. Mean follow up was 4.18±2.36 years.

Overall patient survival at 1,3 and 5 yrs was 98.3%, 94.9% and 92.5% respectively. Death censored allograft survival was 96.0%, 90.8% and 87.0% at 1,3 and 5yrs and the corresponding rejection free survival was 84.2%, 77.9% and 75.2%. 42/927[4.5%] patients died with a functioning graft.8/927[0.86%] died secondary to cardiac causes, 9[0.97%] from malignancy, 9[0.97%] infection,10 [1.08%] cases were unknown and 6[0.65%] had other defined causes. 104/927[11.2%] allografts failed, the causes of which are shown below.



Although AZ induction is associated with good patient and allograft survival, rejection remains the leading cause of allograft failure. This is similar to outcomes achieved with other lymphodepleting induction agents such as ATG.

P143

Audit of risk stratified immunosuppression protocol for kidney transplants

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Background: A 2008 audit of kidney transplant outcomes at Guy's Hospital revealed unacceptably high rejection rates (around 40%) using predominantly cyclosporin-based immunosuppression. Tacrolimus-based regimens with reported rejection rates around 11%[1] are increasingly regarded as the standard of care, but published data do not reflect our patient demographic where nearly 40% of patients are non-Caucasian. We therefore adopted a risk-stratified protocol assigning patients to low, standard or high-immunological risk protocols using two different tacrolimus target ranges.

Methods: We retrospectively reviewed electronic records for all patients transplanted at Guy's Hospital between 1stNovember 2010 and 31st October 2011 (n=198). Follow up data was available for those patients followed up either at Guy's or at King's College Hospitals (n=79).

Results: 26 (33%) patients were stratified as low-risk, 51 (64%) as standard risk and 2 (3%) as high-risk. 20 patients (25.3%) had at least one episode of rejection (Banff '07 category 2 or 4). There was no significant difference between rejection rates in the three groups ($p = 0.74$). DCD kidney recipients had high rejection rates (50%) whereas living donor kidney recipients had low rejection rates (10%). There was no significant increase in the rates of NODAT, BK nephropathy and CMV viraemia.

Conclusions: Immunological risk stratification has enabled introduction of tacrolimus-based immunosuppression in our centre with an overall reduction in rejection and without significant increase in complications. High rejection rates in DCD kidney recipients and low rates in living donor kidney recipients suggest scope for further optimisation of our protocol.

References: 1 Reduced Exposure to Calcineurin Inhibitors in Renal Transplantation Ekberg et al, NEJM 2007; 357: 2562-75a

P144

Does belatacept improve outcomes for kidney transplant recipients? a systematic review of randomised controlled trials

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Introduction: Belatacept (Nulojix), which blocks costimulation, was developed with the intention of providing better patient and graft outcomes for transplant recipients by allowing minimisation or withdrawal of CNIs and steroids.

Methods: A systematic literature search was performed using Ovid Medline, Embase, Cochrane Central, the Transplant Library, and clinical trial registries to identify all randomised controlled trials (RCTs) in adult kidney transplantation (KT) comparing belatacept with standard CNI therapy. Methodological quality was assessed using the Cochrane risk of bias tool. Where more than 1 RCT was found for an outcome a meta-analysis was performed. Odds ratios (OR) or mean difference (MD) including 95% confidence intervals (CI) were calculated.

Results: Six RCTs compared belatacept to CNIs. Five RCTS reported belatacept from the time of KT whilst one RCT included patients who were switched from a CNI to belatacept 6 - 36 months post KT. A moderate/low risk of bias was found across studies. Incidence of NODAT was less with belatacept at 12 months (4 trials, n=1516; OR 0.43, CI 0.26 - 0.70). Renal function (cGFR) was better with belatacept at 12 months (4 trials, n=1467; MD 11.72 ml/min/1.73m2, CI 0.09 to 23.35) and 24 months (2 trials, n=982; MD 13.72, CI 6.34 to 21.10). Lower systolic (2 studies, 755 patients, MD= -7.20, CI -10.08 to -4.33) and diastolic blood pressure (2 studies, 755 patients, MD= -3.06, CI -4.75 to -1.37), and reduced triglycerides were observed in the belatacept group at 12 months (2 studies, 1209 patients, MD=-32.82mg/dL, CI -50.17 to -15.47) and 24 months (2 studies, 1209 patients, MD=-41.65, CI -56.27 to -27.04). There were no statistical differences regarding acute rejection, patient/graft survival, PTLD or malignancies.

Discussion: Belatacept has a definite benefit over existing CNI therapies resulting in improved renal function, reduction in triglycerides, lower levels of hypertension and less NODAT. There may be an increased risk of PTLD in EBV negative patients and the cost of the agent and need for regular IV infusion are other negative factors in determining its role in renal transplantation.

P145

History of tacrolimus-induced hypomagnesaemia. risk factors and treatment

Khaled Abdulnabi[1], Jane Moberly[2], Niki Skaltsa[1], Adham Al-bakry[2], Sanjay Mehra[2], Ajay Sharma[2], Dan Ridgway[2], Mathew Howse[1,2], Abdul Hammad[1]

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Background: Tacrolimus (tac) induced hypomagnesaemia is known to be caused by renal magnesium wasting. This could be due to down-regulation of magnesium (Mg) transport proteins in the distal tubules. We studied the nature history of hypomagnesaemia, risk factors and treatment in tac-treated kidney transplant patients.

Methods: Retrospective study of 101 patients with12 month follow up from transplantation

Results: 83% are hypomagnesaemic by week 4 after transplantation with the lowest mean of 0.61 mmol//L. 28% recovered from hypomagnesaemia at month 9 follow up with significant improvement in Mg mean (0.61±0.10, 0.67±0.07, p=0.001). No correlation was found between Mg and Tac levels during the same period. However, multivariate analysis shows significant negative correlation between Mg levels at week-26 and Tac week 2 and 4 (r =0.191, p=0.046; r =0.233, p=0.019 respectively). No significant correlation was observed between Mg level and age, gender, HLA matching, early graft dysfunction, induction therapy, source of kidney (live donor, DBD, DCD), recipient's CMV status or polyuria.

A negative correlation was found between Mg levels at week 4, and Cr and PO4 at week 1 and age (r =0.79,p=0.051; r =0.195,p=0.037;r=0.206,p=0.029 respectively). Supplementing Mg (14.6±8.4mmol/day) did not normalise low Mg levels and made no significant difference in Mg (change of mean) (0.09 compared to 0.08). None of the patients developed notable complications of hypomagnesaemia, other than one who had refractory hypocalcaemia treated with IV Mg and Ca.

Paired sample T test was done on 62 patients with low mg at 4 weeks post-transplant

On Mg	No	Mg week 4	Mg week 26	Change in the mean	P
Yes	44	0.58±0.08	0.66±0.08	0.09±0.10	.0001
No	18	0.60±0.05	0.68±0.08	0.08±0.08	.001

Conclusion: A higher incidence of hypomagnesaemia identified in Tac-treated patients than in the literature (88% compared to 45%) with up to 28 % recovering within a year from kidney transplant. A negative correlation with the Tac level slope and early graft dysfunction was noticed. No rule for mg supplementation in treating low mg was observed.

P146

De-novo advagraf immunosuppression in category III DCD kidney transplantation – a single centre experience

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Background: Once-daily tacrolimus (Advagraf) has potential advantages over twice-daily dosing in terms of concordance and ease of monitoring. Kramer *et al* have demonstrated equivalent 1 year kidney transplant function between patients treated with de-novo Advagraf compared to Prograf with organs from donation after brain death (DBD) donors.

Methods: This is an observational study of 83 consecutive kidney transplant recipients from Maastricht category III donors with a mean follow up of 2 years. 73 patients received basiliximab induction and maintenance therapy with advagraf, azathioprine or mycophenolate mofetil and prednisolone. The target 24 hour trough tacrolimus levels were maintained between 5-8µg/L. Outcome data assessed includes eGFR (MDRD method) at 3, 6, 9, 12 and 24 months respectively, graft loss, rejection rates at 6 months and at 1 year, incidence of NODAT, PTLD, CMV infection, BK nephropathy and mortality.

Results: Total Number of transplants N = 73 with a mean age being 55 ± 11yrs

Mean	1m	3m	6m	12m	18m	24m
Cr	202	163	136	154	159	156
eGFR	36	41	47	45	42	44

The mean cold ischemia time was 11 hrs 40 min ± 4 hrs 07 min. There were 21 episodes in 21 patients of biopsy proven rejection (15.3%) within 6 months. The incidence of NODAT was 5.1%, CMV infection 6.5%, PTLD 2.1%, and BK nephropathy 1.4%. There were two (1.4%) graft losses (Banff 6 on biopsy). One patient died of PTLD within 4 months of transplant. In the subsequent 6 months there were no new episodes of biopsy proven acute rejection.

Conclusion: This study demonstrates that the outcomes following the use of de novo once daily tacrolimus (Advagraf) in Maastricht Category III deceased donor kidney transplantation are comparable to those that have been observed with the use of once daily (advagraf) and twice daily (prograf) in Maastricht category II deceased donor kidney transplantation.

Category: Marginal Transplantation 2

P147

The early economic costs of delayed graft function in DCD kidney transplantation

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Introduction: Multiple publications, in the last century, have shown that delayed graft function (DGF) is associated with extra hospital costs in DBD and live donor renal transplantation. Further publications have shown that this is associated with reduced long term graft survival. We hypothesised that the effects of DGF would lead to a similar economic effect in DCD transplantation.

Methods: We reviewed all complete DCD renal transplant procedures between January 1st, 2012 and November 1st, 2013. Patients who did not leave the hospital with a functioning graft(s) were censored from the analysis (n=3).

Results: 71 patients were admitted and discharged with a functioning renal graft(s) in the time period. 34 patients (48%) had immediate function and did not require postoperative dialysis. The two cohorts were equally matched in terms of demography (age and sex). Patients with DGF stayed nearly twice as long in hospital and had more investigations and interventions (Table 1).

Conclusions: Interventions, beyond cold machine perfusion, are still urgently needed to reduce the economic costs of delayed graft function in DCD transplantation.

Table 1: Median and (range) Sig. (Mann-Whitney *U* test)

	Immediate Function (n=34)	Delayed Graft Function (n=37)	Sig.
Hospital Stay (days)	12.5 (7 - 22)	20 (12 - 149)	**p<0.001**
Hypothermic perfusion preservation	74%	62%	Fisher's (p=0.32)
Graft biopsy	0 (0-1)	1 (0-3)	**p<0.001**
Steroid treatment courses	0 (0-1)	0 (0-2)	**p=0.0023**
Ultrasounds	1 (1-2)	2 (2-6)	**p=0.0066**
Extra cost for DGF (per median patient)	NA	£**4325.55**	NA

P148

The feasibility of utilising DCD kidneys for paediatric recipients: early outcomes

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Introduction: Despite the widespread uptake of transplantation of kidneys from DCD donors, allocating such organs to paediatric recipients remains controversial; with no large case series available to inform decision making. We present our experience of paediatric kidney transplant recipients of DCD organs.

Methods: 10 paediatric kidney transplants recipients (from DCD donors) affiliated to two hospitals were retrospectively studied. Data was collected on recipient and donor demographics, transplant type (enbloc v single kidney), biopsy results, renal function and complications.

Results: Median recipient age was 7.5 years (3.5 – 15yrs) and median donor age was 13 years (1 – 47yrs). Median follow up was 24 months (1- 72 months). 7/10 patients were dialysis dependent for 1 year or more prior to transplantation; 2/10 were pre emptive and 1 patient had vascular access issues. Donor kidneys from patients under 2yrs (n=2) were implanted as en bloc double, otherwise single kidneys were implanted (n=8). There were five cases of delayed graft function and 1 case of primary non function. The remaining 9 transplants continue to function at last follow up. Median calculated GFR (Schwartz method) at 3 months and 24 months was similar (54mls/min/1.73m^2 v 57 mls/min/1.73m^2, p=0.87). Time 0 biopsy performed in 5/10 patients revealed minimal cortical changes and normal glomeruli. Complications included ureteric reimplantation (n=1), surgical re-exploration for bleeding (n=2) and non-critical transplant renal artery stenosis (n=1). There were 6 episodes of (successfully treated) immune rejection in 3 patients.

Discussion: Utilising kidneys from DCD donors in children can be beneficial in specific circumstances and is associated with good outcomes. The data presented suggests that including selected paediatric recipients in any future national DCD kidney allocation scheme may be justified.

P149

Transplantation of kidneys with cancer: initial experience from a single centre

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Introduction: Transplantation of a kidney with known cancer and of the contralateral kidney from the same donor is generally regarded a contraindication. A 2% risk of bilaterality is quoted for renal cell cancer (RCC) at the time of diagnosis. Transplantation of such kidneys after excising the primary tumour has been carried out in the live donor setting. We review our experience of transplanting living and deceased donor kidneys with malignancy at the point of transplantation.

Methods: Our institution's prospectively maintained database was interrogated for patients receiving renal transplant with diagnosis of renal cancer in the donor kidney during the ten years between April 2003 and March 2013.

Results: 6 recipients of renal transplants received grafts with renal cancer (5 identified before transplant): 3 in the kidneys that were transplanted and 3 in the contralateral kidneys. Of the three kidneys with primary RCC, the diagnosis was made before transplant in two cases (1 living donor, 1 deceased donor), wide excision of the RCC performed and kidneys subsequently transplanted. In one, the diagnosis was made post-operatively on implantation biopsy and kidney was removed on patient's request. Of the three contralateral kidneys, the diagnosis of RCC in two kidneys and malignant oncocytoma in one was established pre-transplant. All cancers were Fuhrman stage I.

There were 3 male & 3 female recipients with a median age of 52 (range 3-69) and a median follow up of 638 days (range 9-1930). Post–transplant surveillance included 3 monthly ultrasound of transplant kidney for 1 year, and subsequent 6 monthly scans. No malignancy was detected in five transplanted patients. One patient died 5.3 years after transplant of an unrelated lymphoma. 1 and 3-year graft survival was 83.3% and 75% respectively. 1, 3 and 5 year patient survival was 100%, 100% and 84% respectively.

Discussion: No patient in this series developed renal cancer after a median follow up of just under 2 years. Judicious use of donor kidneys with a small cancer after wide excision or of contralateral kidney from the same donor is appropriate particularly when considering the quality of life and mortality on waiting list. Informed consent is particularly important in such cases. We suggest a rigorous ultrasound follow up protocol for patients receiving such grafts.

P150

Transplantation of extended criteria deceased donor kidneys is not associated with inferior quality of life outcomes

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Introduction: An increasing number of organs are transplanted from extended and super-extended criteria deceased donors. As this trend continues it is becoming progressively more difficult to know whether a kidney from an extended criteria donor results in a better quality of life for the recipient than remaining on the waiting list. The aim of this study was to compare different measures of quality of life in recipients following deceased donation from both standard and extended criteria donors. A comparison with a living donor cohort was also made.

Methods: Recipients of deceased donor kidneys were asked to complete a questionnaire containing validated measures of life satisfaction, mood, distress and health-related quality of life (SF12). They were also asked about regret, perception of a net benefit and whether their expectations had been met.

Results: 47 deceased donor recipients participated (mean age 55.4yrs). 26 received a DBD kidney (55.3%). 21 organs (44.7%) were from standard criteria donors. There was no statistically significant difference demonstrated between the DBD and DCD groups or between the different criteria categories (standard, extended, super-extended) across each of the measures used ($p>0.05$). There was also no significant difference between recipients of deceased and living donor kidneys ($n=38$; $p>0.05$). Where expectations were unmet and where no net benefit was perceived, life satisfaction was worse ($p=0.004$ and $p=0.011$). In addition, those recipients whose lives were deemed the same or worse than before transplantation demonstrated more distress (9.9 vs. 17.4; $p=0.009$) and inferior health-related quality of life scores.

Discussion: Transplantation with extended criteria deceased donor organs is not associated with deceased quality of life. Those recipients whose expectations are unmet and where life is not seen to have improved have worse mood, life satisfaction and quality of life. Transplant teams need to elicit recipients' expectations and be aware of possible issues when expectations are unmet in order to counsel patients appropriately both before and after transplantation.

P151

Short term outcomes of recipients transplanted with Lifeport machine-perfused kidneys from elderly donors after circulatory death

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Background: The use of the elderly (age>60 years) DCD donors in UK has risen in recent years. Hypothermic pulsatile machine perfusion (MP) of donor kidneys results in lower incidence and duration of DGF. The use and potential benefit of machine perfusion of kidneys retrieved from elderly DCD donors is not well established.

Aim: To investigate the impact of hypothermic pulsatile machine perfusion on short term outcome of recipients transplanted with kidneys from elderly DCD donors.

Material and methods: From 10/2009 to 06/2013 sixty patients were transplanted with kidneys from DCD donors which were machine perfused prior the implantation. Recipients were grouped in two groups. Group A: donor age< 60 years and Group B: donor age>60years. Donor and recipient characteristics, renal function, 1 year patient and graft survival and perfusion characteristics were compared between the two groups.

Results: The overall DGF rate in patients transplanted with kidneys from DCD donors decreased to 28% compare to 40% prior the machine perfusion era.

	Group A	**Group B**
Number of patients	40	20
Donor age (year; mean)	47	67*
Recipient age(year; mean)	47	59*
PNF (%)	0	2
DGF (%)	25	35
MP resistance at the start (mmHg/ml)	0.64	0.89*
MP resistance at the end (mmHg/ml)	0.24	0.31
Creatinine (µmol/l) at 3 month (mean)	162	219*
Creatinine (µmol/l) at 1 year (mean)	152	171
1 year patient survival (%)	97.5	100
1 year graft survival (%)	95	90

*=p<0.05 Group A vs Group B

Summary: The overall DGF rate is decreased using machine perfusion to 28%. The short term results of recipients transplanted with kidneys from elderly and younger donors are comparable. The beneficial effect of machine perfusion on donor kidneys retrieved from elderly DCD donors merits future studies.

P152

Evolution of DCD renal transplantation, lessons learnt and improved outcome - a decade of experience from a single centre

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Introduction: Donation after Circulatory Death (DCD) has evolved from a mere 5% of our transplant programme in the first year to almost 50% in recent years. We present the outcome of DCD renal transplantation carried out in our institution over last 8 years and improved outcome in recent years.

Methods: A prospectively maintained record of all DCD renal transplants between April 2002 and September 2010 (8 ½ years) was analysed. The analysis included donor and recipient characteristics, immediate graft outcome, patient and graft survival and effect of the era of transplantation.

Results: Our institution performed 1200 renal transplants in the study period. Of these, 288 (24%) were from living donors, 672 (56%) were from deceased DBD donors and 240 (20%) from DCD donors. 236 were single transplant, 2 were dual and 2 en-bloc transplants. The median DCD donor age was 46 years (6 months–79 years) with 40% female donors. The most common cause of donor death was intracranial haemorrhage (45%) followed by trauma (16%). The median recipient age was 51.5 years (6–82) with M:F ratio of 2.6:1. Patients had spent a mean of 1108 (30-4755) days on dialysis with median wait time for transplant of 898 days (11–4547), 19 patients receiving a pre-emptive transplant. The mean first warm ischaemia time was 14min (2min – 33min), the cold ischaemia time 15hr 6min (8hr 25min – 24hr 40min) and the second warm ischaemia time 33 min (16min – 90min).

Primary function was seen in 38.8% (93) of cases, delayed graft function in 55.8% (134) and primary non-function in 5% (12). The median hospital stay following a DCD transplant was 13 days (2-60). One month and 1 year mortality were 1.25% (n=3) and 2.5% (n=6) respectively. Graft and patient survival at one year were 93% and 97.5% respectively. The mean serum creatinine at 1 month, 3 month and at one year were 213, 172, 159 µmol/L respectively with corresponding estimated GFR of 38.5, 44 and 53 mL/min/1.7m^2 respectively. We compared the outcome for the two eras: initial 4 years (n=100) and the last 4 years (n=140). There was a trend of increasing donor age. The mean cold ischaemia time (16:01 vs 14:42) was shorter with increased rate of primary function (34% vs 42%) and shorter hospital stay (16 days vs 12 days) in the second era.

Conclusions: DCD renal transplantation in our centre has produced a medium to long-term results comparable to that of deceased donor DBD renal transplantation. The short term outcomes have improved over time and may be attributable to several factors.

P153

Pre-implantation kidney biopsies – a survey of attitudes and usage

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Introduction: There is an increasing use of kidneys from older deceased donors and those with multiple co-morbidities, and therefore a growing need for organ 'quality' assessment to support decisions on usability. Pre-implantation kidney biopsies (PIKB) are used in some units to help decide whether a kidney should be implanted or discarded. We surveyed UK consultant renal transplant surgeons on their attitudes to PIKB, their current practice, and their opinions on a possible round-the-clock national histopathology service for PIKB.

Methods: One hundred and nineteen surveys were posted to consultant surgeons at all 23 UK renal transplant centres in August 2013. Data were analysed for each question, and free text responses were collated to determine whether a pattern of responses emerged.

Results: Fifty seven responses were received from 21 centres (48% response rate). Eighty three percent of responders agreed that PIKB can be useful in assessing the usability of kidneys. In practice, the majority of surgeons (51%) perform a PIKB on less than 25% of deceased donor kidneys received at their unit. Needle (core) biopsy (44%) and formalin fixation (39%) were the most widely-used techniques and the Remuzzi (Karpinski) score was the most common histopathological score used (23%). The overwhelming majority of surgeons (84%) felt that there were difficulties in the provision of a PIKB service in their unit, most commonly due to lack of a pathologist or pathology technician. Only 23% of responders worked in units where there was a round-the-clock PIKB service available. Seventy six percent of respondents agreed that there should be a national round-the-clock histopathology service for the analysis of PIKB.

Conclusions: This study suggests than many consultant renal transplant surgeons feel that PIKB can be useful in assessing deceased donor kidney quality, but that current service provision is highly variable. There was significant support for a national round-the-clock histopathology service for PIKB, although survey response bias cannot be excluded.

Category: Transplantation Medicine 2

P154

The natural history of bone and mineral disorders following renal transplantation

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Introduction: Hyperparathyroidism is a common complication of end-stage renal disease. In many patients it persists following renal transplantation. We present observational data to describe the natural history and management of hypercalcaemia/ hyperparathyroidism following renal transplantation.

Methodology: Data were collected prospectively for 216 renal transplants. Serum calcium and parathyroid hormone (PTH) levels were recorded pre-transplant, 1 week, 3 months, 6 months and 12 months post-transplant. Treatment (both medical and surgical) and complications of hyperparathyroidism were recorded, along with measures of graft outcome (1 year graft and patient survival and eGFR at 1 year).

Results: 52.8% (n=114) of patients had hyperparathyroidism prior to transplantation. 11.1% (n=24) had previous parathyroidectomy and 9.3% (n=20) were on cinacalcet at time of transplantation. 32.9% (n=72) had persistent hyperparathyroidism necessitating treatment following transplantation. 8.4% (n=18) were managed with calcimimetics and three patients underwent parathyroidectomy in the year following transplantation. Two patients developed calciphylaxis post-transplant (one had PTH 216pmmol/l, the other had PTH within the normal range). Mean PTH level decreased significantly in the first 3 months following transplantation (3.95+/-0.14 vs. 3.61+/-0.13pmol/l; $p<0.01$), thereafter it remained relatively static until 1 year post transplantation (3.39+/-0.14pmol/l). Similarly mean adjusted calcium level rose in the three months following transplantation and then remained largely unchanged until 1 year (2.39+/-0.2mmol/l, 2.49+/-0.21mmol/l, 2.47+/-0.23mmol/l at pre-transplant, 3 months and 12 months respectively.) There was no association between PTH or adjusted calcium levels at 6 months and eGFR at 1 year.

Conclusions: Tertiary hyperparathyroidism following renal transplantation is common, however no association between either post-transplant PTH or adjusted calcium and graft function.

P155

Live donor work up – what lies beneath the tip of the iceberg

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Background: Living donation is one of the ways to bridge the gap between numbers of donors and recipients on the waiting list for kidney transplantation. The potential living donor requires extensive investigative work up to ensure fitness to donate safely. This assessment adds complexity, time and cost to the overall costs of transplantation. The current study is an assessment of workload implications of live kidney donor assessment at a single centre in the UK.

Methods: Data collected prospectively over a 1 year (2012 – 2013) period was reviewed. The end-points were proceeding to donation or not and if not then why not. All the donors were assessed as per an established protocol.

Results: Of a total of 141 potential donors investigated, only 18 went on to donate their kidney yielding a ratio of approximately 1 donor for every 6 screened. In 43 cases (31%), live donor work ceased after preliminary telephone interview as the donor was clearly medically unfit or had a BMI >40.Donor factors that precluded kidney donation included medical co-morbidity including hypertension, perceived cardiac risk and history of malignancy or urological problems (25%), Donor withdrew during assessment process (22%), Low donor isotopic GFR (11%) and Anatomical reasons in the donor (1%).Recipient factors that precluded kidney donation included Donation suspended due to recipient medical problems (3%),Donor not needed – recipient transplanted with cadaveric donor (2%), Donation suspended - recipient stable renal function (4%) and Recipient subsequently declined to accept the live donation (4%).32 potential donors (23%) were being worked up at the conclusion of the study.

Conclusion: A significant proportion (31%) of unnecessary clinic assessments are avoided by nurse led telephone screening. Despite this donor medical issues are the commonest reason for non-progression to donation A significant number of donations fail to proceed because of recipient factors and addressing these can potentially reduce the cost of unnecessary or too early assessments that then need repeating.

P156

Post transplant glomerulonephritis following alemtuzumab induction in kidney transplantation

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Background: The incidence and nature of Post Transplant Glomerulonephritis (PTGN) in patients receiving Alemtuzumab induction has been rarely reported. In this study we investigate the incidence of PTGN and its effect on outcomes in kidney transplant recipients receiving a steroid sparing immunosuppressive regime with Alemtuzumab induction.

Methods: We retrospectively reviewed the medical records of 848 (544 male, mean age 48.4 +/- 13.3 years) kidney transplant recipients in our centre between November 2005 and June 2013 for the occurrence of PTGN. All the patients received a steroid sparing immunosuppressive regime with Alemtuzumab induction and tacrolimus monotherapy. Steroids and MMF were only introduced to treat rejection.

Results: 66 out of 848 patients (7.8%) developed biopsy proven PTGN. A male predominance was found in the PTGN group (9.56% male vs 4.8% female, p=0.01), while PTGN was found not to be related to ethnicity (p=0.404), or donor type (p=0.167). Mean follow up of PTGN patients was 40.3 (±24.5) months and mean time from transplantation to diagnosis was 20.4 (±20.2) months. Out of 66 PTGN patients, 16(1.9%) were diagnosed with Focal Segmental Glomerulosclerosis (FSGS), 37(4.4%) IgA Nephropathy (IGAN), 2(0.2%) Lupus nephritis(LN), 3(0.4%) Membranous Mephropathy (MN) and 8(0.9%) with other PTGN's. (Table 1) There was no difference in patient survival between the PTGN and the non-PTGN groups at 1 (98.4 vs 97.8%) and 3 years (96.7% vs 94.3%) post transplantation. (p=0.2) Censored allograft survival did not differ between the 2 groups (95.6% and 91.1% in the PTGN vs. 100% and 88.3% in the non-PTGN group at 1 and 3 years; p=0.11). When stratified according to diagnosis, censored allograft survival was found to be lower in the patients diagnosed with FSGS (100% and 67.3% at 1 and 5 years) when compared to the non-PTGN group (95.6% and 87.1%% at 1 and 5 years). (p=0.02)

Table 1	Frequency	Percent
NO PTGN	782	92.2
FSGS	16	1.9
IGAN	37	4.4
LN	2	0.2
MN	3	0.3
OTHER	8	0.9
Total	848	100.0

Conclusion: Although these are medium term data, the incidence of PTGN in patients receiving Alemtuzumab induction is similar to other induction agents. Post transplant FSGS is associated with a poor prognosis and we are developing new strategies to deal with this problem.

P157

Early relapse of atypical HUS following ABO incompatible living related paediatric renal retransplant successfully treated with eculizumab

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Introduction: We present a paediatric case of successful treatment of an early relapse of atypical haemolytic uraemic syndrome (aHUS) following ABO incompatible (ABOi) living related renal transplant (Tx) using eculizumab at 9.3 years. The female patient presented at 3.8 years of age with clinical aHUS confirmed genetically as complement factor I mutation (heterozygous for CFI c.1216C>T,p.(Arg406Cys) in patient (who had Factor H antibodies) and asymptomatic mother. She was initially treated with forty plasma exchange sessions over two months. Four months after presentation, she commenced peritoneal dialysis converted to home haemodialysis. An en bloc DCD renal transplant failed to perfuse and was removed at the time of transplantation at 8.8y.

Methods: Prospective case study of paper and electronic records.

Results: ABOi live related kidney transplant from father using quadruple therapy (basiliximab, MMF, tacrolimus and corticosteroids) with B lymphocyte depletion (rituximab 1 month pre-transplantation) with 0% calculated reaction frequency. Recipient and donor (father) blood groups were O and A respectively with anti-A titres of 1 in 128 pre-Tx. Four sessions of immunoadsorption reduced anti-A titres to 1 in 4 at time of Tx without intra-operative complications. Six hours post-Tx, she received first dose of eculizumab due to signs of recurrence of aHUS with allograft dysfunction, LDH 1291U/l, Hb 83g/l and thrombocytopenia at 109 x 10^9/l. LDH rose to maximum value of 3334U/l on day 2 post-Tx with ongoing anaemia and thrombocytopenia (49g/l and 82 x 10^9/l respectively) with second dose of eculizumab administered with histopathological evidence of TMA and good clinical response: reduction in LDH and normalisation of Hb and platelets. Six weeks post -Tx, renal function has stabilised with plasma creatinine of 75-93µmol/l (eGFR of 45-55mls/min/1.73m^2), with EBV reactivation, BK viraemia and normal LDH, Hb and platelets, negative anti-A titres and HLA antibodies on regular eculizumab.

Discussion: This is the first report of a paediatric ABOi living related renal Tx in whom early relapse of atypical HUS was successfully treated with eculizumab.

P158

Low rates of perioperative mortality and cardiovascular events in the West of Scotland renal transplant population

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Introduction: Renal transplantation entails the stress of major surgery plus immunosuppression. Published rates of mortality and cardiovascular morbidity are significant and necessitate careful selection of candidates. Ultimately, all screening protocols inform the subjective question of whether the risk of perioperative morbidity/mortality is acceptable or not. We describe our clinical protocol of cardiovascular risk assessment with highly selective further investigation based on a 1st line combination of resting ECG, echocardiography plus exercise tolerance test and report the rates of mortality and perioperative CV events in the resulting transplants performed.

Methodology: Prospective demographic and clinical outcome data was collected in an electronic database (SERPR) for consecutive adult renal transplants performed in Glasgow between 1/1/2007 and 31/12/2012. All major perioperative morbidity and mortality was identified and validated via case note review.

Results: 555 transplants were performed in the study period incorporating 56.8% males with a population mean age of 47.5 ±13.5 years, 12.8% retransplants and 11.2% previous cardiovascular event (defined as CVA, TIA, STEMI, NSTEMI, CABG, PCI). 28 day mortality was 2/555 (0.4%) 28 day Major cardiovascular event rate was 9/555 (1.3%).

Conclusion: Clinical cardiovascular screening, supplemented by highly selective further, stepwise, investigation/intervention is associated with more than acceptable mortality and cardiovascular morbidity rates. This is demonstrated in a population known to have higher background rates of cardiovascular disease and lower life expectancy than most other UK geographical areas. These results suggest aggressive interventional approaches to the optimisation of cardiovascular risk may be unnecessary or at least be successfully delayed until after transplantation and therefore not be a source of delay in patient access to transplantation.

P159

Pre-donation cardiac assessment of potential living kidney donors: a survey of renal transplant units in the United Kingdom

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Introduction: The annual number of living kidney donors has more than doubled over the last decade. The operation is of no clinical benefit to the donor, and a robust assessment of medical fitness prior to donation is therefore essential. Comprehensive national guidelines were published in 2011 and provide a framework for the cardiac evaluation of potential kidney donors, recommending a low threshold for formal screening for cardiovascular disease. This study aimed to ascertain how renal transplant units across the United Kingdom evaluate the cardiac risk in potential living kidney donors.

Methods: A questionnaire was sent to all adult UK renal transplant units.

Results: Twenty of the 23 transplant units responded. The individual units each carry out between 20 and 140 living donor transplants annually. Eight units report using a local protocol, and two report following the recently published guidelines. All units perform electrocardiography, and four routinely perform transthoracic echocardiography. Four units use the Duke Activity Status Index to calculate the metabolic equivalents (METS) of activity, and use the result to guide the need for formal exercise testing. Ten units request exercise testing in all potential donors. Four of these units specify the use of treadmill testing, and two use cardiopulmonary exercise testing. Stress testing in the other units is dependent on age or clinical concerns. No unit reported the use of CT coronary calcium scoring.

Conclusion: All units undertake a careful cardiac evaluation of potential kidney donors, Relatively few units report recording an estimation of activity status according to a published tool such as the Duke Index. There is variability in the threshold for requesting a formal evaluation of functional capacity, with units tending to err on the side of caution.

P160

Pre-listing cardiac assessment of potential renal transplant recipients: a survey of renal transplant units in the United Kingdom

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Introduction: A recipient cardiac evaluation is usually carried out prior to renal transplantation, with the aim of identifying clinically significant coronary artery disease. There is currently no consensus on appropriate investigations, as none have a clear and unequivocal predictive value for future cardiovascular events. This survey analysed the approach to cardiovascular risk assessment in the different adult renal transplant units in the UK.

Methods: A questionnaire was sent to all adult UK renal transplant units.

Results: Twenty of the 23 transplant units responded. Seventeen units followed their local guidelines, which were supplied by thirteen. The majority of units (19) use risk stratification to guide investigations, but there is variability in the risk factors taken into account. Routine transthoracic echocardiography is undertaken in 12 units (60%). Exercise testing is requested routinely in 16 units (80%), of whom 8 use treadmill testing (40%). Myocardial perfusion scanning or stress echocardiography are used if indicated in 19 units, with the choice of modality according to local expertise. All units would proceed to coronary angiography if clinically appropriate. Three units (15%) report increasing use of cardiopulmonary exercise testing. Multidisciplinary (MDT) meetings with cardiologists are held routinely in 5 units (25%), and on an informal basis in a further four. The estimated waiting time to complete cardiology investigations is 6 – 10 weeks in the majority of units (12, 60%), but these were completed in 4 – 6 weeks in two (10%), and delayed beyond 10 weeks in six (30%). There was no difference in time to completion of investigations between those units with regular cardiology MDT meetings and those without.

Conclusion: A risk stratified cardiac assessment is undertaken prior to renal transplantation in the majority of UK transplant units, however there is considerable variability in the individual approach of each unit. This reflects the lack of a robust evidence base to guide appropriate investigations and optimise the use of resources.

Category: Translational Science

P161

The effects of temperature during *ex-vivo* normothermic perfusion

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Background: The optimal perfusion conditions during *ex-vivo* normothermic perfusion (EVNP) remain undetermined. The aim of this study was to assess the effects of different normothermic perfusion temperatures in a model of renal IRI.

Methods: Porcine kidneys underwent static cold storage (CS) for 23hrs followed by 1h of EVNP using leukocyte depleted blood at a mean temperature of 32°C, 38°C or 42°C. Following this, kidneys were reperfused with whole autologous blood at 38°C for 3h to assess renal function and injury. This was compared to a control group that underwent 24h CS followed by reperfusion at 38°C.

Results: During EVNP, kidneys perfused at 38°C had a higher level of renal blood flow (RBF 38°C 246.3±60.8, 32°C 89.7±23.2, 42°C 149.6±22.6 ml/min/100g P=0.001.) They also had higher oxygen consumption compared to kidneys perfused at 32°C and 42°C (O_2 consumption 38°C 53.4±17.6, 32°C 27.5±3.9, 42°C 29.4±8.8 ml/min/g P=0.002). During reperfusion, the mean RBF (P=0.003) and oxygen consumption (P= 0.004) were higher in kidneys perfused at 32°C, compared to CS control and kidneys perfused at 42°C. Kidneys perfused at 32°C had a lower level of renal function (P=0.016) compared to the control, 38°C and 42°C. Kidneys in the 38°C group had a lower level of tubular function compared to CS and kidneys perfused at 32°C and 42°C (AUC Fractional Excretion of Na^+ CS control 120±17.2, 38°C 64.7±31.0, 32°C 162.0±38.7, 42°C 142.9±37.9%.h P=0.0006). After reperfusion, Hsp70 expression was higher in all the normothermic groups compared to the CS control. Expression was higher in the 32°C and 42°C group compared to 38°C (P<0.001).

Conclusion: During EVNP renal and tubular function were improved at the physiological temperature of 38°C compared to sub-normal or supra-normal temperature in this porcine kidney model.

P162

Soluble complement receptor 1 attenuates complement and inflammatory response in rat renal ischemia-reperfusion injury

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Introduction: Renal ischemia reperfusion injury involves complex interactions of adaptive and innate immunity, and the complement system has been shown to be one of the mediators. Soluble complement receptor-1 (sCR1) accelerates the decay of C3/C5 convertase and aids inactivation of C3b and C4b of the complement pathways. There is evidence regarding its protective role in renal IRI.

Methods: Adult Lewis rats (n=8) underwent unilateral renal ischemia (40 minutes) and reperfusion (48 hours). Sham group (n=6) underwent laparatomy without renal ischemia. sCR1 (25mg/kg) was administered IV prior to the operation, and regular blood samples were retrieved for CH50 assay. Kidneys harvested at 48 hours were analysed for histological damage. Immunohistochemistry and real-time PCR were used to assess complement deposits and cellular infiltration.

Results: A comprehensive histological scoring showed a mean score of 13.5 (range 12-15) for the ischemic group, and 9.8 (7-12) for the sCR1 group. IHC showed decreased C3 and C9 deposits in sCR1 group, along with significant reduction of inflammatory cells (CD3, CD4, CD8, CD68, CD15 cells) compared to the ischemia and sham groups. qPCR showed downregulation of kidney injury molecules – KIM1 and NGAL in the sCR1 treated group. CH50 assay showed complete ablation of complement activity at time of reperfusion, with return of complement activity at 24 hours.

Discussion: sCR1 offers protection, but an element of injury persisted in this single dose 48 hours reperfusion model and suggests a role of other mediators in propagating the injury. Further experiments are underway to determine the effects of repeated dosing of the agent to evaluate whether longer duration of the complement inhibition would offer more protection.

P163

Mitochondrial dysfunction and metabolic dysregulation are important aetiological factors in brain death-induced kidney injury

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Introduction: There is a growing disparity between the number of transplants that are performed every year and the number of patients on the waiting list. This has led to increased utilization of kidneys from extended criteria brain dead donors; however these kidneys have inferior outcomes. We used proteomics to identify the effect of brain death (BD) on the protein signature of cortical samples from rodent BD donors. Subsequent to this we went on to evaluate the effect of BD on the metabolic signature using cortical samples from the same kidney.

Methods: Cortical samples were compared from BD rats (n=6) against sham controls (n=6). BD was induced in male Fischer rats F344 (250-300g) using a Fogharty balloon catheter inflated in the epidural space as previously described[1]. Following confirmation of BD, anaesthesia was stopped but ventilation continued. Mean arterial pressures were maintained between 80-120mmHg using colloid administration. BD was maintained for 4 hours. Kidney samples were subsequently snap frozen and cortical peptide samples prepared following homogenization using in-solution trypsin digestion and subjected to shot-gun proteomic mass-spectrometry analysis using LC-MS. Proteins were identified based on a >2 peptide sequence homology. Protein data was analysed using Progenesis (Non-linear Dynamics) and Ingenuity Pathway Analysis (IPA, Qiagen). Proteins were shortlisted according to whether they were either at least two fold up or down regulated and whether they were significantly different between the two groups, significance was set at $p<0.05$. To evaluate the metabolic signature, cortical samples were prepared and the aqueous fraction subjected to 1H-nuclear magnetic resonance (NMR) spectroscopy analysis to evaluate the metabolic signature of kidney from BD rodents compared to sham controls. Data was analysed as normalised intensity ratios and significantly differentially expressed metabolites determined ($p<0.05$, Prism 6 Graphpad).

Results: Over 1400 proteins were identified, with 43 proteins being differentially expressed between BD and BD Sham cortical samples (2 fold up or down regulated, $p<0.05$). Principle component analysis in 2D could differentiate between the two study populations. IPA revealed mitochondrial proteins and proteins concerning small molecule biochemistry and metabolism as being the top canonical pathways which were dysregulated (Fig 1). Evaluation of the metabolome revealed significantly increased amounts of lactate ($p=0.04$) in addition to alterations in other metabolites and intermediaries including increased isoleucine ($p=0.002$) and decreased AMP ($p= 0.004$), TMAO ($p= 0.015$) and aspartate ($p=0.015$). Creatinine signifying renal dysfunction was higher in the BD group in comparison to controls ($p=0.009$).

Conclusion: Kidneys from BD organ donors are subjected to profound injury which leads to kidney dysfunction through dysregulation of a number of homeostatic mechanisms including hormonal, haemodynamic and inflammatory. Our research highlights the importance of mitochondrial dysfunction and metabolic disturbances and draws parallels with the cellular injury induced by ischemia reperfusion injury (Fig 2). We speculate that to address and prevent kidney injury in the brain dead donor requires a multifaceted approach, optimising donor physiology, but also using cellular conditioning to prevent against mitochondrial damage and metabolic disturbance.

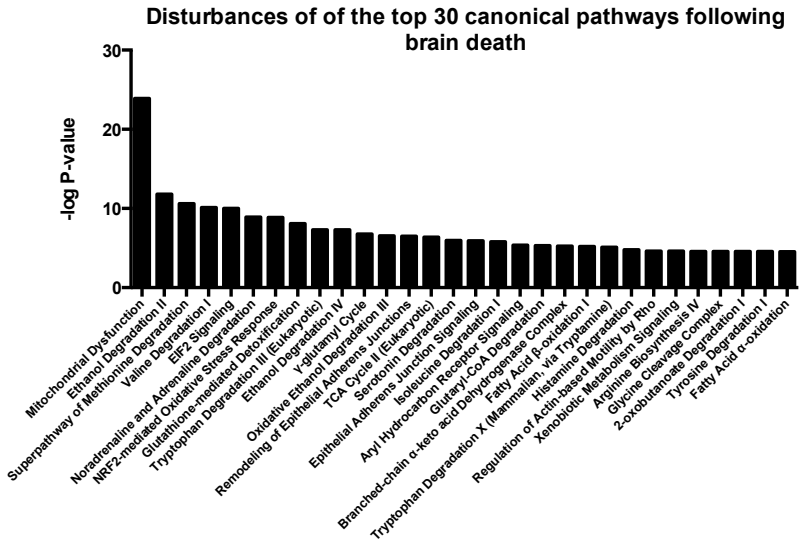

Fig 1: Top 30 canonical pathway disturbances following 4 hours of BD in comparison to sham controls (IPA analysis). Mitochondrial dysfunction and metabolic disturbances predominated the canonical pathways which are disturbed following BD.

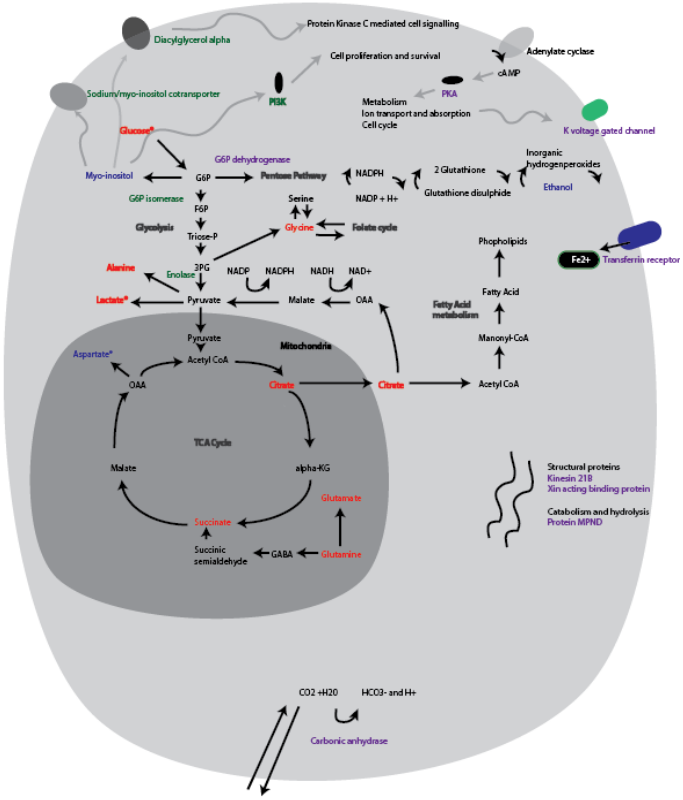

Fig 2: Metabolic and protein disturbances following BD in the renal cortical cells of rat kidneys. Metabolites: Red signifies increased abundance blue decreased abundance relative to the sham brain death model (* $p<0.05$). Proteins: Green signifies increased protein expression and purple decreased protein expression, all of which were significantly different between BD and BD sham. Alterations suggest profound metabolic dysregulation in the kidney as a consequence of BD. [1] Kolkert JL, 't Hart NA, van Dijk A, Ottens PJ, Ploeg RJ, Leuvenink HG. The gradual onset brain death model: a relevant model to study organ donation and its consequences on the outcome after transplantation. Lab Anim. 2007 Jul;41(3):363-71.

P164

Impaired endothelium dependent relaxation - a proxy of viability for donation after circulatory death (DCD) kidneys

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Introduction: DCD kidneys are at increased risk of delayed and primary non function. This study investigated the endothelial response to acetylcholine with increasing cold time in a porcine DCD model. The response of a blood vessel to acetylcholine is the resultant of endothelially secreted nitric oxide and direct vasoconstrictive effects on smooth muscle.

Methods: Kidneys were harvested with 15 minutes of warm ischaemia and then underwent 2 (n=7) or 16 (N=8) hours of static cold storage. Kidneys were reperfused with a normothermic oxygenated autologous blood based solution containing creatinine on an isolated organ perfusion circuit.

Results: Mean (±SD), urine output (2h 624±37ml vs. 16h 335±164; P=0.0014) and creatinine clearance (2h: 12±5.4ml/min/100g.h vs. 16h 5.1±3.7; P=0.0159) were higher in the 2h group. Renal blood flow (2h 441.3±153.5ml/min/100g.h vs. 16h: 573±255; P=0.244) and intra-renal resistance (2h 7.5±2.8, 16h 8.7±8.2 mmHg/min/100g; P= 0.714) were equivalent. There was a significant acetylcholine-induced vasodilatation in the 2h (Renal blood flow baseline 67.0ml/min/100g±26.2 vs. 10^{-8} mM 81.2±34.7; P=0.0338) but not the 16h group (P>0.05).

Conclusions: The reduction of function in the 16h group may result from greater cold ischaemic injury. The loss of acetylcholine-induced vasodilation after 16 hours of cold storage suggests that endothelium is more sensitive to cold ischaemia than vascular smooth muscle. Endothelial response to acetylcholine may form the basis for a test to determine viability of DCD kidneys after prolonged cold ischaemia.

P165

The effect of localised ischaemic preconditioning (IPC) on mRNA expression of acute kidney injury markers and cytokines in a rodent model of ischaemia-reperfusion injury (IRI)

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Introduction: IRI is responsible for delayed graft function and primary non-function in kidney transplantation. Several strategies have been proposed to ameliorate the deleterious effects of IRI. We evaluated whether the previously described use of a continuous immediate localised ischaemic preconditioning (IPC) regime had any effects at the histological and molecular level.

Methods: Twenty adult male Lewis rats were subjected to surgery via an abdominal incision under general anaesthesia and divided into 3 groups: Sham operation; Left unilateral warm ischaemia (IRI) (45 minutes left renal pedicle cross clamping); and IPC+IRI (15 minutes of ischaemia followed by 20 minutes of reperfusion (IPC) prior to 45 min of IRI). Kidney tissue was retrieved at 48 hours. Paraffin sections were made for H&E. RNA extraction and RT-qPCR were performed for markers of acute kidney injury and cytokine profile.

Results: Forty-five minutes of unilateral IRI in the rat caused marked histological damage at 48 hours, characterised by endothelial loss, tubulo-interstitial damage (inflammation, cast formation and necrosis), and glomerular tuft retraction. There was no measurable histological difference between the IRI and IPC+IRI groups. RT-qPCR was performed for acute kidney injury markers (NGAL and KIM-1), cytokines (IL-17, IL-18, and TNF-alpha) and ICAM. There was a significant increase in the expression of NGAL and KIM-1 from sham to IRI, however no difference was found between IRI and IPC+IRI groups. Similarly, there was an increase in the mRNA expression of IL-17, IL-18, and ICAM between sham and IRI, but no significant difference between IRI and IPC+IRI groups. The expression of TNF-alpha was significantly increased in the IPC+IRI group compared to the IRI group, suggesting that inflammation may be an early process in the underlying mechanisms of IPC.

Conclusion: Immediate localised IPC, as utilised in this model does not ameliorate IRI at the molecular or histological level. Further investigation is underway to assess other models of IPC and to analyse functional markers.

P166

Prolonged warm ischemia in an experimental model of renal transplantation

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Background: Donation after circulatory death (DCD) donors provide a large source of kidneys but there is a reluctance to use uncontrolled DCD kidneys due to prolonged warm ischemic times. There is limited data on the tolerance of kidneys to prolonged warm ischemia.

Methods: Porcine kidneys underwent 15, 60, 90 and 120 minutes (min) (n=8, 7, 6 & 4 respectively) warm ischemia and 2 hours cold ischemia followed by normothermic reperfusion with autologous blood for 3 hours. Various perfusion characteristics, markers of renal function and of tubular injury were analyzed.

Results: Renal blood flow was significantly lower in the 60, 90 and 120 (vs. 15) min groups at the start of reperfusion (13.8, 12.5, 12.6 vs. 27.9 ml/min/100g, p=0.0123). However, the blood flow increased in all groups during reperfusion, more so in the 60, 90 and 120 min groups, and there was no difference between the groups from 60 minutes (p=0.215) through to 3 hours (p=0.522). Urine output (UO) and creatinine clearance (CrCl) were significantly lower in the 90 and 120 (vs. 15) min groups throughout (total UO 69, 82 vs. 563ml, p=0.001; CrCl area under curve 0.70, 0.56 vs. 11.1ml/min/100g, p=0.002). Notably, the UO and CrCl in the 90min group improved with reperfusion and were significantly increased by the third hour compared to the first (UO 31 vs. 12ml/hr, p=0.003; CrCl 0.53 vs. 0.12ml/min/100g p=0.0004). This was not seen in the 120min group.

Conclusion: Prolonged warm ischemia caused a significant degree of injury and loss of renal function. However, kidneys appeared to recover during reperfusion suggesting that even after 90 minutes of warm ischemia (but perhaps not 120 min) the injury processes can be reversed. This study suggests that the warm ischemic time can be extended significantly when the cold ischemic time is limited.

P167

Novel rat model of severe renal ischemia-reperfusion injury with therapeutic intervention via renal artery injection and characterization of gfr by inulin clearance

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Introduction: Renal ischemia reperfusion injury (IRI) is major cause of acute kidney injury and allograft dysfunction. Currently no evidence-based protective or restorative treatments exist for clinical use. This reflects the limitations of current *in-vivo* models, which cannot mimic the severity of IRI observed in clinical practice without suffering excessive post-procedure animal deaths from acute renal failure.

Methods: We have developed a novel rat model of severe left renal IRI without a *contralateral* nephrectomy. To mimic the drug administration route most likely used clinically, we test the efficacy of therapeutic agents by injecting directly into the left renal artery, maximising renal exposure whilst minimising systemic distribution. We then utilize inulin clearance studies as a secondary procedure to most accurately determine renal response to injury +/- intervention.

Results: Compared to sham operations, in saline treated animals we observe a long-term reduction in GFR of around 40%, with histological, immunohistological and genetic markers of renal injury. Despite the severity of renal injury, animal losses in the post-operative period using this model are less than 5%.

Conclusion: We believe this model is a useful tool for screening potential therapeutic agents, prior to their use in a more technically complex transplant model. This reduces animal numbers needed to test drugs for clinical transplantation and allows for refinement of dosing schedules.

P168

The suitability of haematopoietic stem cells expanded in a novel clinical grade media for use in the management of acute kidney injury - preliminary results

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Background: Post-operative acute kidney injury is a relatively common complication following numerous types of surgical procedures, particularly following cardiac and transplant surgery. Its occurrence has been associated with an increase in patient mortality, morbidity, and in graft failure following transplantation.

Aim: The aim of the study is to examine the effect of expanding CD34+ haematopoietic stem cells in a novel serum-free and GMP compliant expansion media that has been developed in our lab. W assessed 1) whether the cells expanded in this media remain undifferentiated and maintain a pluripotent state. 2) The ability of the cells to express renoprotective cytokines post-expansion. 3) The immunogenicity of the cells post-expansion.

Methods: CD34+ HSCs were expanded in the novel culture media for twelve days. Cell samples were collected at five time points; day 0, 3, 6, 9 and 12 for gene, protein, and cell surface marker analysis. The analysis was done through the use qRT-PCR, Western blot and FACS analysis. At day 12, Cells were collected and a cytotoxicity assay was performed. (n=2)

Results: CD34+ surface marker was unexpectedly downregulated in the majority of the expanded HSCs. The gene transcripts for the relevant cytokines was found to be expressed through the expansion time points. However, while VEGF-A and FGF-2 saw an upregulation of expression compared to baseline level at day 0, ANG-1, IGF-1 and HGF were downregulated. FACS data shows that both HLA-Class I and II were downregulated in CD34+ cells.

Conclusion: while the data presented here is preliminary data, the successful expansion of CD34+ cells which maintains expression of pluripotent markers suggests these cells may be useful for regenerative medicine. The loss CD34 expression warrants further testing to determine its fate and to confirm that the cells maintain their stemness, although this observation also highlights that CD34 expression may not be the ideal candidate to screen for this purpose. The cells appear to express the relevant cytokines though out their expansion period, however, as a majority of them seem to downregulate expression compared to baseline, methods of increasing expression need to be devised. MHC expression of CD34+ cells appear to be downregulated but since the majority of cells show loss of CD34 expression, future tests should be performed to confirm MHC expression in this setting.

Category: Clinical and Experimental Immunosuppression

P169

Kidney transplant patients' experiences of switching to generic immunosuppressants

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Introduction: Many UK kidney transplant units are switching patients to generic immunosuppressants. In the absence of a central outcomes database, patients switched from branded therapies were invited to respond to a pilot survey. The aim was to assess the feasibility of a larger survey to provide important information for both healthcare professionals and patients.

Methods: A short (13-question), online survey was compiled via SurveyMonkey and ran between May 30th and August 31st 2013.

Results: 76 complete and partial responses were received. Patients reporting switches were taking tacrolimus (42%), MMF (37%) or ciclosporin (8%). Most switches (84%) were undertaken by the transplant unit. Reasons given for the switch were: financial (45%); medical benefit (40%); no reason (15%). Time taken to achieve stable levels after switching varied from immediately to 6 months. When patients were asked how often drug levels were monitored, responses ranged from not at all through once after the switch, to weekly, fortnightly and quarterly. After switching, 60% of respondents reported remaining on their previous immunosuppressant dose, 16% a lower dose and 13% a higher dose. 11 patients (31% of those answering the question) reported suffering new or worse side effects, 4 of whom classed these as 'serious' (mostly changes in creatinine levels). Of patients responding to the question, 13% reported that they needed to be changed back to their original immunosuppression. When asked their views on the switch, around 70% of respondents were unhappy, uncertain or did not know, and 60% felt less than fully consulted.

Discussion: Whilst there are limitations in such research, this survey has highlighted consistent trends in patients' reactions to immunosuppressant switches. There is also evidence of inconsistent adherence to recommended monitoring protocols that could negatively affect patient safety. We hope to build on this pilot to carry out more extensive, scientifically robust, research among a wider group of transplant patients who have undergone switches.

P170

Drug compliance and related issues in young adult kidney transplant recipients transitioning from paediatric to adult service

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Background: Young adult (YA) kidney transplant recipients are at a higher risk for drug non-compliance and subsequent graft loss, particularly during transition from paediatric to adult services. We investigated compliance in our Young Adult Kidney Transplant Clinic (YAKTC) for patients aged 16 to 23 to assess this and whether our specialist service helps with drug compliance.

Methods: Questionnaires were given to 23 patients (mean age 18.8 $\pm$ 1.4) from the YAKTC staffed by paediatric and adult nephrologists. 7 were accompanied by carers who were given the same questionnaire. Comparisons were made on awareness of drugs, frequency and adherence.

Results: 87% reported complete compliance. Reasons for missed medication were forgetfulness (48%) and too busy (4%). 70% of patients reported that the YAKTC helped them to be more responsible for drug adherence. 52% of YA report the YAKTC helped them to reduce the frequency of missed medication. 50% of YA who reported non-compliance said that once daily preparations would improve compliance. Comparisons made between the response from YA and their corresponding carers showed marked inconsistencies with regards to frequency of missed medications. 4/7 YA reported missing some medication, while their corresponding carers thought they did not. Furthermore, we identified 5 incidences of YA reporting taking medications that their carers were unaware of (or vice versa), including azathioprine, tacrolimus, BP mediations and antibiotics.

Conclusions: A significant percentage of YA admit to not taking their medication regularly. Most think that the specialised service we offer for their age group helps them with adherence. Interestingly, there are common discrepancies between what the YA are taking and what their carer think they are taking. YAKTC such as ours may reduce the incidence of drug non-adherence and improve graft survival.

P171

CYP3A4*22 and POR*28 genotypes did not predict drug concentrations for cyclosporin A as assessed by C0 and C2 measurements

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Background: Ciclosporin has a narrow therapeutic index and considerable individual variation in its pharmacokinetics. However, unlike tacrolimus, this has proved challenging to predict by use of genetic markers. Recent reports have suggested that the SNPs *CYP3A4*22* (variant T allele predictive of reduced enzyme activity) and *POR*28* (variant T allele appears to augment CYP3A activity) may affect ciclosporin dose requirements.

Methods: DNA samples from patients commenced on ciclosporin post transplant were analysed by rapid realtime PCR using a LightCycler 2.0 Carousel System to identify expression of the polymorphisms *CYP3A4*22* and *POR*28*. Statistical analysis was performed using SPSS 17.0 (IBM).

Results: 174 samples were analysed: 63 (36.2%) female, 131 (75.3%) Caucasian, 11 (6.3%) Black and 32 (18.4%) Asian. 15 (8.6%) had the mutant CT genotype for *CYP3A4*22* and 83 (48%) had mutant T-alleles at *POR*28*. Groups were compared for equality of distribution, variance and means. No significant difference was found between groups for either genotype with C0 or C2 ciclosporin blood concentrations.

Conclusion: *CYP3A4*22* and *POR*28* genotypes do not influence ciclosporin dose requirements in renal transplant recipients.

P172

The distribution of CYP3A5, CYP3A4*22 and ABCB1 polymorphisms in a healthy Scottish population and liver, kidney and pancreas transplant patients

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Introduction: Polymorphisms (SNPs) of cytochrome P450 isoenzymes CYP3A5 and 3A4, along with SNPs of ABCB1 influence drug pharmacokinetics in transplant patients. The aim of this study was to examine the distribution of these genotypes across a healthy Scottish population, transplant recipients (liver, kidney and SPK) as well as a cohort of deceased organ donors.

Methods: Generation Scotland (GS) is a bioresource of DNA from healthy blood donors in Scotland. 4899 GS subjects, 605 transplant recipients (305 kidney transplant patients, 252 liver transplant patients, 48 SPK recipients) and 385 organ donors were genotyped for SNPs of ABCB1 exon 26 (3435C>T), CYP3A5 (6986A>G) and CYP3A4 intron 6 (CYP3A4*22) using a Taqman® drug metabolism genotyping assay and a real time PCR technique. Basic demographic data including age group, sex and ethnic group were also collected.

Results: Overall 85.5% of subjects had the *3/*3 CYP3A5 genotype, making no functional CYP3A5, with no difference between GS or the transplant groups. Overall 11.9% of the subjects expressed a single A allele (*1/*3) with no difference between the GS or transplant groups. AA (*1/*1) expression was seen in 0.3% of GS subjects, 3.0% of kidney transplant patients, 2.1% of kid-panc transplants, 0.8% of liver transplant patients, and 0% organ donors. ABCB1 CC expression was 20.1%, CT 47.5% and TT 28.9% overall with no difference between GS and transplant groups. CYP3A4*22 CC expression was 88.0%, CT 9.4% and TT 0.2% with no difference between the transplant groups. 31.6% of Asian patients expressed CYP3A5 *1/*3 and 15.8% *1/*1, higher than the population mean of 11.9% and 0.5% respectively. No variation among ethnic groups was seen for CYP3A4 or ABCB1 genotypes.

Conclusion: The distribution of these genotypes is comparable to other Caucasian populations in the literature. The healthy Scottish population and transplant cohort were comparable. In the UK, Asian ethnic patients expressed more CYP3A5.

P173

Bespoke immunosuppression: targeting alloreactive T-cells using c-flip sirna prolongs allograft survival

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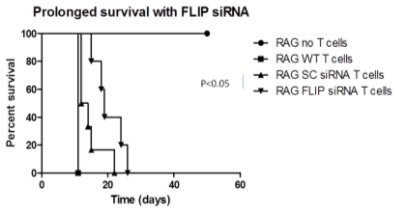
Introduction: If alloreactive T-cells specifically could be removed from the host, allograft tolerance would result, without blanket pharmacologic therapies which suppress all immune responses. The goal of this project is to increase longevity of transplanted organs by inhibiting T cell c-FLIP expression, an important physiologic apoptosis inhibitor, thereby promoting activation induced cell death (AICD) of alloreactive effector T-cells. As an important anti-apoptotic regulator of T-cells in normal immune responses, c-FLIP represents a novel target for manipulating the allograft immune response.

methods: BALB/c and C57/BL6 RAG/WT mice were from Jackson. T cell purification used Miltenyi Biotech magnetic beads. siRNA to cFLIP was from Sigma. siRNA transfer into T cells used Amaxa nucleofector. T cell apoptosis was measured using annexin V flow cytometry. Skin grafting used colloidian glue.

Results: Electroporation of BALB/c T-cells with siRNA to cFLIP resulted in knock-down of cFLIP protein expression as measured by Western Blot and increased T cell apoptosis, measured by flow cytometry, and significant prolongation of skin allograft survival in a full major mis-match model.

Discussion: cFLIP knock-down in T cells can be achieved using siRNA nucleoporation and leads to increased T cell apoptosis and allograft survival.



P174

CHBP and caspase-3 siRNA protect mouse epithelial TCMK-1 cells against cyclosporine a nephrotoxicity via suppressing caspase-3 and apoptosis

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Introduction: Cyclosporine A (CsA) nephrotoxicity is one of main causes of chronic allograft dysfunction, which was characterized by tubular cell apoptosis and interstitial fibrosis. In this study, the effects of cyclic helix-B peptide (CHBP, a novel peptide derived from erythropoietin) and/or synthetic small interfering RNA (siRNA) targeting caspase-3 (an executing enzyme of apoptosis) on mouse epithelial TCMK-1 cells stimulated by CsA were investigated.

Methods: The dose and time responses of CsA or CHBP on TCMK1 cells were observed. Three sequences of caspase-3 siRNAs (s201121, s63385 and s63386, Ambion) were then transfected to TCMK-1 cells with or without CsA treatment. The changes in caspase-3 mRNA and apoptosis were detected by real-time qPCR and flow cytometry.

Results: There are gradual increases in both caspase-3 mRNA and apoptosis induced by 2.5, 5, 10, 20 and 40 ug/ml CsA at 24 h; 20 ug/ml CsA was chosen for further investigation with CHBP or caspase-3 siRNA. The CsA raised caspase-3 mRNA was gradually decreased by 2.5-40 ng/ml CHBP, with 27.2% significant difference at 20 ng/ml; and apoptotic cells were decreased by 53.7%. In addition, the CsA increased caspase-3 mRNA was also significantly down-regulated by three caspase-3 siRNAs at 30 nM after 24 h compared with the negative siRNA control, with 33.9% maximal silencing, while the level of apoptosis was also reduced 22.2%. Simultaneous administration of 20 ng/ml CHBP and the best performed siRNA even better reduced CsA induced apoptosis by 67.5%.

Conclusion: The renoprotection of CHSP against CsA nephrotoxicity might be partially through suppressing caspase-3 and apoptosis. CHBP and caspase-3 siRNA might have synergetic benefits in the treatment of CsA nephrotoxicity.

P175

Cyclosporine A induced vasoconstriction and impaired endothelial dependent relaxation during normothermic reperfusion of experimental kidneys.

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Introduction: The immediate nephrotoxic impact of cyclosporine is unknown in DCD kidneys. This was investigated in a porcine DCD model, during 3 hours of normothermic reperfusion.

Methods: Kidneys were harvested with 15 minutes of warm and 16 hours of cold ischaemia. They were reperfused with warmed oxygenated autologous blood to which creatinine had been added on an isolated organ perfusion apparatus. Cyclosporine (300ng/ml) (n=5) was compared with control (n=6). Dose response of renal blood flow after addition of acetylcholine was used as an index of endothelial function.

Results: Mean (±SD) renal blood flow (control 573±255ml/min/100g.h vs. cyclosporine 306±65; P=0.022) and oxygen consumption (control 47±13.3ml/min/g vs. cyclosporine 25±5.5; P=0.002) were significantly lower in the cyclosporine group. Creatinine clearance (control 5.1±3.7ml/min/100g.h vs. cyclosporine 3.5±1.4; P=0.299) and fractional excretion of sodium (control 106±54%.h vs. cyclosporine 105 ± 49; P=0.978) were equivalent. Acetylcholine had a vasoconstrictive effect in the cyclosporine group (Renal blood flow: baseline 38.4±8.7ml/min/100g vs 10^{-5} mM acetylcholine; P=0.0003) but not control (P>0.05). Concentrations of urinary IL-1β, TNF-α, IL-8 and ET-1 were equivalent, (P>0.05).

Conclusions: We have demonstrated that the vasoconstrictive effects of cyclosporine occur immediately on reperfusion in a porcine DCD kidney model. The failure of endothelium dependent relaxation after cyclosporine suggests that functional endothelial impairment also occurs during this timescale. Calcineurin inhibitor avoidance may reduce delayed graft function in DCD kidney transplants.

Abbreviations: DCD (Donated after cardiac death), AUC (Area under the curve).

Category: Transplantation Medicine 3

P176

New onset post-transplant hypercalcaemia: a retrospective cohort analysis

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Introduction: Renal transplant recipients frequently develop new onset post-transplant hypercalcaemia (NOPTH). In addition to causing unpleasant symptoms, this may worsen patient and graft survival. This analysis sought correlations between NOPTH and recipient, graft, and post-operative factors.

Methods: Retrospective, single-centre, cohort analysis of 138 kidney-alone transplants performed in 2011. Data collected included demographics, pre-operative clinical status, graft type, immunosuppressive regimen, and biochemical follow-up at 3, 6, 9 and 12 months post-operatively.

Results: Of this cohort, 31.8% (n=44) experienced NOPTH, defined as pre-operative normocalcaemia with serum Corrected Calcium above 2.55mMol/L at any follow-up point. In the NOPTH group, mean serum Corrected Calcium was normal at 3 and 6 months follow up (2.46 & 2.52mMol/L), increased to above normal at 9 months (2.61mMol/L), and rose further at 12 months (2.67mMol/L). Compared to normocalcaemic patients, significantly more patients with NOPTH received a DCD kidney (30% (n=13) v 14% (n=13) respectively, p=0.004). Patients with NOPTH had slightly poorer graft function at 9 months (eGFR 42.1 v 46.9, p=0.05). There were no statistically significant differences in recipient age, gender, ethnic origin, duration of dialysis, dialysis modality, pre-operative biochemistry, immunosuppressive regimen, post-operative bicarbonate and tacrolimus trough levels between the 2 groups.

Discussion: This data suggests that NOPTH is a late complication of renal transplantation. The association with DCD kidneys and reduced eGFR poses the interesting question of whether NOPTH is a consequence of reduced graft function. Further work is needed to confirm these links, and determine the underlying mechanisms.

P177

Assessment of feasibility, safety & adequacy of day-case renal transplant biopsies in a single centre

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Background: Renal protocol transplant biopsies are playing an increasing role in the early detection and treatment of subclinical rejection and also allow the detection of unexpected pathology. With increasing transplant rates and increasing pressures on inpatient beds, we have looked at safety and adequacy of day-case transplant renal biopsies in our centre.

Methods: A total of 125 serial day-case biopsies over a 2- year period (2012 & 2013) in a single transplant centre were analysed retrospectively. All were renal transplant biopsies and were performed as day-case procedures majority in a dedicated area. Biopsies were performed under direct ultrasound guidance using a 16 gauge 10cm Tru-Core™ disposable biopsy needle. Patients with an eGFR of < 20mL/min were given desmopressin (0.3 micrograms/kg) and all patients had 6 hours bed rest following procedure. All patients were required to have a haemoglobin of ≥ 100g/l, blood pressure of < 150/90 and INR ≤1.2, adequacy was assessed according to the Banff' 97 criteria. Biopsies were not performed on 2 patients due to potential risks outweighing benefit. None of the patients requiring protocol transplant biopsy were planned as overnight ward admissions. Complications were identified *via* departmental spreadsheet/patient records.

Results: The demographics were as follows 77% of the biopsies were on males, age range was 20yrs to 74yrs and all patients had a BMI < 35. The biopsy uptake was 100% and 67 (54%) of the biopsies were protocol biopsies. The average pre-procedure creatinine was 165µmol/L and desmopressin was given in 16 cases (12.8%). Complications were as follows- 8 patients (6.4%) had visible haematuria following the procedure. Admission overnight was required in 4 cases (3.2%) for observation due to persistent visible haematuria- none of the patients required blood transfusions, radiological or surgical intervention. None of the patients required more than paracetamol for analgesia. Adequate or marginal adequacy was reported for 94.4% of the biopsies with an average of 18.6 glomeruli across all of the biopsies. The mean haemoglobin was 119.7 g/l before the procedure and average of 119.4 g/l post-procedure. Significant pathology was identified in 22 of the protocol biopsies (32.3%), borderline (Banff criteria) or active (Banff 1A onwards) rejection: 8 (36.3%), Calcineurin inhibitor toxicity: 3 (18.1%), recurrence of original disease or de novo glomerulonephritis 2 (9%), viral nephropathy and rejection 2 (9%), chronic allograft nephropathy (CAN) 3 (13.6%) and other pathology 3 (13.6%).

Discussion: We have demonstrated that transplant protocol biopsies can be performed safely as a day-case procedure with minimal complications and with minimal analgesic requirements. Sufficient tissue for diagnosis can be obtained in most cases. We have also shown that renal transplant protocol biopsies can allow early detection and treatment of a range of different pathologies. Whether day case transplant renal biopsies provide improved patient experience requires further assessment. We have however shown that the service can be operated with an excellent uptake by patients by incorporating the practice into patient care pathways.

P178

Pregnancy outcome after kidney donation

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Although pregnancy post donor nephrectomy appears to be generally safe, data on pregnancies in kidney donors are rather limited. Given that many donors are women of childbearing age, the impact of donation on future pregnancies is crucial when advising patients who consider kidney donation. We report our centre experience regarding outcomes of pregnancies post donor nephrectomy.

Data were prospectively collected on consecutive live donors who had pregnancies following nephrectomy from 2007-2012. We used Friedman's test to compare variables at several time points before and after pregnancy.

We identified 10 donors who had 12 pregnancies post donor nephrectomy. Three of them had six deliveries before donation without complications. A total of 11 deliveries were identified. The median age at transplantation was 31.5 (24-35) years and median age at pregnancy was 33.5 (27-38) years. The delivery occurred at 28.5 (13-62) moths post donation. The follow up period following delivery was 12 months (1- 85).

Regarding complications, one donor had two pregnancies, which were complicated by preeclampsia without negative maternal or foetal outcome. The second pregnancy occurred on the background of significant proteinuria and was against medical advice. One donor developed gestational diabetes during pregnancy, and one donor reported one miscarriage followed by delivery without complications. No other complications were reported. There was no statistically significant difference regarding serum creatinine [Chi-square (5)=8.235, p=0.144], 24-hour protein excretion [Chi-square (4)=0.421, p=0.981], systolic [Chi-square (5)=5.882, p=0.318] and diastolic blood pressure [Chi-square (5)=0.294, p=0.998] before pregnancy, at 16, 30 weeks of pregnancy, post-delivery and at the end of follow up.

Although the number of donor pregnancies in this series is small, we demonstrate that pregnancy post donation is safe and that maternal and foetal outcomes are comparable to the outcomes in the general population.

P179

VTE prophylaxis, outcomes and bleeding risks in adult kidney transplant recipients

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Introduction: A lack of national guidelines for venous thromboembolism (VTE) prophylaxis in renal transplant (RT) recipients reflects the unique complexities of RT patients and concerns regarding post RT bleeding. Our local protocol, for patients without high VTE risk factors, is graduated compression elasticated stockings, intraoperative intermittent pneumatic compression devices and aspirin.

Methods: A retrospective audit of 90 day post op VTE incidence, VTE prescribing practice between January 2012 and October 2013. VTE episodes were recorded from hospital electronic notes. Follow-up data was requested from referring hospitals. For a subgroup of patients, the prescribing practice was noted with reasons for protocol deviation. A second subgroup was assessed for post transplant bleeding events.

Results: 395 renal transplants were performed. 4 patients died (2 cardiac, 2 sepsis). 8 patients (2.0%) had a VTE; 4 lower limb DVTs (1 prolonged immobility in nursing home, 1 at site of previous DVT, 1 line-related, 1 unexplained), 1 upper limb line-related DVT and 3 renal vein thromboses (all right kidneys with technical factors +- post transplant identified pro-thrombotic factors). 82% received planned RT VTE protocol. 18% received additional pharmacoprophylaxis mainly low dose subcut unfractionated heparin for pre-existing risk factors (n=6), surgical concerns (n=4), prolonged stay (1) and unknown (n=2). Overall there was an average post-RT haemoglobin drop of 3.8g/dl (range 1.2-9.4). Major post-RT bleeding complication rate (return to theatre and/or blood transfusion) was 12%.

Discussion: Our 2% VTE rate is comparable to international standards. Combined with our bleeding rate, these results support the attention to mechanical VTE prophylaxis but question the requirement for routine pharmacoprophylaxis in RT patients. Comparison with other UK centres may inform specific RT guidance.

P180

Urinary tract amyloidosis in patients with end stage renal failure awaiting renal transplantation

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Introduction: Amyloidosis is a heterogenous group of diseases that can be localised or systemic in distribution and primary or secondary in aetiology. Dialysis related Beta-2 microglobulin amyloidosis (DRA) is a recognised complication of long term haemodialysis. Localised bladder amyloid is uncommon. Our aim was to review recent experience in managing urinary amyloidosis, to highlight some of the management issues in pre-transplant patients.

Methods: In the past 3 years 2 patients with dialysis dependant end stage renal disease who were on the renal transplant waiting list and diagnosed with renal tract amyloidosis were identified. Case notes were retrospectively reviewed. A review of the literature on localised bladder amyloidosis was performed.

Results: Patient 1) A 51 year old male with HUS dialysis dependant for 22 years. Investigations for haematuria revealed an inflamed small bladder with biopsy proven amyloidosis. Video cystometrogram demonstrated poor compliance, high pressure, reduced capacity, reflux and bladder outflow obstruction. Systemic screening has not yet been performed. Patient 2) A 56 year old male with Hereditary Fibrinogen Amyloidosis (HFA), A alpha chain, causing end stage renal disease. Cystoscopy, biopsy and VCMG were unremarkable. Systemic screening at the National Amyloidosis Centre revealed renal and splenic deposits. Approximately 200 cases of bladder amyloid are reported in the literature.

Discussion: Renal transplantation reduces progression of DRA but not other forms of amyloidosis such as HFA, unless other treatments are pursued e.g. combined renal-liver transplant. However there is no literature on how bladder amyloid responds to transplantation and fibrotic, high pressure bladders (e.g. patient 1) may require augmentation before a renal allograft could be sited. Case series in non-transplant populations suggest that most patients symptoms can be managed endoscopically with approximately 10% requiring cystectomy due to massive amyloid involvement. Patients with diagnosed amyloidosis awaiting transplantation should be referred for consideration of systemic screening.

P181

Audit of three month protocol transplant biopsies

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Introduction: For all transplant patients at our hospital, two protocol biopsies are recommended: Pre-implantation 'time zero' biopsy and three month staging 'protocol' biopsy. We wanted to ascertain whether this three month protocol biopsy made any impact on long term treatment and eGFR in the era of tacrolimus immunosuppression.

Method: Data was collected in the data collection table.Patients were selected from the transplant list from 01/01/2012 to 31/12/2012. All patients transferred out prior to 3 months were excluded. ABOi and HLAi transplants were included. eGFR at three months, whether biopsy was performed, histology results, treatment change and improvement in eGFR were documented.

Results: 8 of 53 patients (15%) who required a biopsy did not have one and had no reason documented. 18% of patients with eGFR <50ml.min at 3 months had already had an indication biopsy. Biopsy minor complications were not well documented but no major complications were recorded. eGFR in 21% of patients improved.

Discussion: Three month protocol biopsy in tacrolimus treatment regime led to treatment change and eGFR improvement in some patients, so should be considered in anyone with eGFR < 50ml.min at three months. Perhaps we should be more selective and decide on donor/recipient characteristics rather than umbrella biopsy for all. If decided not for biopsy, reason to be clearly documented. Biopsy appears safe with no major complications in our cohort.

P182

Urinary sodium excretion one year post transplantation does not predict subsequent transplant failure

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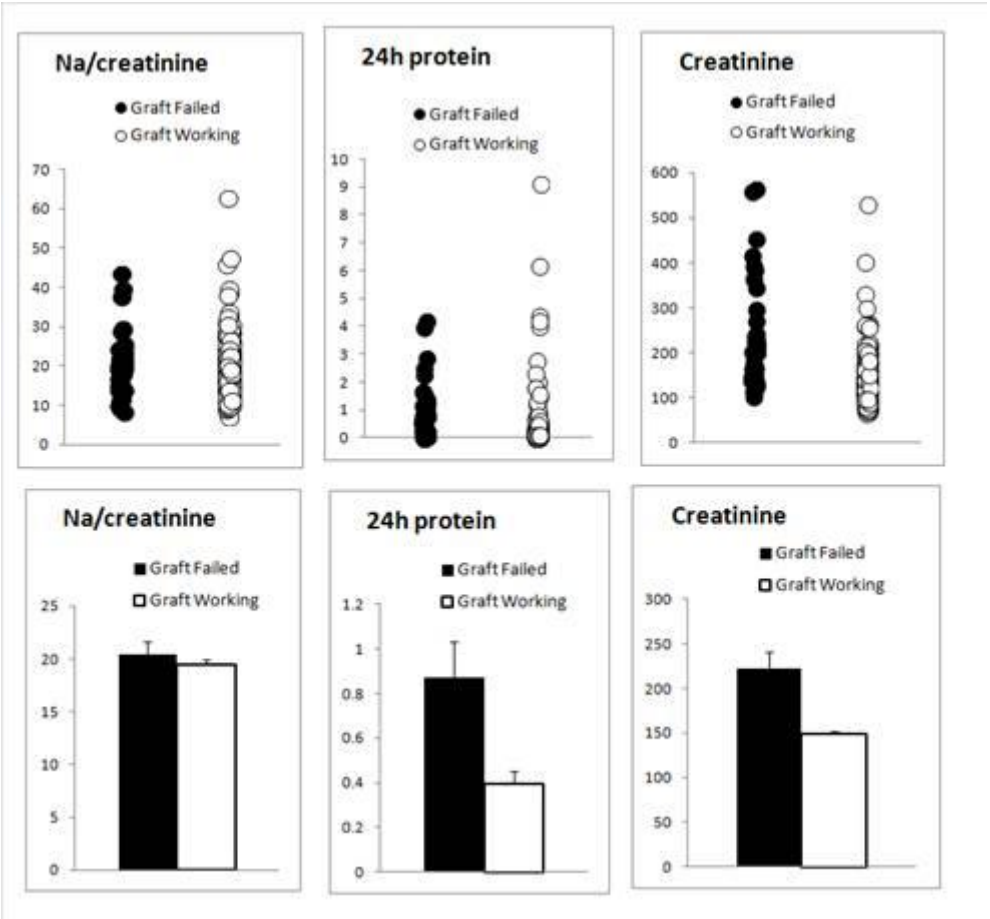
Introduction: Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines recommend dietary sodium intake of less than 2.4 g/d (less than 100 mmol/d) in most adults with CKD and hypertension (A).There is evidence in patients with CKD that high sodium intake limits the antihypertensive and antiproteinuric effects of angiotensin converting enzyme inhibitor (ACE-I) and hence leads to progression of CKD independent of blood pressure (BP) control. However there has not been any study in patients with renal transplant and the effect of high sodium intake on renal transplant survival.

Objectives: We assessed the effect of urinary sodium corrected by urinary creatinine at one year post renal transplant on the graft survival.

Method: Data was retrospectively collected from the 385 patients who had renal transplant from 2000 to 2005. Statistical tests (T-Test) were done to determine if the one year urinary sodium had any effect on renal graft survival.

Results:



The two positive results (24h protein and creatinine at 1 year post transplant) confirm what we would expect and therefore this is a valid sample. There was no statistically significant difference in 1 year urinary Na/creatinine with subsequent transplant failure. We are performing a multi-variant Kaplan-Meier survival analysis on this data and the results will be presented.

Category: Nurses/Coordinators

P183

A review of perioperative staffing and competence levels for national organ retrieval teams in the United Kingdom

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Organ retrieval from cadaveric donors in the United Kingdom is undertaken by National Organ Retrieval (NORS) teams. Organ preservation techniques are developing rapidly, with new technologies including Normothermic Regional Preservation and ex-situ normothermic preservation now emerging into clinical practice. Currently organ preservation is often undertaken by Specialist Nurses in Organ Donation who already have significant other commitments during the organ retrieval process. Increased complexity in surgical retrieval and organ preservation requires highly trained individuals working to a national competence framework to undertake these roles. As workload increases, and roles become more complex, Specialist Practitioners in Organ Retrieval and Transplantation are emerging. Adequate staffing numbers and competence levels are critical for quality in organ retrieval and preservation. The staffing levels recommended in the NORS standards fall below that required by the A ssociation for Perioperative Practice. Additionally, new competencies need to be developed to support staff from different disciplines that are developing specialist knowledge in organ retrieval and preservation. The composition and competence levels of NORS teams should therefore be reviewed to ensure cadaveric organ donors receive the same level of care as other patients in the operating room.

P184

A multifaceted approach to raising awareness of organ donation

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Introduction: The presentation will explore the multifaceted approaches trialled by a healthcare trust to raise awareness of organ donation and propose a transferable model for implementation across the UK.

Methods: Following review of national data it was identified that 20-40 year old males were under-represented in their registration on the organ donor register (ODR). Local iniatives were developed to specifically target this demographic. There were multiple strands to the project, including: developing a social media campaign, art competition and ODR status opinion asked on admission to hospital.

Results: The success of the various iniatives was measured by a combination of statistical analysis of ODR registration, review of social media activity and utilising a qualitatative approach in order to gauge general public perceptions of organ donation. This was analysed pre and post campaign commencement. The results of the iniatives show a 2.1% increase in the number of people in the local geographical registered on the ODR. This contributes to the overall regional ODR registration rate, which is 6.6% above the current national average of 31.5%. There has been a variation of impact that each strand of the campaign has achieved, notably the most successful has been the social media project which has achieved international recognition.

Discussion: We will present the strengths, weaknesses and results of the approaches used and propose a transferable model reflecting the successes of the campaign that can be utilised by other trusts to continue raising awareness of organ donation throughout the UK.

P185

The use of a treatment choices table and an annual consent form to improve patient decision making in renal transplantation

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Introduction: All Adult patients considering renal transplant from a deceased donor must complete a consent form at the time of initial transplant waitlisting and then on an annual basis. The consent form details their choices re whether to accept a kidney from a DBD (deceased after brain death), DCD (deceased after cardiac death) and ECD (expanded criteria donors).

Methods: The patients have the opportunity to read the "What do I need to know about Deceased Donor Renal Transplantation?" leaflet and also to discuss their options with a member of the renal transplant team – though many patients make decision independent of staff. The treatment choices available are:

1. Consider all offers
2. Consider DBD and DCD but not ECD offers
3. Consider only DBD offers

Results: For 2013 (to end 2013) 87% of patients have returned their annual consent forms or are within a year of initial listing – indicating their deceased donor treatment choices. Factors influencing their choices include: 1. Age 2. Are they on dialysis? 3. Are they sensitised or not? 4. How well/ill do they feel? 5. How long have they been on the waiting list? 6. Have they had a previous transplant? 7. Prior knowledgeor experiences influencing choices 8. ? Professional bias at time of counselling re choices. 84% of patients who returned forms indicated they would be willing to consider DBD and DCD offers but not ECD kidneys.57% of patients opted for all kidney offers (i.e. DBD, DCD and ECD offers). If consenting for ECD – patients can still decline without future offers being affected.

Conclusion: Having prior documentation of patients treatment choices re deceased donor offers means we are able to optimize the time used to decline promptly if a patient has clearly indicated "no" to ECD. This form and the treatment choices form has streamlined the decision making process for transplant co-ordinators and the renal transplant team though some offers and recipient choices are still reviewed further as needed.

P186

Avoidance of patient-controlled analgesia systems after laparoscopic live donor nephrectomy

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Background: Patient controlled analgesia systems (PCAS) are commonly used after laparoscopic live donor nephrectomy (LLDN). Nonetheless, opioids are associated with postoperative complications that may delay recovery. The aim of this study was to assess whether donors can be managed safely and effectively without PCAS.

Methods: A consecutive series of 77 LLDN patients from August 2011 to October 2013 were analysed. All donors underwent a full laparoscopic procedure. Forty four received PCA with morphine, and 33 received a morphine based oral analgesic (Oramorph), with intravenous opioids as required. Outcome measures were the amount of intravenous morphine required, duration of PCA, the amount of Oramorph used, antiemetic use, donor complications and the length of hospital stay.

Results: Donor demographics were similar in both groups. The mean (± SD) duration of PCA used was (1 ± 1) days, with the mean dosage used was 41 ± 32 mg. Patients that did not receive a PCA did not require any intravenous morphine, however, they used significantly more Oramorph (PCAS 3950mg vs No PCAS 2150mg P = 0.002). Antiemetic use was similar in both groups (P=0.505). The incidence of urinary retention was greater in donors receiving a PCAS (PCAS 6/44 vs No PCAS 0/33 P = 0.034). Length of hospital stay was similar in both groups of donors (2.8 ± 0.87 vs 2.5 ± 0.87days; P = 0.186).

Conclusion: Avoidance of PCAS is a safe and effective approach to pain management in patients undergoing laparoscopic surgery for live kidney donation.

P187

Are nurse-led clinics an established and valuable means of improving care following renal transplantation?

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Introduction: The role of the specialist nurse in the care of patients following renal transplantation has necessarily evolved with ever increasing pressures for early post-operative discharge and changes in SpR training. The aim was to examine the role of specialist transplant nurses in educating and managing patients at the time of discharge, who else in the multi-disciplinary team delivers this and whether nurse led clinics provide a viable and valuable addition to medical led care.

Methods: A questionnaire was sent to 21 renal transplant centres to establish who delivers education on medication and after care of the graft, whether out-patient clinics have teams of specialist transplant nurses, are nurse led and have independent nurse prescribers.

Results: 10/21 units responded. On-going education begins prior to discharge and involves nurses, doctors, pharmacists and dieticians. Nurses deliver education on medication more often than pharmacists and give more education about after care of the graft than doctors. Transplant specialist nurses both contribute to, and manage, patient care. Only 3 nurse led clinics were identified, but transplant nurses are almost always present in medical consultant led clinics. All centres have a team of out-patient transplant nurses. 6/10 units have nurse prescribers in post. Planned length of stay was predominantly 5-7 days. Unplanned readmission within 4 weeks was not significantly higher where the care was nurse led.

Discussion: Although nurse led clinics are still in the minority, nurses manage care more often than doctors which may reflect their increased experience compared to SpRs. This does not impact adversely on unplanned readmission rates. It is unclear if this correlates with who delivers post-transplant education. More nurse led clinics would seem to offer greater continuity of care and be safe and viable.

P188

Education of secondary school children using medical school applicants: a new messenger for awareness about organ donation?

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Background: We have previously demonstrated that primary school children can promote organ donation amongst their friends and families after attending a workshop. We extended our pilot scheme for secondary school children but this time selected applicants for medical school to promote the message.

Methods: Year 13 students wishing to study medicine were invited to attend a training workshop run by a consultant transplant surgeon, supported by a renal transplant recipient, a medical student and the NHSBT press team. The workshop covered the basics of organ donation and common misconceptions. Students practised giving the talk to the group. They were set a challenge of delivering a talk in their school or community. Questionnaires were used to gauge audience response.

Results: Ten out of the 13 students who attended the training workshop gave a talk. All but one were from BAME backgrounds. Overall their talks reached over 500 school students aged 11-18 years old. Prior to the talk, the majority of students knew about organ donation but less than 40% had discussed it with others. Post-talk questionnaires were returned by 70% of students and of these, 93% felt the session on organ donation was valuable. After the talk, 50% of students had spoken to family and friends as a result of the session. Importantly, over 78% of students who gave feedback said they felt this issue was suitable for their age group to discuss, with 81% saying it was easy to talk about.

Conclusion: We have shown that applicants for medical school can act as excellent messengers in promoting awareness of organ donation amongst secondary school children.

P189

Can we tackle medication adherence in renal transplant patients using a care planning approach?

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Problem: Non-adherence to medication is a major cause of graft failure. What strategy can we use to tackle this problem effectively?

Strategy: The recommendations Nice have made to improve patient adherence are:

- Improve communication and increase patient involvement
- Understand the patient perspective and provide information
- Assess adherence, and implement interventions to increase adherence.

Can a care planning approach tackle all these areas?

Design: We received NHS Kidney Care funding to develop a care plan with particular focus on adherence to medication. The aim is to help patients into a routine particularly during the first year, monitor this annually and enable them to take more control and develop coping strategies. This approach is based on findings from Nevins and Thomas (2009), and Ruppar and Russell (2009).

Working in collaboration with the CKD team adaptations were made to their pre-dialysis care plan:

- To include a section devoted to medication and transplantation
- Amendments to the information section to include information on medication and outcomes
- Information added regarding when reviews were needed and questionnaires designed to detect problems with adherence
- Inclusion of a questionnaire to assess attitudes to medication immediately after transplant.

Methods used were piloting and informal interviews to obtain feedback.

Findings: Some problems were encountered with the care plan process:

- Very few patients remembered to bring the document with them to appointments initially although this has improved
- Some couldn't see the relevance as they felt doctors wouldn't have time to look at them
- Some patients would prefer an application on their phone or computer

Care plan process benefits:

- Increased and more structured interaction between patients and nursing staff:
- Patients have more in depth information regarding the importance of their medication
- Improves patient focus on adherence in the first year

Conclusion: Increased intervention with a care planning approach could help to get patients into a routine with their medication during the first year, therefore improving their chances of subsequent adherence and improved graft survival.
The development of an application for smart phone or web site would be the next stage in this process.

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