

British
Transplantation
Society

British Transplantation Society and Nederlandse Transplantatie Vereniging Joint Congress 2015

Wednesday 11th March – Friday 13th March 2015
Bournemouth International Centre



ABSTRACT BOOK

Thursday 12th March
Tregonwell Auditorium – 10:00
Medawar/Van Rood Awards
Chairs: Prof Luuk Hilbrands and Prof Anthony Warrens

M001

CD8+ T cell senescence predicts cutaneous squamous cell carcinoma development in renal transplant recipients

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Background: Malignancy is a leading cause of death in long-term renal transplant recipients (RTR). Cutaneous squamous cell carcinoma (SCC) represents 75% of malignancy in this cohort, causing considerable morbidity. Risk stratification utilising clinical (e.g. skin colour and sun exposure) and immune (CD4+FoxP3+ regulatory T cells [Treg]) phenotype has had limited success in predicting SCC risk in RTR. We hypothesised that quantifying CD8+ T cell senescence (by CD57 expression) may aid in identification of RTR at increased risk of SCC.

Methods: Long-term, stable, Caucasian RTR were recruited at routine transplant follow-up. Isolated PBMC were analysed by flow cytometry for CD8 and CD57. Phenotypic and clinical data were collected at time of recruitment. Hazard ratios for variables were calculated by stepwise Cox regression.

Results: 117 RTR were recruited: 59 had a history of previous SCC. During follow up (median 403 days), 23 RTR developed SCC. Age at sampling and first transplant and previous SCC were predictive of SCC development within 500 days of assessment; duration or type of immunosuppression, chronic UV exposure, CMV serostatus, smoking history and gender were not. Two of three phenotype risk scores were predictive of subsequent SCC on univariate analysis, but both lost predictive value when adjusted for age. Number and proportion of Treg were not predictive of SCC. The percentage of CD8+ T cells expressing CD57 was strongly predictive of SCC development. When stratified into those with a majority (>50% - CD57hi) and minority (CD57lo) expressing CD57, CD57hi RTR were four times as likely to develop SCC, independent of age or history of previous SCC.

Conclusion: Stratifying senescence on CD8+ T cells using CD57 expression is the best performing predictor of SCC in RTR, who may benefit from timely reduction of immunosuppression and enhanced dermatological surveillance.

Kidneys from uncontrolled donors after cardiac death: an offer you can't refuse? A 10-year evaluation in the Netherlands

Hessel Peters-Sengers¹, Jaap J. Homan van der Heide¹, Martin B.A. Heemskerk², Ineke R.J.M. ten Berge¹, Fred C.W. Ultee¹, Mirza M. Idu³, Michiel G.H. Betjes⁴, Arjen D. van Zuijlen⁵, Maarten H.L. Christiaans⁶, Luuk H. Hilbrands⁷, Aiko P.J. de Vries⁸, Azam S. Nurmohamed⁹, Stefan P. Berger¹⁰, Frederike J. Bemelman¹

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Introduction: Despite the relatively high rate of donation after cardiac death (DCD) in the Netherlands, the median waiting period for a post-mortem kidney was still over three and a half years in 2013. The majority of DCD kidneys are from controlled DCD (cDCD). Further expansion of the donor pool can be done by also accepting uncontrolled DCD (uDCD).

Methods: In this retrospective cohort study in which all Dutch transplant centers participated we examined various donor-related and recipient-related factors on several renal endpoints between firstly transplanted uDCD (n=97) and cDCD (n=1444) procured from 2002 till 2012.

Results: PNF was higher in the uDCD than in the cDCD (19.6% vs 9.4%, $p < .001$, respectively). Delayed graft function was also higher in uDCD than in cDCD, but not significant (73.7% vs 63.3%, $p = .069$, respectively). Estimated glomerular filtration rate after one-year and five-year graft survival rates were comparable between uDCD and cDCD, if censored for primary non-function (PNF). The main variables affecting the differences in PNF between uDCDs and cDCDs were first warm ischemic period, cold ischemic time, and donor age.

Discussion: We conclude that uDCD can be a valuable expansion of the donor pool when limiting these risk factors for PNF.

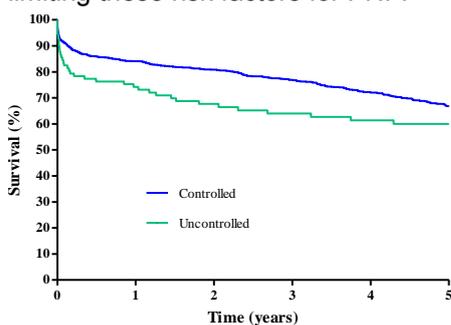


Figure 1: Kaplan-Meier curves of 5-year crude graft survival for the uncontrolled (green line) and the controlled (blue line) circulatory-death donors. Crude graft survival was defined as time from transplantation to either graft nephrectomy or return to dialysis or patient death, whichever was earlier.

M003

Transplantation with kidneys from deceased donors with acute renal failure: the United Kingdom experience

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Introduction: Kidneys from deceased donors with acute renal failure (ARF) are generally not accepted for transplantation due to concerns of inferior outcomes. We present one of the largest studies in the world examining the outcomes of kidney transplantations from deceased donors with ARF performed in the United Kingdom.

Methods: NHSBT data of all deceased adult kidney transplants in the UK from 2004-2014 was analysed to identify donors with or without ARF, defined as terminal serum creatinine level >150 $\mu\text{mol/l}$. Comparison was undertaken for both standard (SCD) and extended criteria (ECD) donors (as defined by UNOS criteria). Outcome measurements include; delayed graft function (DGF), primary non-function (PNF), eGFR, graft survival (GS) and overall survival (OS) at 1 & 5 years.

Results: In SCD, 649 and 8328 patients received kidneys from donors with and without ARF respectively. Mean eGFR at 1 & 5yr was 56 & 58ml/min ($p=0.448$) and 55 & 55ml/min ($p=0.137$) in the ARF & non-ARF groups respectively. DGF and PNF rates were 39%vs.23% ($p<0.001$) and 3%vs.2% ($p=0.645$) respectively. No statistical difference in GS & OS between study groups at 1 and 5 yrs. (1 yr: 90% vs. 90%, 5 yr:76% vs.73%) and (95% vs.96%. 88% vs. 85%) respectively.

In ECD, 223 and 3206 patients received kidneys from donors with and without ARF. Mean eGFR, DGF, PNF and GS & OS at 1 & 5 yrs. between ARF & non ARF: 38 & 38ml/min ($p=0.210$) & 39 & 41ml/min ($p=0.281$), 48%vs.33% ($p<0.001$), 3%vs.4% ($p=0.876$), 80%vs.83% ($p=0.366$), 65%vs.62% ($p=0.812$) and 90%vs. 92% ($p=0.498$) & 81%vs.76% ($p=0.192$) respectively.

Conclusion: Despite the increased incidence of DGF in both SCD & ECD groups, the UK national data supports the transplantation of kidneys from selected deceased donors with ARF. Graft and overall survival outcomes are comparable to kidneys from non-ARF donors and provides a valuable resource to increase the donor pool and address the current challenge of the waiting list.

VR004

Genetic variants of recipient PD-1 and donor PD-L1 affect risk of acute rejection after liver transplantation

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Introduction: Co-inhibitory receptor-ligand interactions fine-tune immune responses by negatively regulating T-cell function, and are involved in transplant tolerance in experimental animal studies. Whether they affect transplant rejection in humans is still unclear. The aim of this study is to examine whether single nucleotide polymorphisms (SNPs) in co-inhibitory receptors or their ligands in donors and recipients influence the rate of rejection after liver transplantation (LT).

Methods: 10 SNPs of PD-1, PD-L1, CD244, and TIM-3 were genotyped in 528 LT recipients and 410 donors. Associations with both early (≤ 6 months after LT) and late (> 6 months after LT) acute rejection were analyzed by a likelihood ratio test. Multivariate analysis of SNPs in combination with patient characteristics were performed using cox regression model. PD-L1 expression on hepatic leukocytes of donors with different genotypes was measured by flow cytometry.

Results: Donor PD-L1 rs1411262 ($p=0.008$), CD244 rs3766379 ($p=0.034$) and rs6682654 ($p=0.023$), were associated with early acute rejection. Meanwhile, recipient PD-1 rs11568821 ($p=0.019$) and donor PD-L1 rs4143815 ($p=0.006$) were associated with late acute rejection. After adjusting for baseline characteristics, donor PD-L1 rs1411262 was the only SNP independently associated with early acute rejection (AA versus AG/GG; HR=3.592; 95% CI=1.775-7.269; $P=0.002$), while the A allele of recipient PD-1 rs11568821 (AA/AG versus GG HR=2.951; 95% CI=1.269-6.861; $P=0.014$) and the C allele of donor PD-L1 rs4143815 (CC/CG versus GG; HR=0.236; 95% CI=0.086-0.648; $P=0.002$) remained to be independent factors associated with late acute rejection. In vitro analysis showed that C allele of PD-L1 rs4143815 is associated with higher PD-L1 expression on donor hepatic BDCA1⁺ dendritic cells upon IFN- γ stimulation.

Discussion: Functional SNPs in donor PD-L1 and recipient PD-1 are associated with the development of acute rejection after liver transplantation. Donor PD-L1 and recipient PD-1 interaction is involved in the regulation of allogeneic immune responses to liver graft in humans.

M005

B cells from a tolerant environment can control a T cell allograft response in an antigen specific, IL-10 dependent mechanism

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Introduction: B cells can have multiple functions in transplant recipients, alloantibody and cytokine production, alloantigen presentation, as well as immune regulation. This study tested the hypothesis that the context and microenvironment in which B cells act plays a critical role in determining their function after transplantation.

Methods: The immune regulatory role of B cells was investigated using a mouse model of transplantation tolerance. Briefly, mice were pre-treated with a non-depleting CD4 antibody and DST, which permits cardiac allografts to survive long term. B cells within the allograft and spleen were analysed and purified at day 35-post transplant. After purification splenic B cells were transferred into CBA.*RAG*^{-/-} mice along with naïve effector T cells. The following day recipients received a skin transplant, which was monitored for survival.

Results: We show that IL-10 producing B cells with a regulatory surface phenotype infiltrate long term surviving mouse cardiac allografts. No donor specific alloantibody was detectable. Furthermore, the splenic compartment contains a 1.5-fold increase in IL-10 producing B cells. Adoptive transfer of purified splenic B cells into immunodeficient recipients along with naïve T effector cells prolonged allograft skin graft survival (MST 57 days vs 13 days for T effector cells alone) in an alloantigen specific mechanism. Blockade of IL-10R at time of transplantation, abrogated graft survival. These IL-10 producing regulatory B cells affect T cell function via altering inflammatory cytokine production and triggering the development of an increased number of regulatory T cells.

Conclusion: Together these data suggest that exposure to alloantigens in a tolerant environment can lead to the development of an antigen specific splenic B cell population that can control alloreactive T cell responses through IL-10 dependent regulatory mechanisms.

M006

Does HLA-incompatible transplantation confer a survival advantage in the UK?

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Introduction: HLA-incompatible transplantation is perceived as being a 'high-risk' option with increased mortality and morbidity for transplantation of sensitized recipients of renal transplants. Data from the USA has indicated that HLA-incompatible transplantation confers an increased patient survival compared to 'dialysis only', or 'dialysis and transplant'. This study aims to determine whether this survival advantage applies in the UK, where options for deceased donor transplantation are different.

Methods: UK patients listed for transplantation at 1.1.2007, and all subsequent listings to 31.12.2013 were accessed from the NHSBT waiting list on 6.11.2014. LD HLA-incompatible (HLAi) transplants were identified, and compared with LD compatible transplants (LDc, excluding paired scheme recipients), DD compatible transplants (DDc) and untransplanted (U) patients. **Main outcome measures:** Post-listing survival, time from listing to transplant.

Results: During the study period, of total cohort of 25089 patients listed for transplantation, 219 recipients received an HLAi transplant; 4498 an LDc; 11313 a DDc and 9059 were untransplanted. Using cox regression modelling of post-listing survival, adjusting for age at registration, gender, blood group, CRF at registration and duration of ESRF, compared to LDc, DDc had a hazard ratio (HR) for death of 1.6 (95% CI 1.31-1.88, $p < 0.05$); HLAi a HR of 2.5 (95% CI 1.55-3.98, $p < 0.05$) and remaining untransplanted conferred a HR of death of 6.9 (CI 95% 5.75-8.39, $p < 0.05$). For the transplanted recipients, mean time from listing to transplant was 540d for LDc (SD 622), HLAi 1091d (SD 848) & DDc 1078d (SD 1331), $p < 0.05$.

Discussion: HLAi transplantation confers a quantifiable survival advantage in the UK, compared to remaining untransplanted. Time from listing to transplant is significantly longer for patients receiving an HLA-i living donor transplant, compared to a compatible living donor. There may be scope to improve survival for patients coming forward with an HLA-incompatible living donor, by expediting the time from listing to transplantation. Further work with a fully matched cohort is planned.

VR007

First clinical series of end-ischemic hypothermic oxygenated machine perfusion via hepatic artery and portal vein in donation after circulatory death liver transplantation

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¹Section of HPB Surgery and Liver Transplantation, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands, ²Surgical Research Laboratory, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

Introduction: Hypothermic oxygenated machine perfusion (HOPE) is a promising method to improve preservation of livers prior to transplantation. Animal studies have suggested that HOPE can restore hepatic energy status and reduce reperfusion injury in donation after circulatory death (DCD) liver grafts. Aim of this clinical study was to assess the safety and efficacy of dual HOPE via both hepatic artery and portal vein in DCD liver transplantation.

Methods: In 10 patients undergoing DCD liver transplantation, the donor liver was treated with 2 hr of dual HOPE. Livers were procured in a conventional manner using rapid flush out and static cold storage (SCS) in UW solution at 0-4°C. Upon arrival at our center livers underwent HOPE with Belzer UW - Machine Perfusion Solution at 12°C using a pressure controlled device (Liver Assist, Organ Assist). During HOPE, mean arterial pressure was 25 mmHg and portal pressure 5 mmHg. Outcome after transplantation was compared with a historical control group of 20 DCD liver transplantations matched for donor age, donor warm ischemia time, and recipient MELD score.

Results: There were no technical problems during HOPE. Median SCS time until HOPE was 5.2 hr (IQR 4.7-5.9). Total preservation time was not significantly different between the two groups (8.4 hr [IQR 7.0-9.3] vs 7.6 hr [IQR 7.0-8.1]; p=0.143). During HOPE, hepatic ATP content increased >10-fold from 4 (IQR 3-7) to 56 µmol/g protein (IQR 41-71) (p=0.03). All HOPE preserved livers showed excellent early function after transplantation. Postoperative peak serum ALT was significantly lower compared to controls (median 933 U/L [IQR 610-1631] vs 1641 U/L [IQR 1086-2343]; p = 0.03). At a median follow up of 2.5 months (range 0.1-7.4) none of the HOPE preserved livers had developed non-anastomotic biliary strictures (NAS). In contrast, early NAS occurred in 6/20 (30%) control DCD livers (p=0.07).

Discussion: This first clinical study of end-ischemic dual HOPE in DCD liver transplantation demonstrates that this technique is safe, can restore cellular energy levels, and reduce reperfusion injury. Our data suggest that HOPE can reduce the incidence of NAS after DCD liver transplantation.

M008

Ex-vivo lung perfusion impairs direct allorecognition reducing recipient T cell infiltration

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¹Manchester Collaborative Centre for Inflammation Research, University of Manchester, Manchester, UK, ²The Transplant Centre, University Hospital of South Manchester, Manchester, UK, ³Department of Pathology, Rikshospitalet, Oslo, Norway, ⁴Department of Cardiothoracic Surgery, Lund University and Skåne University Hospital, Lund, Sweden

Introduction: Depletion of immune cells from the donor organ prior to transplantation prevents rejection, whereas restoration of the depleted immune compartment restores the alloresponse. Strategies to remove donor immune cells prior to transplantation may therefore represent a potential therapeutic intervention. For the purpose of this study, we used a pig lung ex-vivo lung perfusion EVLP transplant model to determine if donor immune cell depletion impacts on recipient T cell responses.

Methods: 12 female recipient pigs were randomised to receive either i) a left male lung following 2 hours of EVLP or ii) a left male lung retrieved using standard protocols, followed by right pneumonectomy. Recipients were monitored for 24hrs and samples were collected at 0, 6, 12 and 24 hours. Donor or recipient cells were identified via Y chromosomal selection. T cell infiltration was assessed and graded using standard guidelines. In all cases EVLP transplantation was compared against standard lung transplantation

Results: At all timepoints EVLP reduced donor leukocyte transfer following transplantation, determined by total donor DNA quantification and Y+ cell counts. Donor leukocyte migration to the recipient spleen and liver lymph nodes was also reduced (spleen – 0.16ug/ml vs 0.09ug/ml, p=0.006, liver 0.17ug/ml vs 0.12ug/ml, p=0.038). Recipient T cell infiltration of the donor lung was significantly lower in EVLP when compared to the standard transplant group (p=0.039).

Conclusions: This data suggests that passenger leukocyte removal during EVLP leads to a reduction in direct allorecognition and T cell priming, leading to a loss in recipient T cell infiltration of the donor lung.

Poor renal function and increased mortality in elderly recipients transplanted with kidneys from elderly deceased donors: a Dutch cohort study

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Introduction: An increasing number of elderly patients (65+) are transplanted with kidneys from elderly donors both after cardiac death (DCD) or brain death (DBD). Concerns rise that this may lead to poor transplant outcome. We compared renal outcomes of elderly DCD and DBD kidneys within the Eurotransplant Senior Program (ESP) to the outcome of young (65-) kidneys transplanted in elderly recipients.

Methods: In this retrospective cohort study we included all recipients (at least 18 years old) from all Dutch centers transplanted from 2002 to 2012 with a first DBD or DCD kidney (Maastricht category III). We categorized young and elderly recipients either transplanted with young or elderly donors, and classified them on donor type. Data were retrieved from the Dutch Organ transplantation Registry (NOTR).

Results: The mortality risk within 5 years was significantly higher for elderly recipients with elderly DCD (n=245, HR 2.27 CI (1.34-3.84) or elderly DBD kidneys (n=137, HR 1.71 CI(1.06-2.77)) as compared with elderly transplanted with young DBD (n=144) kidneys. Elderly DCD kidneys also resulted in more 5-year crude graft loss (HR 1.75 CI 1.11-2.75) as well as a significantly increased incidence of delayed graft function and acute rejections within 3 months compared with elderly transplanted with young DBD kidneys. Concerning renal function, 1 year after transplantation 63.8% of elderly DCD kidneys had an eGFR below 30 ml/min/1.73m² (including primary non-function) compared with 45.5% in elderly DBD kidneys, and 26.0% in elderly recipients with young donors.

Discussion: Acceptance of elderly DCD or DBD donors to transplant elderly recipients is associated with increased risk of mortality compared with elderly transplanted with young DBD. Renal function at one year of elderly recipients transplanted with elderly DCD kidneys was severely inferior as compared to all other categories. The current practice of transplanting vulnerable kidneys to vulnerable recipients needs reconsideration.

M010

Kidney transplantation using kidneys from donation after circulatory death donors: results from the UK experience

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Introduction: Kidneys from donation after circulatory-death donors currently make up over 40% of deceased donor kidney transplants in the UK. In addition, 34% of deceased donor kidneys transplanted in the UK are from kidneys from older donors (>60 years). We used the largest international cohort of recipients of such kidneys to assess long-term transplant outcome.

Methods: A comprehensive analysis of adult recipients of DCD and DBD (donation after brain death) donor kidneys performed in the UK between 2001 and 2012 was performed, using data from the UK transplant registry. Cox proportional hazards and multiple linear regression were used to compare graft survival and function.

Results: 3626 DCD and 9683 DBD donor kidneys were included in the analysis with a median follow-up of 7.5 years (IQR 4.5-10.7). 1013 (27%) of DCD kidneys and 2110 (22%) of DBD kidneys were from donors aged over 60 years. Unadjusted 5 and 10 year death-censored graft survival was 85.9% and 74.9% for recipients of DCD kidneys and 84.5% and 74.3% for recipients of DBD kidneys with an adjusted hazard ratio (DCD compared to DBD) for 10 year graft survival of 0.95 (95% CI 0.8 to 1.1, p=0.42). There was no interaction between donor age over 60 years and donor type (p=0.40). There was no significant difference in the incidence of primary non-function 3.1% vs 2.6% (p=0.06) for DCD and DBD donors, respectively. Graft function (estimated glomerular filtration rate) was 49.6 ml/min/1.73m² and 48.1 ml/min/1.73m² for DCD and DBD recipients 5 years post transplant respectively, and risk-adjusted regression analysis demonstrated no difference between the groups (regression estimate 0.02 (95% CI -1.1 to 1.2, p=0.97).

Discussion: Recipients of kidneys from DCD donors have equivalent graft survival up to 10 years post transplant and equivalent graft function 5 years after transplantation to recipients of DBD kidneys, irrespective of donor age. DCD donor kidneys have provided an excellent source of kidneys for transplantation.

Wednesday 11 March
Tregonwell Auditorium – 15:00
Clinical
Chairs: Dr Antonia Bouts and Dr Rachel Hilton

O001

Vaccination to prevent the high herpes zoster incidence after renal transplantation

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Introduction: Herpes zoster (HZ) is the clinical manifestation of varicella zoster virus (VZV) reactivation and occurs more frequently in people with a suppressed immune system. We studied the incidence of HZ in a cohort of renal transplant recipients. Moreover we assessed the efficacy of vaccination to increase VZV IgG titres in kidney transplant candidates to comparable levels as in healthy persons.

Methods: In a cohort of 522 renal transplant recipients, transplanted between 2003-2008, incidence and complications of HZ were analysed up to July 31, 2013. In a prospective study, patients ≥ 50 years awaiting renal transplantation (n=23) were vaccinated with Zostavax®. Gender and age-matched kidney transplant donors (n=22) were included as controls. VZV-specific IgG titres were determined before, 1 and 3 months after vaccination.

Results: HZ prevalence was 21.3%. HZ incidence was 12.5 cases/1000 person years (PY) under immunosuppressive therapy (IS) in patients < 50 years, and 22.7 cases/1000 PY in patients ≥ 50 years. HZ incidence in the general population is significantly lower (7-8 cases/1000 PY). Complications (bacterial infections, systemic dissemination, and death) only occurred in HZ cases under IS. After vaccination, VZV-IgG titres significantly increased at 1 and 3 months compared to before vaccination in both patients (1 mo: $p=0.0003$, 3 mo: $p=0.0006$) and donors (1 mo: $p=0.0002$, 3 mo: $p<0.0001$). The increment in VZV-IgG titers from pre-vaccination to 1 and 3 months post vaccination was comparable between patients and donors. One patient had a mild HZ episode at 11 months post-transplantation (16 months post-vaccination).

Discussion: HZ incidence post renal transplantation is high. Remarkably, in contrast to hepatitis B vaccination, VZV vaccination equally increased virus specific IgG titres in patients with renal failure compared to healthy individuals. ESRD patients can be effectively vaccinated to prevent herpes zoster.

O002

Proteomics of urinary exosomes to identify biomarkers of BK virus infection and acute rejection

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Introduction: Acute cellular rejection (ACR) and BK virus associated nephropathy (BKVAN) are frequent causes of graft dysfunction after renal transplantation with similar symptoms but requiring different treatments. We investigated whether patients with an ACR episode or BKVAN could be distinguished based on proteins present in urinary exosomes.

Methods: Urine samples (50 mL) were collected from renal transplant patients with ACR, BKVAN or stable graft function. Urinary Exosomes were isolated by ultracentrifugation (110' at 200.000×g). For each group (ACR, BKVAN, controls) we pooled equivalent amounts of exosome proteins of 4 patients (first set) and repeated this with 4 different patients in each group (second set). Subsequently, exosomes were lysed and 40 microgram of protein was resolved by a 4-12% SDS-PAGE. After electrophoresis, gel lanes were cut into 5 pieces according to molecular mass. Proteins were in-gel digested with trypsin, and peptide mixtures were analysed using LC-MS/MS. Proteins were identified using the NCBI database. Partial least squares enhanced discriminant analysis was used, to classify the patient groups based on exosomal protein content.

Results: A total of 340 individual proteins was detected in the first set of samples and 385 proteins in the second set, with 204 proteins overlapping between both sets. Our preliminary findings show a number of proteins for which the exosome content differed between ACR and BKVAN. Specific candidate proteins that can serve as urinary biomarkers include acid ceramidase, low density lipoprotein-related protein 2, copine VIII, alpha-1-acid glycoprotein 1 syndecan 4, and lactate dehydrogenase.

Conclusion: In this study we show that profiling of urinary exosomes is a promising tool to identify urinary proteins which allow differentiation between ACR and BKVAN in renal transplant patients.

O003

Primary tubular epithelial cells; the Trojan horse for BK polyoma virus

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Method: Activation and/or reactivation of BK polyoma virus (BKV) is an important cause of renal transplant dysfunction and graft loss. BKV-associated nephropathy develops in 1-10% of renal transplant patients, and no therapy is available other than decrease in immunosuppression. We studied mechanisms used by BKV to suppress and/or evade anti-viral immunity. As an *in vitro* model, we used human primary tubular epithelial cells (pTEC), isolated from the cortex of healthy tissue surrounding Grawitz tumors. pTEC were infected with BKV Dunlop strain or influenza A (H1N1) as a control. Moreover, pTEC were stimulated with genomic double-stranded DNA (dsDNA) with Lyovec as transfection reagent or with Interferon- α (IFN α). Optimal concentration and incubation time were established. mRNA was isolated, and expression of CXCL10, ZBP1, IFN α , BKV and influenza were determined by quantitative RT-PCR,.

Results: pTEC failed to mount any response to BKV infection (24, 48, 72 hours) as was previously shown by Abend *et al*, Virology 2010;397. However, pTEC are able to respond to viral nucleic acids and IFN α (Heutinck *et al*, Kidney Int. 2013;664). To assess whether BKV actively suppressed the anti-viral response of pTEC, we first stimulated pTEC with dsDNA and subsequently infected them with BKV. BKV infection did not dampen the effect of dsDNA on pTEC. By pre-stimulating pTEC with IFN α , bringing pTEC in an activated state, followed by BKV infection, we expected to see a reduced viral replication within pTEC. However, BKV showed the same amount of replication. To ascertain that pTEC can respond to viral infection, pTEC were infected with influenza virus. Influenza infection elicited a rapid and pronounced anti-viral response and showed reduced viral replication when pTEC were pre-stimulated with IFN α .

Conclusion: We conclude that although pTEC are capable of mounting an anti-viral response, they fail to do so when infected with BKV. We hypothesize that BKV has a way of hiding within pTEC to ensure it is not detected by the cells who subsequently fail to elicit an anti-viral response.

O004

Renal protection against Ischaemia-Reperfusion in transplantation, the REPAIR study

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Background: Ischaemia reperfusion (IR) injury sustained at transplantation contributes to damage that limits allograft longevity. Remote ischaemic preconditioning (RIPC) has been reported to be beneficial in cardiac, renal and neurological protection in small trials. REPAIR investigated whether RIPC improves kidney function following living donor kidney transplantation.

Methods: 406 adult live donor/recipient pairs were randomised. Patients on ATP sensitive potassium channel opening/blocking drugs or ciclosporin, with known iodine sensitivity, undergoing an ABO incompatible transplant or requiring HLA antibody removal therapy were excluded. Pairs were randomised using a factorial design to either: sham RIPC, early RIPC (immediately pre-surgery), late RIPC (24 hours pre-surgery) or dual RIPC (early and late RIPC). Donor and recipient received the same intervention (active or sham RIPC) at the two time points. The primary outcome was iohexol glomerular filtration rate (GFR) 12 months after transplantation. Important secondary outcomes were eGFR and safety.

Results: There was a trend towards early RIPC having a small but clinically important effect to increase iohexol GFR (ml/min/1.73m²) at 12 months (58.3 vs. 55.9: adjusted mean difference 3.08; 95% CI -0.89 to 7.04; p=0.13). There was stronger evidence for a treatment effect when eGFR was used to impute missing values (adjusted difference 3.41; 95% CI -0.21 to 7.04; p=0.065) and when eGFR was used to assess kidney function (adjusted difference 4.98; 95% CI 1.13 to 8.29; p=0.011). There was no evidence for an effect of late RIPC, or that combining early and late RIPC had additional benefits. RIPC was safe and well tolerated.

Conclusion: RIPC is a safe, low cost intervention in living donor kidney transplantation. The evidence for an effect of RIPC on GFR as measured using iohexol was weak, but eGFR measures provided stronger evidence of a clinically important improvement of kidney function after transplantation.

O005

Pretransplant non-HLA antibodies in renal transplant recipients

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Introduction: Pretransplant donor-specific anti-HLA antibodies are associated with a shorter kidney graft survival, whereas the relevance of non-HLA antibodies remains uncertain. The aim of this study was to determine the relation between kidney graft failure and the presence of pretransplant non-HLA antibodies.

Methods: We evaluated the presence of anti-Endorepellin (C-terminal fragment LG3), anti-Peroxisomal-trans-2-Enoyl-CoA-Reductase (PECR) and anti-Agrin antibodies in pretransplant sera of 438 patients transplanted between 1990 and 2008 at the UMC Utrecht. A multiplex non-HLA antibody assay was set-up on a luminex platform where magnetic beads were coated with human recombinant proteins. Patient sera were incubated with the magnetic beads and the presence of anti-IgG non-HLA antibodies was evaluated.

Results: anti-Endorepellin antibodies were found in 89 (20%) sera; whereas 52 (12%) sera had anti-PECR antibodies and 1 serum was positive for anti-Agrin antibodies. In 14 (3%) sera we found anti-Endorepellin as well as anti-PECR antibodies. Patients with pretransplant anti-PECR antibodies had a 10 year graft survival of 40% versus 80% in patients without anti-PECR antibodies ($p < 0.02$). No significant difference was observed in graft survival between patients with or without anti-Endorepellin antibodies.

Discussion: From these preliminary results, we can conclude the presence of anti-PECR antibodies is associated with a shorter graft survival. Concurrently we have been setting up additional non-HLA antibody Luminex assays to determine the relation between kidney graft failure and the presence of these antibodies, and we are investigating whether the presence of anti-PECR antibodies strengthen the negative effect of donor specific HLA antibodies on graft survival.

O006

Treatment of subclinical rejection identified on surveillance biopsy may prevent the development of chronic alloimmune injury

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Introduction: Surveillance biopsies [SBx] are not universally performed following renal transplantation. In patients in whom protocol biopsies are performed, how best to manage subclinical rejection [SCR] is not known. The aim of this study to determine the outcomes of treated SCR compared with a historic control group with untreated SCR.

Methods: We included 550 patients who underwent a SBx in the first year post-transplant. In a previous study we showed that 26 patients with untreated SCR [uSCR] had higher risk of clinical rejection than patients with no SCR on SBx, with a rejection free survival of 90.0% and 76.9% respectively, $p=0.0078$. Following this analysis a change in protocol was made at our centre and SCR is now treated conventionally with corticosteroids and MMF [tSCR]. We have subsequently treated 16 patients with SCR and in this study compare their clinical outcomes with our historic group of 26 patients with uSCR.

Results: Allograft survival was 100.0% and 65.9% in the tSCR and uSCR groups respectively, $p=0.62$. Clinical rejection free survival was 83.3% in the tSCR and 58.8% in the uSCR groups, $p=0.42$. AMR free survival was 83.0% and 64.1%, $p=0.83$ and ACR free survival was 100.0% and 85.6%, $p=0.19$ in the tSCR and uSCR groups respectively. TG free survival was 100.0% and 55.6%, $p=0.22$ and de novo DSA free survival was 100.0% and 78.1%, $p=0.35$ in the tSCR and uSCR groups respectively. Histological features on follow up biopsies in 9/16 tSCR showed a decrease in g, c, t and C4d scores but an increase in c, cg and C4d scores was seen in the 20/28 u SCR group.

Conclusion: Although these data are preliminary and patient numbers are small, treatment of SCR results in better allograft survival, less rejection and histological improvement in repeat biopsies Longer follow up is required but this study suggests treating SCR may reduce the development of chronic alloimmune injury.

O007

Outcomes after hand-assisted laparoscopic donor nephrectomy can be improved by an Enhanced Recovery After Surgery programme

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Introduction: An Enhanced Recovery After Surgery (ERAS) programme reduces perioperative morbidity, length of stay and improves patient outcome by limiting the physiological stress response to surgery. The aim of this study was to compare outcomes of an ERAS programme with standard care in live kidney donors.

Methods: A sequential cohort study was performed. An enhanced recovery protocol was developed using guidelines from the ERAS Group (Lassen et al, Arch Surg. 2009 Oct; 144(10):961-9). A hand-assisted laparoscopic donor nephrectomy (HALDN) via an upper quadrant transverse incision was performed in all patients. Standard perioperative care (SPC) involved preoperative overnight fasting and administration of 1L 0.9% saline IV followed postoperatively by 3L of 0.9% saline IV, intravenous morphine via a Patient Controlled Analgesia (PCA) device and a return to diet with removal of the urinary catheter after 24 hours. The ERAS group received an intraoperative rectus sheath nerve block followed by insertion of an indwelling rectus sheath nerve catheter containing 0.25% bupivacaine administered at 5ml/hr. Patients in the ERAS group had their urinary catheter removed in the theatre recovery area, received no postoperative IV fluids and were encouraged to eat, drink and mobilise on the evening of surgery.

Results: One hundred patients received either SPC (n=50) or the ERAS protocol. There were no differences in the patient demographics (Mean age SPC 46.1yrs v ERAS 45.1yrs; Male 18/50 for each). Post-operative length of stay was shorter in the ERAS group (Median SPC 4.0 days v ERAS 3.1 days p<0.001). At 48 hours post-operatively, codeine, tramadol and total opioid requirements were lower in the ERAS group (mean codeine SPC 257mg v ERAS 135mg p=0.010; median tramadol SPC 250mg v ERAS 150mg p=0.034; total opioid SPC 99.5mg v ERAS 62.5mg p<0.001). There were fewer complications and less constipation in the ERAS group (SPC 48% v ERAS 24% p=0.021; SPC 50% v ERAS 22% p=0.006 respectively).

Conclusion: This ERAS protocol can be applied safely to HALDN patients with the benefits of reduced length of stay, opioid requirements and complications.

Wednesday 11th March
Purbeck Lounge – 15:00
Translational – Cell Death
Chairs: Prof Cees van Kooten and Dr Richard Baker

O008

Prevention of human skin rejection by selective blockade of CD28 costimulatory signaling

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Background: Targeting the CD28-CD80/86 co-stimulation pathway with CTLA-4 immunoglobulin (Ig) is a promising alternative to current immunosuppressive regimens. However, clinical trial data have revealed an increase in the rate of acute rejection of renal transplants with CTLA-4 Ig treatment when compared with conventional immunosuppression. This may be related to interference with physiological CTLA-4 signalling that is crucial to regulatory T cell function. In order to preserve this regulatory function, selective blockade of CD28 is theoretically advantageous as coinhibitory signals are preserved. In the current study we have investigated the hypothesis that a non-activating monovalent anti-CD28 antibody (FR104) would suppress alloimmune responses and prevent rejection of human skin allografts *in vivo*.

Methods: Using a humanised mouse system, we treated mice that had received human skin transplants with FR104 (5 mg/kg), CTLA4-Ig (10mg/kg) or vehicle control intravenously twice a week for three weeks. All mice were started on the treatment regimen three weeks post-adoptive transfer of allogeneic human peripheral blood mononuclear cells (PBMCs) to ensure adequate levels of human leukocyte chimerism in recipient mice.

Results: FR104 significantly prolonged skin allograft survival in humanised mice compared with CTLA4-Ig (median survival time, MST=56 vs. 31 (p=0.002)) or saline (MST=31). While FR104 treatment significantly impacted the level of human leukocyte chimerism in the peripheral blood, it remained above the required reconstitution level known to cause skin rejection. The number of graft infiltrating CD4⁺ (47.8±24.8 vs 83.3±5.1 cells/HPF, P<0.02) and CD8⁺ (50.0±11.9 vs 111±34.0 cells/HPF, P<0.04) cells was significantly reduced by FR104 treatment as compared with CTLA-4 Ig treatment. Importantly, only CTLA-4 Ig, but not FR104 treatment significantly reduced the number of graft infiltrating FoxP3⁺ cells. In addition, FR104 significantly suppressed the serum cytokine production of IL-2, IFN γ , and TNF α .

Conclusion: FR104 is an effective immunosuppressant *in vivo*. By sparing CTLA-4 coinhibitory signals, FR104 may theoretically lead to improved therapeutic responses compared with CTLA-4-Ig.

O009

Vascularised composite allografts and intestinal transplantation: Does the skin component provide a pre-rejection marker for the visceral organ?

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Introduction: Can the skin component of a synchronously transplanted vascularised composite allograft (VCA) be used as a pre-rejection marker for the intestinal transplant (IT)?

Methods: Recipients of a combined IT and VCA were studied and compared to those an earlier cohort who only received an IT.

Results: From October 2008 to January 2014, 32 patients had an IT. Fifteen patients had an IT without the VCA and 17 had an IT with a VCA. In the latter group, 15 had abdominal wall transplants (AWT) and 2 sentinel skin flaps (SSF). Induction immunosuppression was similar in both groups with Campath-1H (Genzyme, USA), 30 mg intravenously, 6 hours after reperfusion and 24 hours later. Maintenance was with Tacrolimus at a trough level of 8-12 ng/ml. At a mean follow-up of 40 months (range 5-65), 22 patients are alive and well. All VCA's were successful. There were 5 intestinal rejections in the IT alone group and 1 intestinal rejection in the IT + VCA group (lead time of 10 days between VCA and IT). There were 5 rejections in the VCA part of the IT+ VCA group. A further 5 patients in the IT group were falsely treated for biopsy proven rejection. This was later labelled as infection. False positive diagnosis of rejection was not observed in the IT+VCA group. Rejection of the intestine in the IT alone group resulted in a mean hospital stay of 45 days (range 15-63). Rejection of the VCA in the IT+VCA group resulted in a mean hospital stay of 4 days (range 3-5).

Discussion: VCA to complement IT provides a visual, dynamic canvas for remote immune monitoring of their visceral graft. The skin component of the VCA may act as an immunologic 'ghost target' that may help divert the cellular affect away from the IT. Conversely, intestinal graft dysfunction with a clear VCA is a dynamic visual canvas for the clinician. This helps to refute the diagnosis of rejection.

O010

Cytotoxic CD8 T cell recognition of acquired, intact MHC alloantigen on host dendritic cells promotes acute allograft rejection

Jason Ali, Simon Harper, Margaret Negus, Eleanor Bolton, J. Andrew Bradley, Gavin Pettigrew

University of Cambridge, Cambridge, UK

Introduction: Although there is increasing evidence that recipient DCs can acquire intact MHC class I by trogocytosis from parenchymal cells, the functional relevance of the 'semi-direct' antigen presentation to CD8 T cells that this permits, to allograft rejection, has not been previously demonstrated.

Methods: Murine heterotopic cardiac transplant models were utilised. Balb/c donors were lethally irradiated to eradicate haematopoietic cells (HPC) (Balb/c^{HPC-}), such that parenchymal cells were the only source of alloantigen. Recipients included: 1) 2C transgenic mice (monoclonal population of CD8 T cells against Ld MHC class I); 2) Splenectomised aly/aly (aly/aly^{spl}) mice, to investigate the importance of secondary lymphoid tissue (SLT); 3) CD11c-DTR transgenic mice, in which host DCs can be selectively depleted by treatment with diphtheria toxin. Recipient CD4 T cells and B cells were depleted with monoclonal antibodies.

Results: 2C transgenic mice rejected Balb/c^{HPC-} grafts as rapidly as non-irradiated Balb/c grafts (MST = 5d vs. 4d respectively; p=0.4) suggesting an effective mechanism for parenchymal cell driven CD8 T cell mediated rejection. Balb/c^{HPC-} allografts showed prolonged survival (>50d) in aly/aly^{spl} mice given 2C CD8 T cells whereas in non-splenectomised controls all grafts rejected (MST = 17d; p=0.01). In addition, when aly/aly^{spl} mice were given activated 2C CD8 T cells (from a 2C recipient of a Balb/c cardiac graft) they rapidly rejected Balb/c^{HPC-} allografts (MST = 7d; p=0.01) suggesting an essential role for SLT in this pathway. Wildtype recipient CD8 T alloreactivity acutely rejected Balb/c^{HPC-} allografts in CD11c-DTR recipients lacking B cells, with rejection significantly attenuated if either CD4 T cells, or DCs were additionally depleted (MST = 12 vs >50 and 26 respectively; p<0.01), highlighting an essential role for both recipient DCs and CD4 T cells in driving CD8 alloreactivity.

Conclusion: These results provide support for the semi-direct pathway of allorecognition having the potential to contribute to allograft rejection. Recipient DCs can acquire intact MHC class I from donor parenchymal cells, and upon transit to SLT, receive indirect CD4 T cell help to activate directly alloreactive CD8 T cells.

O011

Host NK cell allorecognition of passenger donor lymphocytes within allografts is essential for preventing augmentation of recipient adaptive alloimmunity

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Background: Memory T cells reside in peripheral non-lymphoid tissue, but how their presence within solid organ allografts impacts upon transplant outcomes is not known. We have previously described how graft-versus-host (GVH) allorecognition by passenger CD4 T cells within MHC Class II-mismatched bm12 heart grafts provokes humoral autoimmunity in B6 recipients. Here we aimed to examine how such GVH recognition impacts upon the alloresponse

Methods: An MHC class I and II mismatched murine model of cardiac transplantation was developed (bm12.Kd.IE to B6). Following transplantation, cellular and humoral responses against disparate antigens were assayed by ELISPOT and ELISA and the impact of GVH recognition assessed by depleting donor CD4 T cells prior to graft procurement. Anti-nuclear autoantibody development was assayed by HeP-2 indirect immunofluorescence. The role of recipient NK cells was examined by depletion with anti-NK1.1 antibody.

Results: Bm12.Kd.IE heart grafts provoked strong germinal centre allo- and auto-antibody responses in B6 recipients and developed vasculopathy. In contrast, heart grafts from CD4 T cell-depleted donors developed minimal vasculopathy, and the alloantibody responses were weaker, without observable autoantibody. Bm12.Kd.IE CD4 T cells survive long term in RAG hosts suggesting that avoidance of killing by host NK cells may be essential for autoantibody development. In support, in a model of alloantibody mediated vasculopathy, depletion of NK cells from a B6 recipient of a Balbc heart graft resulted in autoantibody development, amplification of the alloantibody response and rapid graft rejection. This amplification was abrogated by depleting donor CD4 T cells.

Conclusion: Although host adaptive immunity is expected to effect destruction of passenger lymphocytes within heart allografts, this occurs too slowly to prevent GVH-mediated augmentation of the alloresponse to the graft. Rapid killing of donor lymphocytes by host alloreactive NK cells is instead essential. Passenger CD4 lymphocytes may therefore contribute to chronic rejection in recipients who receive an allograft that does not prompt innate NK cell recognition.

O012

Heterologous immunity: T-Cell receptor affinity of virus-induced cross-reactive CD8⁺ T cells differs for alloantigens compared to viral epitopes

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Introduction: Virus-specific T-cells can recognize allogeneic HLA antigens by means of T-cell receptor (TCR) cross-reactivity. The potential impact of such cross-reactivity on transplantation greatly depends on the TCR affinity for the allogeneic targets. This affinity could in theory be highly variable, as it is not restricted by positive and/or negative thymic selection in the recipient. We therefore aimed to evaluate the differences in TCR affinity for allogeneic HLA antigens versus viral epitopes.

Methods: Cold target inhibition assays were performed to assess differences in TCR affinity for allogeneic versus viral epitopes. Stimulator cells were labeled with radioactive ⁵¹Chromium (hot targets) and incubated with cross-reactive virus-specific CD8⁺ T-cell clones. Inhibitor cells without radioactive labeling (cold targets) were added in different hot:cold target ratios. Inhibition of hot target lysis indicated a stronger TCR affinity of the cold target. Both viral peptide-loaded as well as allogeneic immortalized B-cell lines were used as hot and cold targets respectively.

Results: Allogeneic cold target cells were not able to inhibit the anti-virus response, whereas viral-peptide loaded cold targets were able to inhibit the alloresponse.

Discussion: The results indicate that the TCR affinity of cross-reactive T-cell clones is lower for allogeneic HLA antigens compared to viral epitopes. This could be the result of skewing of the TCR repertoire, as the TCRs were selected for optimal recognition of virus rather than allogeneic antigens. Currently, we are investigating whether the opposite could also apply: if repeated allogeneic target stimulation could skew the TCR repertoire towards TCRs with higher affinity for allo- than viral antigens.

O013

Alpha-1-antitrypsin treatment to prevent ischemia-reperfusion injury in liver transplantation

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¹Erasmus MC - University Medical Center, Rotterdam, the Netherlands, ²CSL Behring R&D, King of Prussia, PA, USA

Background: Extensive ischemia-reperfusion injury (IRI) negatively effects early graft function and long-term survival in organ transplantation. Treatment with the acute phase protein alpha-1-antitrypsine (A1AT) showed protective effects on kidney IRI. In this study, we investigated whether A1AT treatment is protective in liver transplantation, using different models of hepatic IRI.

Methods: *In vitro*, the effects of clinical grade human A1AT (Zemaira, CSL Behring, 2.5 mg/ml) on cell viability were tested on the human hepatocyte-like cell line (Huh7) under normothermic and hypothermic conditions. *In vivo*, the effects of A1AT were tested in male C57BL6 mice that were subjected to partial hepatic warm ischemia for 75 minutes. Mice were either sham operated without induction of hepatic IRI (n=3), or intravenously injected with 100 µL of PBS (controls, n=7) or 10 mg/kg A1AT (n=5) 10 minutes prior to IRI. Finally, A1AT was supplemented during isolated hypothermic-oxygenated machine perfusion (HOPE) of human liver grafts, followed by isolated normothermic-oxygenated reperfusion.

Results: *In vitro*, A1AT-treatment led to significantly higher viability in Huh7 cells (p=0.009), which was even more pronounced after cooling and rewarming with both medium (p=0.006) or UW (p=0.019). *In vivo*, levels of AST, ALT and LDH were all significantly lower in serum at 6 and 24 hrs after hepatic IRI in A1AT-treated mice compared to controls (p≤0.05). Protective effects were most apparent at 24 hrs after IRI, showing a significant reduction in serum levels of ALT and LDH (p<0.05). In human liver grafts (n=3), supplementation of A1AT during HOPE resulted in less transaminase release during normothermic-reperfusion compared to grafts that did not receive A1AT.

Conclusion: Treatment with A1AT shows cytoprotective effects in culture of Huh7 cells and accordingly attenuates hepatic IRI in mice. The first results on supplementing A1AT during isolated graft machine perfusion suggest that A1AT could optimize graft preservation in liver transplantation (research support from CSL Behring).

Germinal centre autoimmunity mediates progression of allograft vasculopathy, with essential help provided by T follicular cells

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Introduction: In our previous work we have shown that donor CD4 T cells within heart grafts initiate anti-nuclear autoantibody responses. Here we clarify the contribution of host CD4 T cells to progression and maintenance of the response.

Methods: Bm12 heart grafts were transplanted into wild type (WT), T-cell deficient (TCR^{-/-}) or SAP^{-/-} B6 recipients that lack T follicular helper (T_{FH}) cells. Germinal centres (GCs) were quantified by calculating percentages of PNA / GL7^{+ve} splenic B cell follicles, and allograft vasculopathy (AV) and graft rejection monitored.

Results: Bm12 heart allografts developed progressive AV when transplanted into WT recipients and provoked long lasting GC (68±3% PNA^{+ve} splenic B cell follicles) autoantibody responses, with late generation of anti-vimentin autoantibody (relative anti-vimentin IgG levels were 77±3 at week 7 vs 287±2 at week 15, *p*= .007) evident. Depleting CD4 T cells in the donor abrogated autoantibody production and resulted in minimal AV (12±8% luminal stenosis). In contrast, transplantation into TCR^{-/-} recipient triggered autoantibody responses, but GC activity was not observed, and heart grafts survived indefinitely (MST >100d) and ameliorated AV (1±2% luminal stenosis). Critically, heart grafts transplanted into SAP^{-/-} recipients triggered autoantibody generation, but neither GC activity nor late anti-vimentin responses were detectable and grafts developed only minimal AV (% luminal stenosis was 10±8 in SAP^{-/-} recipients vs 74±1 in WT, *p*=0.02) and survived significantly longer (MST was 91d in SAP^{-/-} vs 56d in WT, *p*=0.04) . In support of the role of GC autoantibody responses in mediating allograft vasculopathy, in a wound-induced endothelial cell (EC) migration assay, cultured bm12 endothelial cells showed fivefold less migration upon addition of serum from SAP^{-/-} recipients than when serum from WT recipients was added.

Conclusion: Our results demonstrate that donor passenger CD4 T cells within an allograft can trigger recipient autoantibody responses, but graft rejection is dependent upon progression to a GC response, with essential help for its development provided by host T_{FH} cells.

Wednesday 11th March
Tregonwell Seminar Suite – 15:00
Translational – Stem cells
Chairs: Dr Luc van der Laan and Dr Maria Hernandez-Fuentes

O015

Living and dead mesenchymal stem cells induce an immunosuppressive response in an experimental sepsis model

Franka Luk, Samantha de Witte, Marieke Roemeling-van Rhijn, Sander Korevaar, Ron de Bruin, Michiel Betjes, Carla Baan, Martin Hoogduijn

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Introduction: There is evolving interest in the use of mesenchymal stem cells (MSC) as a cell therapeutic agent after solid organ transplantation. The nature of the immunomodulatory response after MSC infusion is, however, still largely unknown. The *in vitro* immunomodulatory effects of MSC depend on soluble factors and membrane proteins induced on MSC by inflammatory conditions. However, recent data demonstrates that MSC have a short survival time after infusion, suggesting that the mechanisms of MSC mediated immunomodulation *in vivo* are different. In this study we sought to investigate whether MSCs exert their immunomodulatory effect *in vivo* by interaction with immune cells via cell surface molecules or via actively secreted factors.

To distinguish between effects via cell-cell contact or actively secreted factors of MSC, we killed MSC by heat inactivation (HI) at 50 °C and examined their immunophenotype and secretome. Immunomodulatory effects of HI and living MSC were evaluated in healthy and LPS induced septic mice.

Results: FACS analysis for MSC markers showed no difference between HI and living MSC indicating that cell surface markers of MSC are still intact after HI. Measurement of cytokine titers in supernatants showed that HI successfully inactivates the secretome of MSC. After intravenous infusion of living but also HI MSC in healthy mice an increase in mRNA expression of MCP-1 and IL-1 β in the lungs was found. Systemic increases in G-CSF, IL-5, IL-6 and CXCL1 levels were measured, indicative of an immunomodulatory effect of MSC. In LPS induced septic mice infusion of living and HI MSC both induced high serum levels of IL-10 and reduced IFN- γ compared to the PBS controls.

Conclusion: HI of MSC does not affect MSC cell surface epitopes but it does inactivate their secretome. Dead and living MSC induce the same immunomodulatory responses in healthy mice and reduced systemic inflammation in septic mice. These data suggest that viability of MSC is not required for the *in vivo* immunomodulatory effect of MSC. Understanding the immunomodulatory mechanisms of MSC treatment will contribute to the development of effective immune therapy with MSC.

O016

Allogeneic mature human monocyte-derived dendritic cells generate superior alloreactive regulatory T cells in an IL-2-independent manner

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Introduction: Expansion of antigen (Ag)-specific natural occurring regulatory T cells (nTregs) is required to obtain sufficient numbers of cells for cellular immunotherapy. In this study, different allogeneic stimuli were studied for their capacity to generate functional alloantigen-specific nTregs.

Methods: A highly enriched nTreg-fraction (CD4⁺CD25^{bright}CD127⁻ T cells) was alloantigen-specific expanded using HLA-mismatched immature, mature monocyte-derived dendritic cells (moDC) or peripheral blood mononuclear cells (PBMC). The allogeneic mature moDC-expanded nTregs were fully characterized by analysis of the demethylation status within the TSDR of the *FOXP3* gene and the expression of both protein and mRNA of FOXP3, HELIOS, CTLA4 and cytokines. In addition, the antigen-specific suppressive capacity of these expanded nTregs was tested.

Results: Allogeneic mature moDC were superior in inducing nTreg-expansion compared to immature moDC or PBMC. Remarkably, the presence of exogenous IL-15, but not IL-2, was needed for optimal mature moDC-induced nTreg-expansion. Allogeneic mature moDC-expanded nTregs were potent suppressors of alloantigen-induced proliferation. Even at low ratios (<1:320), these expanded nTregs still efficiently suppressed alloAg-induced, but hardly the completely HLA-mismatched-Ag-(3rdP)-induced, proliferation. Mature moDC-expanded nTregs were highly demethylated at the TSDR within the *FOXP3* gene and highly expressed of FOXP3, HELIOS and CTLA4. In addition, hardly any expanded nTregs produced IL-17 whereas a minority of nTregs produced IL-10, IL-2, IFN- γ and TNF- α . Next generation sequencing of mRNA of moDC-expanded nTregs revealed a strong induction of Treg-associated mRNAs.

Discussion: Human allogeneic mature moDC are highly efficient, IL-2-independent, stimulator cells for expansion of stable alloantigen-specific nTregs with superior suppressive function. This opens a new avenue for using Tregs as source for cellular immunotherapy in kidney transplantation.

O017

Persistent immunomodulatory phenotype of mesenchymal stromal cells, after removal of inflammatory stimulation

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Introduction: Mesenchymal stromal cells (MSC) are a promising therapy for inflammatory and auto-immune diseases. Unsorted, they are a heterogeneous cell-population with low inherent immunogenicity and potent immunomodulatory properties. Cell therapy legislation supports the use of a defined MSC population, which was obtained through selection, based on the surface expression of CD362. Preliminary data show that this homogeneous population exhibits similar immunological properties to the unsorted MSC. The immunological properties of MSC can be enhanced by inflammatory stimuli, but the longevity of these changes is unclear, as is the impact on the immunogenicity of MSC.

Method: Human bone marrow-derived unsorted and CD362⁺ MSC were cultured for 7 days in an inflammatory environment (50 ng/ml IFN γ) followed by 21 days without IFN γ . Immunomodulatory gene expression and function were analyzed over time. Recognition by HLA-I and -II mismatched natural killer (NK) cells and memory CD8 T-cells was evaluated at day 7 by analyzing lysis of MSC in europium release assays.

Results: IFN γ stimulation resulted, for both MSC populations, in increased expression of protein and mRNA of the following immunomodulatory factors: IDO, COX2, CCL2, CXCL10, IL-8, IL-1RA, PD-L1, HLA-I and -II and SerpinB9. In addition, increased L-Kynurenine levels were also detected in media, reflecting IDO-activity. When IFN γ was removed, unsorted and CD362⁺ MSC maintained their immunomodulatory phenotype, for a period up to 21 days. Unsorted and CD362⁺ MSC were recognized and lysed by NK cells and CD8 T-cells. Whilst IFN γ treatment of MSC significantly decreased their lysis by NK cells, increased their lysis by CD8 T-cells. Sustained IDO-activity, COX2 and PD-L1 expression indicate an enhanced immunomodulatory capacity of the MSC, whilst upregulation of HLA-I, HLA-II and SerpinB9 changed the immunogenicity of the MSC.

Conclusion: These data show that, regardless of the subpopulation, IFN γ induces a persistent immunomodulatory phenotype of MSC, which has implications for the continued immunosurveillance of MSC after resolution of organ inflammation. The differential effect of stimulation on the immunogenicity of MSC will likely have context-dependent implications for clearance.

O018

The role of Neuropilin-1 in human regulatory T cells

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Introduction: Regulatory T cells (Tregs), whose native function is to regulate immune responses, are a promising approach for the treatment of allograft rejection. If Tregs are to be manipulated for therapeutic applications, it is crucial to understand how human Tregs sense environmental cues that modulate their function. We investigated the hypothesis that Neuropilin-1 (Nrp-1), a co-receptor implicated in mouse Treg function, can sense salient cues that potentiate human Treg function.

Methods: Tregs isolated from human blood were stably transduced with a short hairpin RNA to silence the Nrp-1 transcript. The proliferation of mononuclear cells (PBMCs) in the presence of Tregs, was measured to assess the suppressive potency of Nrp-1-deficient cells. The cytokine concentration was determined using a flow cytometry bead array. Alterations in the cell biology of Nrp-1-deficient Tregs were examined using flow cytometric assays and qRT-PCR for markers of cell viability, proliferation, cytokine secretion and activation status.

Results: Nrp-1 deficient Tregs were significantly impaired in their ability to suppress proliferation and pro-inflammatory cytokine secretion of PBMCs. Nrp-1 deprivation had no effect upon Treg activation or proliferative potential but did enhance apoptosis in these cells. Strikingly, Nrp-1-deficient Tregs secreted diminished levels of the Treg-associated cytokine IL-10, compared with Nrp1-sufficient Tregs. Meanwhile, secretion of the Th17-associated cytokine IL-17A and the Th2-associated cytokine IL-13 was elevated in Nrp-1-deficient Tregs.

Conclusions: We conclude that Nrp-1 is required for optimal human Treg-mediated suppression *in vitro*. The altered cytokine profile in Nrp-1-deficient Tregs suggests that Nrp-1 is implicated directly in the mechanisms of Treg-mediated suppression and the maintenance of Treg phenotypic stability.

O019

Rational development of alloantigen specific regulatory T cell therapy requires insight into longevity of alloimmune pathways

Jason Ali, Margaret Negus, Eleanor Bolton, J. Andrew Bradley, Gavin Pettigrew

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Introduction: We have recently demonstrated that indirect-pathway responses against different alloantigens differ in their strength and longevity; specifically, that indirect responses against MHC class I alloantigen are long-lived, whilst those against class II alloantigen are, in similar fashion to direct-pathway responses, short-lived due to rapid clearance of donor APCs. Here we demonstrate how this knowledge may be used to inform immunoregulatory therapy with antigen-specific regulatory T cells (Tregs).

Methods: An MHC-mismatched murine model of cardiac transplantation was used [bm12.Kd.IE to C57BL/6]. Polyclonal and antigen specific Tregs were generated by culture of CD4 T cells, utilising either syngeneic C57BL/6 or T cell receptor transgenic CD4 T cells specific for self-restricted donor class I (TCR75) and class II (TEa) allopeptide. To limit donor class I expression to haematopoietic cells, bone marrow chimeric donors were incorporated (bm12.Kd.IE bone marrow to lethally irradiated bm12.IE). T-reg were administered either at the time, or 3 weeks after, transplant, and impact on the development of alloantibody and allograft vasculopathy evaluated.

Results: When given on the day of transplant, although polyclonal Tregs attenuated germinal centre allo and autoantibody responses and reduced allograft vasculopathy, monoclonal populations of class I and II allopeptide-specific indirect pathway Tregs were more effective. Moreover, when transferred late (3 weeks) after transplantation, only class I indirect Tregs proved effective at ameliorating chronic rejection, presumably because presentation of alloantigen is limited at this stage to self-restricted MHC class I alloantigen. In support, class I specific Tregs were ineffective at preventing progression of allograft vasculopathy when administered late to recipients of heart allografts from bone marrow chimeric donors, in which indirect-pathway responses against MHC class I alloantigen were truncated due to restricted expression of the alloantigen on short-lived haematopoietic cells.

Conclusion: Antigen specific Treg are more effective than polyclonal Treg at abrogating alloimmune responses and allograft vasculopathy. Their effectiveness when administered at late time points after transplantation is, nevertheless, dependent upon ongoing presentation of target allopeptide.

O020

Modulation of non-autologous regulatory T cell therapy for the prevention of transplant rejection

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Purpose: *Ex vivo*-expanded CD4⁺CD25⁺CD127^{lo} human regulatory T cells (Treg) promote the survival of human skin transplants *in vivo*. These recipient-derived Treg also display improved suppression when expanded against donor alloantigen in a GMP-compliant manner. Clinically, expansion of recipient-derived Treg against a donor alloantigen is logistically challenging. In the current study we investigate the hypothesis that non-autologous human Treg are efficient at controlling allograft rejection.

Methods: Human Treg from HLA typed donors were expanded *ex vivo* and suppressive activity confirmed *in vitro*. BALB/c Rag2^{-/-}cyt^{-/-} mice received human skin grafts and were subsequently reconstituted with allogeneic human peripheral blood mononuclear cells (PBMCs) alone (n=19) or together with Treg derived from the same PBMC donor (autologous Treg, n=12) or non-autologous Treg (HLA haplotype mismatched against the PBMC and skin donors, n=6). Assays were repeated across multiple HLA combinations.

Results: Autologous and non-autologous Treg were equally suppressive *in vitro*. However *in vivo*, non-autologous Treg were less effective at promoting skin survival compared with autologous Treg (median survival, MS, 81.5 days vs. >100 days). *In vivo* killing assays revealed loss of non-autologous Treg secondary to CD8-mediated killing. We aimed to suppress this killing using a subtherapeutic dose of rapamycin. Non-autologous Treg therapy combined with rapamycin promoted survival of Treg *in vivo* and led to a significant prolongation of skin graft survival (MS>100 days, n=4) compared with rapamycin alone (MS=37 days, n=5) or non-autologous Treg alone (MS=43 days, n=5). Cell tracking assays revealed that rapamycin acted through both the prevention of Treg killing as well as promotion of Treg proliferation.

Discussion: Non-autologous Treg are inferior *in vivo* in comparison with autologous Treg due to their killing by recipient CD8 T cells. This loss of Treg may be controlled with low dose Treg-sparing immunosuppression. Such a combination therapy may be a viable clinical alternative, allowing the development of a bank of Treg expanded against a range of donor alloantigens.

O021

Pre-conditioning with heme arginate upregulates heme-oxygenase 1 in renal transplant recipients and may offer protection: reporting the HOT study

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¹University of Edinburgh, Edinburgh, UK, ²Edinburgh Royal Infirmary, Edinburgh, UK, ³Freeman Hospital, Newcastle, UK

Introduction: Despite a wide range of inventive approaches, few interventions have been proven to protect against the inevitable ischaemia reperfusion injury (IRI) that occurs during transplantation. One enzyme of interest is heme oxygenase-1 (HO-1) that degrades heme and protects against oxidative stress. Heme arginate (HA), a form of hemin, can safely induce HO-1 in humans. Clinical renal recipients with higher HO-1 levels show improved graft function. The HOT study (Heme Oxygenase-1 in renal Transplantation) is a randomised, placebo-controlled, single centre, phase IIb trial to evaluate HA effect on HO-1 upregulation after deceased donor kidney transplantation.

Methods: 40 recipients were randomised to either active (two doses 3mg kg⁻¹ HA: pre-operatively, day 2) or placebo (NaCl: same schedule). Recipient blood was taken daily for peripheral blood mononuclear cells (PBMC) extraction. Urine was also collected. Graft biopsies were taken pre-op and day 5.

Results: HA upregulated PBMC HO-1 protein at 24 hours more than placebo: HA 11.1ng/ml [1.0- 37.0] vs. placebo 0.14ng/ml [-0.7- 0.3](p<0.0001). PBMC HO-1 mRNA was also increased: HA 2.73 fold [1.8- 3.2] vs. placebo 1.41 fold [1.2- 2.2](p=0.02). HA increased day 5 tissue HO-1 protein immunopositivity compared with placebo: HA 0.21 [-24- 0.7] vs. placebo -0.03 [-76- 0.15] (p=0.02) and the percentage of HO-1 positive renal macrophages also increased: HA 50.8 cells per hpf [40.0- 59.8] vs. placebo 22.3 [0- 34.8] (p=0.012). Urinary biomarkers were reduced in the HA group but not significantly so. Histological injury scores and delayed graft function rates were similar but the study was not powered to these endpoints. Adverse events were equivalent between groups.

Discussion: The primary outcome was achieved and demonstrated for the first time that HA safely induces HO-1 in renal transplant recipients. Larger studies are planned to determine the impact of HO-1 upregulation on clinical outcomes and evaluate the benefit to patients at risk of IRI.

Wednesday 11th March
Bayview – 15:00
Clinical
Chairs: Prof Teun van Gelder and Dr Iain Macphee

O022

Alemtuzumab induction has been safe in the UK and achieves long-term steroid avoidance in more than 80% of low risk renal transplant recipients

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Introduction: The use of alemtuzumab as an induction agent for renal transplantation is increasing in the UK. There is some evidence to suggest that this is safe in the short and medium term, but concern remains over long term safety because of profound and enduring effects on the lymphoid compartment. This report attempts to address some of the safety concerns of alemtuzumab in standard risk renal transplantation.

Methods: Data was extracted from the NHSBT database. The analysis included standard risk adults (excluding HLAi, ABOi and highly sensitised patients) undergoing a first kidney-alone transplant in the UK between 2005 and 2013. The outcomes of those patients receiving alemtuzumab (group A) were compared with those receiving other agents, mainly IL2-Receptor antagonists (group B). There were 14,027 patients in total, 1,519 in group A and 12,508 in group B.

Results: There was no significant difference in graft or patient survival up to five years post transplantation. Group A did have a significantly higher proportion of patients that were rejection free ($p=0.012$, log-rank test). The median time to rejection was 126 days in group A, vs. 35 days in group B. Graft function was not significantly different at any time point to five years. The proportions of patients who were steroid-free were higher at all time points in group A (1yr 90.8% vs. 20.3%, 3yrs 83.5% vs. 32.6%, 5yrs 85.4% vs. 38.5%). The aetiology of graft loss was similar in both groups.

Discussion: Despite concerns over long term safety regarding the use of alemtuzumab in renal transplant recipients UK registry data is reassuring suggesting similar overall performance to alternative induction agents. However alemtuzumab does permit significantly higher numbers of patients to avoid steroids without any obvious penalty.

O023

Renal ^{123}I -mIBG scintigraphy suggests functional sympathetic reinnervation of the human kidney allograft

Linn C. Dobrowolski, Hein J. Verberne, Bert-Jan H. van den Born, Ineke J.M. ten Berge, Frederike J. Bemelman, C.T. Paul Krediet

Academic Medical Center at the University of Amsterdam, Amsterdam, the Netherlands

Introduction: In human kidney allografts there is histological evidence of reinnervation but whether this is functional is unknown. We hypothesized that parameters of ^{123}I -metaiodobenzylguanidine ^{123}I -mIBG uptake in the human kidney allograft as a measure of organ specific functioning sympathetic innervation, correlate with time after transplantation.

Methods: In 12 patients (median graft survival 8 years (range 1month-34years), median creatinine clearance 59ml/min) planar images were made at 15min and 4hr after intravenous administration of ^{123}I -mIBG and a SPECT-CT at 4hr was made. Regions of interest of the allograft (specific) and muscle (non-specific) were drawn on planar geometric mean images and volumes of interest on SPECT-CT. We calculated ^{123}I -mIBG uptake as a ratio of specific counts vs. non-specific counts and determined washout between 15min and 4hr.

Results: We found no correlation between creatinine clearance and either ^{123}I -mIBG uptake ($R^2=0.039$, $p=0.54$ at 15min, $R^2=0.022$, $p=0.646$ at 4hr) or washout ($R^2=0.002$, $p=0.89$). Relative uptake measured as allograft-to-reference ratio correlated with transplant vintage for 15min ($R^2=0.619$, $p=0.002$) but not for 4hr images ($R^2=0.041$, $p=0.529$). Time after transplantation correlated with ^{123}I -mIBG washout between 15min and 4hr ($R^2=0.366$, $p=0.037$).

Discussion: These data show that renal ^{123}I -mIBG scintigraphy is feasible in human kidney allografts. The technique should be further developed. Our data suggest that there is functional sympathetic reinnervation in human renal allografts increasing over time after transplantation, independent of allograft function.

O024

Optimize the registration of malignancies in renal transplant recipients; the result of linking two databases

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¹Erasmus MC, Rotterdam, the Netherlands, ²NTS, Leiden, the Netherlands, ³IKNL, Utrecht, the Netherlands

Introduction: Underreporting in the Dutch Organ Transplant Registry (NOTR) database may result in unreliable frequencies of malignancies after kidney transplantation. We investigated whether linking the national cancer database with the NOTR significantly alters this outcome.

Materials & methods: The NOTR is operational since 2002 and includes the clinical data from recipients with a functioning organ transplant as reported yearly by the transplant centres. From 1989 onwards, the IKNL (Netherlands Comprehensive Cancer Organisation) collects nationwide pathology results documenting malignancy in a database. All renal transplant recipients (RTR), transplanted between 1966 and 2013, were connected with the malignancy database using surname, sex, date of birth, ZIP code and treatment hospital. Malignancy data of both databases were compared.

Results: The NOTR dataset consisted of 16717 RTR of which 3684 (22%) were diagnosed with a malignancy in the IKNL database. 1760 of these 3684 recipients had no documented malignancy in the NOTR database. The NOTR registers malignancies only during transplant follow-up. This results in missing data before transplantation (n=581) and after organ failure (n=169). Another 27% of the malignancies registered in IKNL was absent in NOTR for no good reason. 596 malignancies that were registered in NOTR were not in IKNL dataset probably due to matching difficulties. This changes the percentage of kidney transplant patients with a malignancy at follow-up from 15% in the NOTR to 21% with additional information from IKNL.

Conclusions: Linkage with the IKNL registry showed a significantly higher frequency of malignancies in RTR, due to underreporting in our national transplant registry. Transplantation is a known risk factor for developing malignancies but not per se diagnosed during follow-up of a functioning transplant. To add this information to the NOTR data, future linkage with a unique patient identifier like citizen service number (BSN) is necessary.

O025

Cancer risk in the renal transplant population: Does immunosuppressive type increase the risk?

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Introduction: Long term immunosuppression is required for patients who have had a renal transplant. This is known to increase the risk of cancer. A previous study in 1995 included 918 renal transplant recipients in the Yorkshire and Humber (YAH) region. Since then there have been significant changes in immunosuppressants, cancer surveillance and cancer registry data collection. An up to date review has been undertaken to estimate the cancer risk in our patient population and the effect that the immunosuppressive medication has had on the standardised incidence ratio (SIR) of cancer.

Methods: A database of renal transplant recipients over the last 40 years was cross-referenced with the local cancer registry to identify cancer incidence in the transplant population. This was compared to the non-transplant and the general population. The effect of immunosuppression on cancer incidence was also analysed. The outcome measures are expressed as hazard ratios and SIRs.

Results: 3392 renal transplants have been performed in 3133 patients since 1967 in Leeds. There were 1230 cancers reported in 677 renal transplant recipients. Of these cancers, 408 patients had 1 cancer, 144 had 2 cancers, 114 patients had 3-8 cancers and 4 had >9 cancers. The median time to first diagnosis of cancer was 7 years 2 months with median follow up of 15.9 years. Cancer incidence in the transplant population increases with age and also increased over the study period. The risk of cancer was shown to be five times greater in the over 50s compared to the under 25s. ($p < 0.001$) All types of cancer show an increased incidence in the >25s, with haematological malignancies ($p < 1.3E-06$) and skin cancers ($p = 0.79$) increased in all age groups. The risk of developing a cancer after one year of treatment with tacrolimus was 1.037, and continues to increase over the next five years.

Discussion: The SIR shown in our population is similar to those identified in other reviews. Treatment with tacrolimus has a higher risk of cancer incidence compared to ciclosporin and azathioprine.

O026

Longitudinal eGFR modelling to understand rates of eGFR decline in renal transplantation in the United Kingdom

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¹UK Renal Registry, Bristol, UK, ²Guys Hospital, London, UK, ³Southmead Hospital, Bristol, UK, ⁴Southampton University, Southampton, UK, ⁵St Georges Hospital, London, UK

Background: The rate of decline in eGFR (slope) has been independently associated with a higher risk of cardiovascular events and all cause mortality in kidney transplant recipients, and may also predict patients at risk of early graft failure. The aim of this study is to investigate how eGFR slope correlates with donor type and its association with specific patient characteristics.

Methods: Using data provided by the UK Renal Registry we analysed all patients aged ≥ 18 years who received a kidney transplant in the UK between 1st January 2007 and 31st December 2009. A mixed model for repeated measurements was used to calculate eGFR slopes, with examination of linear, quadratic and cubic regression models. This multivariable analysis adjusted for age, ethnicity, gender, primary renal diagnosis, social deprivation, time on dialysis and donor type. Patients were followed up to 4 years post transplant and required a minimum of 18 months graft function with three or more creatinine measurements for inclusion.

Results: Of 5226 identified patients, 4829 (92.4% data completeness) were analysed in an adjusted multivariable model. The overall median eGFR (in ml/min /1.73m²) at one year after transplantation was 55.3. This compared to a median eGFR at one year of 57.6 for live kidney donors (LKD), 55 for donation after brainstem death (DBD), and 51.3 for donation after circulatory death (DCD). The overall unadjusted median eGFR decline per year was -1.01 as compared to -0.3 in the adjusted model. Factors associated with a steeper decline included age <40 years (-1.49, p<0.0001), female gender (-0.96, p<0.0001), diabetes (-0.8, p=0.0005), and increasing social deprivation (-0.58, p=0.003). There were no significant differences between donor groups, except for younger DCD recipients (age <40years) who had a significantly better outcome (1.85, p=0.0006).

Conclusions: Despite having a lower initial eGFR, rates of decline in DCD and DBD kidneys is comparable to LKD recipients up to 4 years after transplantation. Further research is needed to understand the lower rate of decline seen in young DCD recipients, and the patient variables associated with steeper decline.

O027

Conversion from immediate to prolonged release tacrolimus did not change intra-patient variability in renal transplant patients

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Iain MacPhee³

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Background: Tacrolimus has a narrow therapeutic index and is characterized by a large inter- and intra-patient variability (IPV). Variable blood tacrolimus concentrations have been shown to be a risk factor for graft loss. It has been reported that IPV was reduced by switch to a prolonged release preparation of tacrolimus (Wu, et al. Transplantation 2011; 92:648).

Objectives: The aim of this study was to investigate the effect of switching stable renal transplant patients to a once a day tacrolimus formulation (Advagraf®) on the IPV of dose-adjusted tacrolimus trough concentration.

Methods: A cohort of 100 stable renal transplant patients aged between 21 to 76 years was included in this study. Switching from twice-daily tacrolimus to Advagraf® was made on a 1mg:1mg basis. The IPV was calculated based on the dose-adjusted tacrolimus C₀. Analysis of tacrolimus trough blood concentrations (C₀) was made during periods of stable tacrolimus doses and over the whole periods before and after conversion.

Results: After the switch, The mean dose-adjusted tacrolimus C₀ concentration fell from 14.6 µg/L SD 10.9 to 13.0 µg/L SD 9.8 (p<0.01) with 8% reduction [90%CI 4 to 14%]. The mean IPV (%CV) of tacrolimus dose-adjusted C₀ was 26.9% SD 18.2 for Prograf® and 24.9% SD 13.0 for Advagraf® (p > 0.05) and also no difference observed between high- and low-variability patients in both formulations. There was no significant change in mean daily dose before and after switching. However the tacrolimus dose was reduced in 39 patients (39%) by a mean change of 28.3% and the dose was increased in 29 patients (29%) by a mean change of 31.5% with 32% of the patients continuing on the same daily dose.

Conclusion: Switching from immediate to prolonged release tacrolimus formulations in kidney transplant patients was associated with a significantly lower tacrolimus trough concentration (C₀), confirming previously published reports but had no influence on IPV.

O028

Predicting obstructive coronary artery disease in asymptomatic renal patients undergoing renal transplantation

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

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Introduction: Almost 50% of asymptomatic patients with End Stage Renal Disease (ESRD) are reported to have significant coronary artery disease (CAD). Our practice involves a relatively aggressive approach and we have shown that this is associated with excellent survival. However, many patients have an unnecessary coronary angiogram. Our aim is to develop a tool to predict significant CAD (>50% stenosis in ≥ 1 vessels) in asymptomatic patients awaiting transplantation.

Methods: We included all asymptomatic patients evaluated in 2002-2013. Patients were excluded if they had ischemic heart disease, cardiac symptoms or electrocardiographic findings of ischemia.

Results: 819 patients (509 m, 310 f) were included. Median age was 56 yrs (range 24-76). 43.9% of patients were Caucasians, 37% South Asians and 13% Afro-Caribbeans. 61% were on dialysis, 35.3% were pre-dialysis and 3.7% had failing transplants. 46.9% were diabetics. Patients were on dialysis for a median of 6 mos (range 0-487). 36.1% had obstructive CAD. 18.4% required treatment (90 patients stent and 52 patients CABG). Male patients ($p < 0.001$), South Asians ($p = 0.01$), older ($p = 0.001$), diabetic patients ($p < 0.001$), were more likely to have obstructive CAD. There was no difference regarding ESRD modality ($p = 0.948$) or duration ($p = 0.157$). A logistic regression model was developed to predict obstructive CAD and need for intervention. Female [odds ratio (OR) 0.632 95% confidence interval (CI) 0.460-0.868, $p = 0.005$], non-diabetic (OR=0.319, 95% CI 0.233-0.436, $p < 0.001$) and younger patients (<50 yrs) (OR=0.675, 95% CI 0.480-0.949, $p = 0.024$) were less likely to have obstructive CAD. Similarly, female (OR 0.622 95% CI 0.414-0.936, $p = 0.023$), non-diabetic patients (OR=0.318, 95% CI 0.241-0.471, $p < 0.001$) were less likely to need intervention.

Discussion: One third of asymptomatic ESRD patients had obstructive CAD. Older, diabetic males were more likely to have obstructive CAD and need aggressive management. Non-diabetic, asymptomatic females are unlikely to have obstructive CAD and a risk score will be derived from this model and validated to confirm accurate prediction in this population.

Thursday 12th March
Tregonwell Auditorium – 14:20
Ethics, Law and Public Policy
Chairs: Prof Willem Wiemar and Dr Antonia Cronin

O029

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

Antonia Cronin^{1,2}, Dale Gardiner³, Bobbie Farsides³, Chris Rudge³, Penney Lewis^{1,3}

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Background: In 2009 in the UK, 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: With the agreement of the DH, the UKDEC has published 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. Guidance on one pre-mortem intervention—extubation—has also been published. UKDEC is working with the DH & NHSBT to finalise draft guidance on another intervention—heparin—in light of the most recent clinical evidence. It is anticipated that this published generic guidance may also be a useful guide for clinicians and clinical scientists when considering the ethical and legal implications of applying novel interventions and developing translational pathways for emerging and future biotechnologies.

O030

A systematic review on brokers' involvement in human trafficking for organ removal

Jessica de Jong¹, Frederike Ambagtsheer², Natalia Codreanu³, Ninoslav Ivanovski⁴, Willem Weimar²

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Background: In 2012 the European Commission awarded 'the HOTT project', an international research project which aims to generate more knowledge and awareness on trafficking in human beings for the purpose of organ removal (THBOR). The project's first report, an extensive literature review, fulfils this objective by describing existing information on the incidence and nature of THBOR, in particular the persons involved. Our sub-study focused on the role of brokers. By conducting a systematic literature review we aimed to a) describe the background, common characteristics and modus operandi of brokers, and b) discuss whether they organize commercial transplantations through THBOR.

Methods: We searched EbscoHost databases, Library of Congress Catalog, OAlster, PubMed, Scopus, Web of Science and Embase Medline. The methodology and results of this systematic literature review are in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. All English studies published in full text after 1 January 2000 were included. Presentations, abstracts, opinion papers and publications lacking methodology were excluded.

Results: We identified 57 records about brokers, who are also called 'middlemen', 'third parties', 'corredors', 'agents' and 'connectors'. Brokers function as invaluable connectors between organ recipients and suppliers. They are thereby key players in the organ trade network and are claimed to financially benefit the most from these transactions. Brokers may include doctors, hospitals and matching agencies and operate individually or work with organized criminal groups. In contrast to the larger degree to which 'brokerage' is mentioned in the literature, only 9 studies address their modus operandi. As brokers exploit the vulnerable position of suppliers by means of deception, force or other forms of coercion, abduction, or fraud, the presence of a broker increases the likelihood of THBOR.

Conclusion: Although the literature reveals that the presence of a broker is likely to enhance the exploitation of suppliers, trafficking is generally assumed, not explicitly established. In order to understand to a greater extent the nature and extent of brokers' involvement in human trafficking for organ removal, ethnographic research and/or in-depth case studies is required to collect reliable and verifiable data.

O031

Patients who paid for kidney transplantations abroad

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Introduction: Patients travel worldwide for living kidney transplants. Although travelling abroad does not directly imply an illegal transplant, it is commonly seen as an illegal and/or immoral endeavour involving risks. The current lack of data makes it difficult to draw conclusions about its nature and potential illegality. We aimed to describe how, where and by whom transplants abroad were facilitated as well as to describe the motivations, experiences and characteristics of patients travelling abroad.

Methods: Between March and May 2014 half-structured interviews were performed with patients from Sweden, Macedonia and The Netherlands who travelled abroad for kidney transplantation.

Results: 22 patients (19 men; born between 1949-1985) travelled abroad from Sweden (N=5), Macedonia (N=10) and The Netherlands (N=7) for transplantation between 2000-2011. The most frequently reported countries were Pakistan (N=13), India (N=3) and Iran (N=2). 7 patients went to their country of origin. For 6 patients a facilitator organized their transplant abroad, the others received help from family or friends. 17 patients directly paid the doctor, hospital or a broker; some paid for the whole transplant service. 14 patients met the supplier; 4 patients said to have paid their supplier. Reported total costs varied from €280-€45.000. Almost all patients mentioned a lack of hygiene and poor hospital conditions. 11 transplantations were uncomplicated; 11 patients had severe complications (e.g. infections or kidney loss). Patients' motivations to go abroad were the long wait time for deceased organs, lack of regular transplant activities, complications of dialysis and discrimination by the health care system.

Discussion: Despite the worldwide prohibition of organ trade, patients still purchase organs. Knowledge about the facilitation of these transplants helps to disrupt and prevent illegal transplant networks. Warning patients against the medical, ethical and legal risks and increasing the supply of organs are strategies to prevent patients from purchasing organs abroad.

O032

Breaching the secrecy oath when patients purchase kidneys: a survey-based plea for guidelines

Frederike Ambagtsheer¹, Linde van Balen¹, Wilma Duijst-Heesters², Emma Massey¹, Willem Weimar¹

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Introduction: The purchase of kidneys is prohibited in almost all countries. Nevertheless, patients buy kidneys and commonly travel overseas in order to do so. Because commercial transplants may inflict harm on donors and recipients, the question arises whether kidney purchase justifies a breach of the doctor's secrecy oath.

Methods: This paper presents the results of a national survey on transplant professionals' (TP) experiences with patients who purchased kidneys and introduces a guideline on breach of the secrecy oath. Of the 546 TPs invited, 241 (44%) completed the survey.

Results: Between 2008 and 2013, 111 professionals (46%) treated patients who traveled abroad for kidney transplantation. The vast majority (100/111) had suspicions or were certain of purchase. Whereas most professionals (85%) understood why patients bought kidneys, they also felt that they have a duty to prevent organ purchase (72%). Participants experienced a conflict of duties (65%) when suspicions of purchase occurred. Eighty percent reported a need for guidelines in dealing with patients who will or have purchased a kidney.

Conclusion: We claim that a breach of the secrecy oath by reporting patients who purchase kidneys is not justified. Nonetheless, TPs can contribute to eradicating the harm and suffering inflicted on patients and donors by anonymous reporting of organ trafficking networks. We propose that guidelines are established for TPs to disclose information that supports the police and judiciary in investigating, disrupting and prosecuting the *facilitators* of illegal transplantations.

O033

Trust, empathy and the ethics of patients advertising online for living donors

Heather Draper, Greg Moorlock

MESH, University of Birmingham, Birmingham, UK

Background: The use of the Internet by potential organ recipients to advertise for living donors is a relatively new development in the UK. Social media and dedicated websites give patients opportunities to advertise their need for an organ and persuade potential donors that they are a worthy recipient. Allowing recipients to find their own living donors via the internet may attract new donors, but it raises many ethical issues. The prospect of relationships being forged online by strangers solely for the purposes of organ donation represents a departure from the existing norms of living donation (where donor and recipient generally have a pre-existing relationship, or in cases of non-directed altruistic donation, donor and recipient rarely meet). This brings issues of sharing, trust and empathy to the fore: for instance, where should the line be drawn between reasonable expectations about what needs to be shared to motivate donors to give to specific individuals and gratuitous or exploitative demands for over-sharing? Is mutual trust sufficient to protect both sides or is further safeguarding required? Do opportunities for on-line sharing dangerously undermine impartial but 'top down' forms of allocation, or do they represent a 'bottom up' response to scarcity that empowers potential recipients?

Method: This project uses the concepts of sharing, trust and empathy in online spaces to underpin a detailed examination of the ethical issues raised by online advertising for organ donors.

Results/discussion: We argue that patients using websites to advertise for donors raises the following significant ethical concerns:

1. Online relationships between donor and recipient are forged for the specific purposes of organ donation, which requires a relatively superficial and quickly-formed trust between donor and recipient. This may leave both recipient and donor more vulnerable to exploitation than when trust has been built over a long pre-existing relationship, which may be difficult to safeguard against. This exploitation could involve the recipient or donor lying to the other about important facts that may influence the other's decisions, or donor and recipient have vastly different expectations of the relationship post-transplant.
2. Although some recipients may be empowered by being able to find their own donors, members of stigmatised groups may feel *powerless* if it proves impossible for them to similarly find donors. Patients advertising for donors has clear potential for increasing inequality in transplantation, and this may undermine trust more generally in the transplantation system.

O034

Live kidney donation to strangers should be encouraged

Willij Zuidema¹, Jacqueline Wetering van de¹, Sohal Ismail², Frank Dor³, Joke Roodnat¹, Emma Massey¹, Lotte Timmerman¹, Michiel Betjes¹, Jan IJzermans³, Willem Weimar¹

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Background: In unspecified living kidney donation there is no relationship between donor and recipient. In our centre this type of donation is on a strict anonymous basis, and there is no material benefit for the donor. In contrast, almost all specified donors are emotionally or genetically related to the recipient. However, a number of them is not, and donate non-anonymously to a specified stranger.

Methods: From May 2000 until December 2014 we prospectively collected data of individuals who approached us with the intention to donate a kidney to a stranger.

Results: After the initial information procedure 193/290 (66%) of the original applicants underwent the screening process including a psychosocial assessment. Twenty-four others were referred to another centre. 116/193 (60%) have donated a kidney to a stranger: 103/116 (89%) in an unspecified way of which 8 donated kidneys that had to be removed for urological reasons and 5 were seriously ill patients. 13/116 specified their recipient. Overall these 116 donors enabled 192 kidney transplants to 113 waitlist patients and 79 recipients of incompatible couples in domino-paired procedures including 55 doublets, 7 triplets and 3 quartets. Medical and psychosocial follow-up revealed no differences compared to specified donations to emotional and genetically related recipients.

Conclusion: We conclude that live kidney donation to strangers makes a significant contribution to the live donation program and that waiting list patients as well as recipients of incompatible couples profit. Methods to increase live donations to strangers should be encouraged.

Thursday 12th March
Tregonwell Seminar Suite – 13:15
Nurses Chapter: Part 2
Chairs: Ms Helen Tincknell & Ms Janneke Vervelde

O035

2 years of experience with stand-alone MOD team Erasmus MC Rotterdam

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Background: In 2009, the Ministry of Health gave instructions to the university hospitals in the Netherlands to implement a Masterplan to increase the number of organ donors. The Erasmus MC started with the realization of a stand-alone Multi Organ Donation (MOD) team to improve quality, reduce the waiting time for the family and relieve the donor hospitals, so that no planned surgery has to be cancelled due to staff utilization. In this abstract we describe the first experiences and results of the first 2 years of this team.

Method: The MOD team contains: a certified surgeon, an assistant surgeon (resident or fellow), an anesthesiologist (graduate) and two surgical assistants (graduate). The team carries out the MOD completely independent. They take all the disposables and reusable materials that the team will need during the MOD. The team will only use an empty OR room in the donor hospital. The team works in 24 hour service connection, and is on call every other week with the Leiden transplant team.

Results: In the first two years, no elective surgery had to be cancelled. Compared with the year before implementation, waiting times for the family of the donor reduced with 300 minutes. Realization of a faster and more efficient procedure by experienced teams led to a reduction in surgery duration of 40 minutes per procedure. In one year the team retrieved 80 kidneys of which 74 were transplanted. In 3 cases preventable damage occurred. In the same period 30 livers were procured and all used for transplantation. A survey showed very good satisfaction of the donor hospitals with the effort of the MOD team. The estimated costs to set up a team were 500.000 euro in the first year and 300.000 euro for the second year. In this estimate the salary of the MOD surgeon is not included.

Conclusion: In all areas the stand-alone MOD team is showing improvement. No donor hospital surgery had to be cancelled. Waiting time for the family was reduced with 5 hours. The procedures are carried out more quickly with good outcome of the procured organs. In conclusion, the implementation of a stand-alone MOD team was a success, and is now structurally implemented in the Netherlands.

O036

Trajectories of anxiety and depression of liver transplant candidates during the waitlist period

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Introduction: Psychological problems like anxiety and depression are common among liver transplant candidates. However, little is known about the evolution of anxiety and depression during the waitlist period and variables that influence these problems. The aim of this study was to explore trajectories of anxiety and depression of liver transplant candidates during the waitlist period and to gain insight into demographic, clinical and psychological variables associated with these trajectories.

Methods: A longitudinal study among 216 liver transplant candidates was performed, in which all participants filled out a questionnaire with measures regarding anxiety, depression, demographic and psychological variables (T0). Measures regarding anxiety and depression were repeated every six months until transplantation (T1-T7). Clinical variables were retrieved from the medical record. Latent class analyses was used to identify trajectories. Bivariate correlation analyses and multinomial regression analyses were used to explore variables associated with the different trajectories.

Results: Three trajectories regarding anxiety were identified that were consistent over time: 1) low anxiety (n=118), 2) moderate anxiety (n=7), and 3) severe anxiety (n=1). Regarding depression four trajectories, also consistent over time, were identified: 1) low depression (n=36) 2) mild depression (n=104), 3) moderate depression (n=66), and 4) severe depression (n=10). Experiencing more liver disease symptoms, a lower level of mastery and the use of emotional coping were significantly associated with higher symptom levels on both trajectories. Male gender was significantly associated with mild and moderate levels of depression.

Discussion: Given the persistent nature of symptoms of anxiety and depression during te waitlist period, it is important to screen liver transplant candidates for psychological problems early in the transplant process. Consequently appropriate interventions can be undertaken to optimize the psychological health of the transplant candidate.

O037

Relationship of psychological problems with non-adherence in Dutch liver transplant recipients

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Introduction: Non-adherence in transplant recipients is widely recognized, and leads to poor transplant outcomes. Psychological problems like depression, anxiety and post-traumatic stress (PTS) might increase the risk of non-adherence. However, evidence about this relationship is inconclusive. This study aimed to determine if there is a relationship between psychological problems and non-adherence regarding medication intake, monitoring signs and symptoms and appointment keeping one year after liver transplantation.

Methods: This study was a secondary analysis from the Psychological Aspects of Transplantation study (PATx-study). The present cross-sectional study involved 71 liver transplant recipients of our center. Data of the PATx-study regarding anxiety, depression, PTS, adherence, coping styles and personality traits were used. Adherence regarding immunosuppressive blood levels, monitoring signs and symptoms and appointment keeping were retrieved from hospital databases.

Results: Of the 71 participants included, 78.9% were non-adherent in some part of their treatment. Non-adherence in reporting vital signs was associated with depression ($r = -0.393$, $p = 0.001$), PTS ($r = -0.374$, $p = 0.001$) and anxiety ($r = -0.407$, $p < 0.000$). Depression increased the risk of non-adherence in noting medications (OR= 11.7, CI [2.40 – 57.14]). PTS showed a significant association with appointment non-adherence (OR= 15.71, CI [3.19 – 77.33], $p = 0.001$). Non-adherence with taking blood tests was associated with anxiety (OR= 4.378, [1.42 – 13.52], $p = 0.010$).

Discussion: Non-adherence is prevalent in most aspects of the treatment regimen after liver transplantation and is associated with psychological problems. Results emphasize the need to screen for adherence and psychological problems after transplantation. Future research regarding the different aspects of non-adherence and how these evolve over time is needed.

O038

The potential of E-health to improve adherence: exploring the patients' view

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Erasmus MC, Rotterdam, the Netherlands

Introduction: Transplant outcomes can be negatively influenced by medication nonadherence. Therefore, there is a need for effective interventions to improve adherence. In recent years due to developments in technology, e-health interventions have gained popularity. However, an e-health intervention for kidney patients will be effective only if patients are willing to adopt the intervention and have the facilities to do so. In this study we explored patients' internet-use, smartphone-use and their willingness to participate in online or offline self-management support interventions (SMSI's). Secondly, we explored if adherence was associated with internet-use and the willingness to participate in a SMSI, and if the willingness to participate in an online SMSI differed with age.

Methods: Patients who received a kidney transplant between 2010 and 2011 were invited to participate in a prospective cohort study. The questionnaires used for this study were administered 18 months post-transplant. Questions for exploring e-health potential were specifically designed. Adherence was measured using the Basel Assessment of Adherence to Immunosuppressive Medication Scale©.

Results: Almost 60% of the patients owned a smartphone, but only 4% used apps for health-purposes. However, 50% of all patients used internet to find information about their disease. Nonadherent patients were significantly more likely to use internet ($p < 0.05$). 70% was not willing to participate in the SMSI's, neither online nor offline. Only 17% would participate in an offline SMSI and 26% would participate in an online SMSI (of which 13% would participate in both). No difference was found in willingness to participate in an offline or online SMSI between adherent or nonadherent patients, ($p = 0.53$, $p = 0.55$, respectively). Patients who would participate in an online SMSI were significantly younger, than patients who would not ($p < 0.05$).

Discussion: The majority of kidney transplant recipients owned a smartphone, and internet is well-used to find health-related information. However, patients are not very willing to participate in SMSI's. For successful intervention-implementation, developers must take this into account.

O039

Case study: PML after lung transplantation, challenges for the nurse practitioner

S.H Smit, W van der Bij

UMCG, Groningen, the Netherlands

Introduction: Progressive multifocal leukoencephalopathy (PML) is caused by reactivation of the polyomavirus JC (JCV), leading to demyelination of the central nervous system (white matter lesions). JCV is highly seroprevalent (>80%), but may reactivate in the context of cellular immunodeficiency, such as organ transplantation (Tx) or AIDS. PML has a variable neurological presentation and is usually progressive and fatal. The diagnosis is based on MRI (white matter lesions) and PCR on JCV in the cerebrospinal fluid.

Case reports: Twenty-two months after bilateral lung Tx because of emphysema a 43 year old male patient developed loss of vision. He was diagnosed with cataract and underwent surgery, with partial visual improvement. Five months later an epileptic insult occurred, followed by hemiparesis of his left leg, hemianopia and dysarthria, Neurological evaluation by MRI and cerebrospinal fluid showed white matter lesions and a positive PCR on JCV DNA, confirming the diagnosis of PML. Ciclosporin-based immunosuppression was minimized. After an initial improvement his neurological deficits increased again, combined with chronic graft failure. He died 3 months later.

The second patient, a 44 year old male patient underwent a heart-lung Tx because of restrictive cardiomyopathy and pulmonary hypertension. Later, everolimus was added to his tacrolimus-based maintenance immunosuppression because of bronchiolitis obliterans syndrome. Five years after Tx he developed shoulder and neck complaints, initially interpreted as bursitis or cervical hernia. After developing sensory deficits of the left index finger and left hemianopia he was referred to a neurologist. A presumptive diagnosis of CVA was reevaluated by MRI and JCV PCR of the cerebrospinal fluid and changed to PML, 3 months after onset of complaints. His quadruple immunosuppression was converted to leflunamide and prednisolone. Although his vision is slightly improving and his lung function is stable, the current follow-up of only 2 months is not sufficient to allow any conclusions on outcome.

Conclusion: PML is a very severe complication after Tx. The diagnosis is often delayed for months and masked by comorbidity and unawareness of medical personnel. For the nurse practitioner taking care of transplant recipients it implicates a high index of suspicion that vague and unexplained complaints may well be the first signs of a rare complication, such as PML. PML implies a drastic change of life expectancy and an uncertain therapy, were the role of the nurse practitioner is relevant in coaching and supporting the patient and his/her family.

O040

Guidance of (potential) kidney donors

Dianne van Dongen - Segeren, Daënn Scheuter - van Oers, Hans Boots, Ton van Kooij, Tahnee van der Marel, Ellen Versluijs - Rovers

Maasstadziekenhuis, Rotterdam, the Netherlands

Introduction: After kidney donation, several living donors missed the possibility to share their experiences. They expected prolonged contact by a social worker or specialised nurse as they had experienced before donation. In addition, an evaluation by the Dutch Kidney Patient Federation revealed that donors experienced significant attention prior to and missed attention after the donation procedure. We enrolled a surveillance programme for donors to accompanying them after the procedure.

Methods: Potential Donors will be accompanied by a social worker, who will contact them every three months from the start of the first appointment until the moment of donation. After the procedure, donors will be at first re-evaluated by the specialised nurse two to four weeks after donation, and the a second time two to four months after the procedure by the social worker. In the first re-visit, the aim will be the consequences of the operation and the physical recovery. The social worker will discuss the further physical recovery, reintegration of work and the relation to the recipient. They will also pay attention to unexpected negative outcome or regret.

Results: Currently, the work is in progress. We expect that donors feel more guided, now also after donation. In addition, we expect to receive a lot of information to improve our work-up programme for potentially new donors.

Discussion: More attention for living kidney donors is essential, especially after the donation procedure. We expect that the proposed guidance programme will improve the donors' feelings and will contribute to a positive image about living kidney donation. In addition, we expect to improve our work-up programme for upcoming donors.

Thursday 12th March
Purbeck Lounge – 16:00
Pancreas
Chairs: Dr Colin Wilson and Dr Dries Braat

O041

What is a 'safe' pancreas cold ischemic time? A UK national registry analysis

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Introduction: To determine the impact of pancreas cold ischemia time (CIT) on graft outcomes in the UK and identify a safe CIT threshold.

Methods: We analyzed the national cohort of simultaneous pancreas-kidney (SPK) and pancreas only (PO - PTA and PAK) transplants from 1.1.05 to 31.12.12. Study parameters included donor age, donor type (DBD, Maastricht III DCD), donor BMI, recipient waiting time, and pancreas CIT. Outcomes were initial graft function, number of laparotomies within 3-months post-transplant, unadjusted and risk-adjusted 1-year and 5-year pancreatic graft survival. Comparisons were performed between 4 groups: CIT<10h, 10h≤CIT<12h, 12h≤CIT<14h and CIT≥14h.

Results: 1180 SPK (1045 DBD, 135 DCD) and 229 PO (165 DBD, 64 DCD) transplants were analyzed. The median (IQR) CIT was 12.1(10.0-14.7)h for SPK and 12.7(10.9-15.0)h for PO. Initial graft function (immediate, delayed, non-function) did not differ between the CIT groups. The number of laparotomies within 3-months post-transplant was also similar. However, unadjusted pancreatic graft survival at 1- and 5-years was significantly higher in DBD SPK recipients with CIT <10h compared to a CIT≥14h (90% vs 80%, p=0.01; 82% vs 68%, p=0.003, respectively). After risk adjustment for donor type, donor age, donor BMI, transplant type (SPK vs PO) and recipient waiting time, there was a stepwise increase in the risk of graft failure at 5 years across the 4 CIT groups (CIT<10h: HR 1.00; 10h≤CIT<12h: HR 1.42; 12h≤CIT<14h: HR 1.54; CIT≥14h: HR 2.11) (p<0.001).

Discussion: Pancreas CIT >10h has a significant independent impact on graft survival. A safe CIT threshold was unable to be identified. Surgeons must strive to ensure that CITs are minimized; national pancreas allocation policies also need to be re-examined.

O042

Pancreas transplantation from controlled DCD: A single centre experience

Anand S Rathnasamy Muthusamy¹, Shruti Mittal^{1,2}, Michiel Voskuil², Srikanth Reddy¹, Isabel Quiroga¹, James Gilbert¹, Rutger Ploeg^{2,1}, Edward Sharples¹, Sanjay Sinha¹, Anil Vaidya¹, Peter Friend^{2,1}

¹Oxford Transplant Centre, Oxford, UK, ²University of Oxford, Oxford, UK

Background: The use of DCD pancreata is gaining popularity in the UK. Isolated pancreas transplantation (IP) is known to have inferior outcomes in comparison to SPK. This abstract summarizes a large single centre experience with transplanting pancreases from controlled DCD (Maastricht III).

Methods: Our pancreas transplant database was interrogated to obtain data on 691 pancreas transplants from 2004 to 2014. DCD pancreata were accepted from 2007, based on donor age <60 years, BMI <30, cardiac arrest <1 hour.

Results: 43 SPK-DCD, 47 IP-DCD, 488 SPK-DBD and 113 IP-DBD were identified, resulting in more IP from DCD ($p=0.0001$). DCD donors were younger ($33\pm 12y$ vs. $37\pm 14y$, $P=0.01$), had less vascular cause of death (35% vs. 59%, $p<0.0001$) and longer cold ischaemia ($701\pm 151min$ vs. $663\pm 156min$, $p=0.02$). DCD had more graft thrombosis leading to early graft loss (8% vs. 1%, $p<0.001$) despite frequent use of therapeutic anticoagulation (16% vs. 7%, $p=0.008$); IP-DCD graft thrombosis required pancreatectomy more frequently (vs. IP-DBD, $p=0.02$ vs. SPK-DCD, $p=0.02$). In IP-DCD, thrombosis was predictive of the need for pancreatectomy ($p=0.001$), delayed graft function ($p=0.015$), and graft failure ($p=0.05$). DCD grafts were also lost to pancreatitis (6%) and/or to rejection (9%). DCD kidneys had more frequent DGF than DBD (34% vs. 16%, $p=0.02$). DCD pancreata had similar DGF (requiring insulin at discharge) (8% vs. 3%, $p=0.06$). PNF incidence and patient survival was similar. DBD pancreas grafts had better survival (79% vs. 71%, $p=0.01$) although graft survival of SPK and IP sub-groups was similar (82% SPK-DBD vs. 86% SDCD, $p=0.8$; IP-DBD 70% vs. DCD 57%, $p=0.2$)

Conclusion: Excellent SPK-DCD results suggest that this cohort is a good additional source to expand the donor pool. IP-DCD pancreata are more at risk of thrombosis related graft loss requiring pancreatectomy. IP-DCD grafts remain a feasible source for pancreases with comparable long-term survival, despite early graft loss risk. Clearly a multipronged strategy is required to improve graft utilization, encompassing donor management, preservation and recipient conditioning.

O043

Validation of the pancreas donor risk index for use in a UK population

Shruti Mittal^{1,2}, Fang Jann Lee¹, Lisa Bradbury³, Isabel Quiroga¹, Srikanth Reddy¹, James Gilbert¹, Sanjay Sinha¹, Edward Sharples¹, Anil Vaidya¹, Rutger Ploeg^{1,2}, Peter Friend^{1,2}

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³*NHSBT, Bristol, UK*

Aim: Pancreas transplantation offers people with diabetes insulin independence; however, graft failure rates remain significant. The PDRI can be used at the time of organ offers, to better assess which pancreases would result in good graft survival. This study aimed to validate the PDRI for use in a UK population

Methods: Data was retrieved from a nationally maintained database for all whole organ pancreas transplants performed between April 2004 and July 2011. The UK dataset was described and compared to the published US dataset. The PDRI was calculated and cases categorised according to PDRI quartile and compared for death-censored one-year graft survival by type of transplant.

Results: 1021 cases were included in the analysis. Statistically significant differences were observed between the UK and US cohorts in all recipient, donor and transplant characteristics examined. Comparison of pancreas graft survival by PDRI quartile showed PDRI to accurately discriminate graft survival for SPK with the lowest to highest risk quartiles achieving 1 year survival of 93.1%, 89.1%, 84.6% and 80.5% respectively. A multivariate Cox regression analysis showed PDRI was associated with graft survival in the SPK group, with a hazard ratio of 1.52 (p=0.009). However, in the PTA and PAK groups, no association between PDRI quartile and graft survival was observed.

Conclusion: To our knowledge this is the largest study to validate the PDRI in a European cohort and has shown for the first time that the PDRI can be used as a tool to predict graft survival in SPK but not PTA or PAK transplantation. Further research into post-transplantation markers of graft failure are needed to improve outcomes in this group.

O044

Damage to the deceased donor pancreas during procurement - a registry analysis

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¹*Guy's Hospital, London, UK*, ²*Freeman Hospital, Newcastle, UK*, ³*Hospital Xeral, Vigo, Spain*

Introduction: Surgical injuries to the deceased donor pancreas are thought to occur commonly during procurement. We analysed the UK Transplant Registry to determine the frequency of pancreatic injuries, identify factors associated with damage, and assess the impact of injuries on graft survival.

Methods: Pancreases procured for solid organ or islet transplantation between 1.1.08 and 31.12.12 were analysed. Univariate and multivariate analyses were performed to determine factors associated with pancreas damage. Data from procuring and implanting surgeons were combined. Pancreas graft survival of SPK transplants was analysed on the basis of organ damage.

Results: 1610 deceased donor pancreases were procured during the study period; 1296 (80.5%) from DBD donors and 314 (19.5%) from DCD donors. Fifty two percent of pancreases had at least one injury, commonly a portal vein <10 mm length (21.5%), capsular damage (13.6%), or parenchymal injury (5.9%). Liver donation, hepatic artery (HA) arising from the SMA, and increasing BMI were associated with increased rates of pancreas damage on univariate analyses. Donor type was not associated with injury. On multivariate analysis, only HA from SMA remained significant ($p=0.02$). 640 SPK transplants were performed; 42.8% had some type of damage. Overall, there was no difference in graft survival between damaged and undamaged organs ($p=0.28$). However, when graft survival was analysed by damage type, graft loss was significantly more frequent in organs with arterial damage ($p=0.04$), and those with parenchymal injuries ($p=0.05$).

Conclusions: Damage to the pancreas during procurement is far more common than for other organs. DCD donors do not appear to have a higher rate of pancreas injury, though the presence of a HA from the SMA was independently associated with pancreas damage. Overall, pancreases with procurement-related damage have similar graft survival to those without, though caution should be exercised in organs with parenchymal or arterial injuries. Meticulous surgical technique is needed to reduce rates of pancreas damage during procurement.

O045

Effect of donor age on pancreas transplantation outcome

Anand S Rathnasamy Muthusamy¹, Giorgios Vrakas¹, Shruti Mittal^{1,2}, Srikanth Reddy¹, Isabel Quiroga¹, Edward Sharples¹, James Gilbert¹, Rutger Ploeg^{2,1}, Sanjay Sinha¹, Anil Vaidya¹, Peter Friend²

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Introduction: The global increase in the average donor age over the last decade has resulted in widespread acceptance of pancreases from older donors for transplantation. This abstract aims to review the effect of this cohort on pancreas graft and patient survival.

Methods: Prospectively maintained database of pancreases transplanted from 2004-2014 at a single centre was analysed, comparing pancreas & kidney, graft & patient survival, delayed graft function (DGF) and non-function (PNF) between all (DCD and DBD) donors aged >50 years (ED) and standard criteria donors (SD).

Results: 684 transplants occurred from 562 SD and 122 ED including 89 SD-DCD and 4 ED-DCD with median follow up of 32 months (SD) and 28 months (ED). There were 422 SPK, 55 PAK and 85 PTA from SD; 105 SPK, 1 PAK and 16 PTA from ED. ED had a median age of 55 yrs (51-67). Recipients of ED grafts were older (47 vs. 42, $p < 0.0001$) reflecting the intention to match donor and recipient age. Actuarial pancreas (90% SD vs. 87% ED, $p = 0.9$), kidney (87% SD vs. 88% ED, $p = 0.9$) and patient survival (90% SD vs. 87% ED, $p = 0.1$) was similar. Overall DGF of the pancreas (9% ED vs. 4% SD, $p = \text{NS}$) and kidney (27% ED vs. 16% SD, $p = 0.06$) was similar, as was PNF rate for pancreas (4% ED vs. 1% SD, $p = \text{NS}$) and kidney (4% ED vs. 1% SD). The isolated pancreas transplants (PAK & PTA) had similar pancreas graft outcomes (76% ED vs. 71% SD, $p = 0.5$). However, when the DCD grafts were excluded, kidney DGF rates became significantly higher in ED (26% vs. 10%, $p = 0.0006$) whereas the pancreas DGF rate remained similar (3% ED vs. 2% SD).

Conclusion: Utilising older donors for pancreas transplantation appears to be safe, providing the increased risk of delayed graft function is duly considered in the risk-benefit analysis. Considering older donors for isolated pancreas transplants merits careful consideration.

O046

Early pancreas graft loss; technical failure or missed rejection?

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Introduction: Technical failure is thought to be the most significant cause of early pancreas graft loss. However, acute pancreas rejection (APR) is increasingly recognised as an important cause of graft failure, though current biochemical markers of rejection lack sensitivity and specificity. We analysed our experience of early graft pancreatectomies and subsequent histopathological analysis, to determine the rate of undiagnosed APR.

Methods: Case notes of all pancreas transplants (SPK, PAK, and PTA) performed at our unit between 1.1.09 and 1.5.14, were reviewed. Patients who underwent graft pancreatectomy within 90 days of transplantation were identified. Histology reports of explanted specimens by specialist renal/pancreas pathologists were analysed.

Results: One hundred and thirty four pancreas transplants were performed (122 SPK, 6 PAK, 6 PTA); 18 graft pancreatectomies occurred within 90 days of transplantation. Surgical diagnoses at the time of pancreatectomy were: duodenal leak 8; venous thrombosis (+/- amylase leak) 5; recurrent peripancreatic collections 3; duodenal bleeding 1; and necrotic pancreas with pseudoaneurysms 1. Documentation of suspected APR prior to pancreatectomy occurred in only one case. On explanted graft histopathology, 9 grafts (50%) showed definite evidence of APR, 2 showed possible APR, and 7 showed no evidence of APR. Of the 8 grafts attributed to duodenal leaks, histopathology showed strong evidence of pancreatic or duodenal rejection in 7 (88%). All duodenal leaks occurred in SPK recipients. Of the 5 grafts removed for presumed venous thrombosis, only one showed possible APR, the other 4 had no evidence of rejection.

Conclusions: Duodenal leaks and venous thromboses are widely considered to be technical causes of early pancreas graft loss. Our analysis suggests that duodenal leaks are strongly associated with findings of APR on histopathology, and that technical factors may be less important. We plan to review our induction immunosuppressive policies in the light of these findings. A higher index of suspicion of APR is required amongst transplant clinicians.

O047

The impact of donor alcohol intake on pancreatic graft survival

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Introduction: Alcohol (EtOH) abuse can damage the pancreas, but outcomes of pancreas transplantation from donors with a high EtOH intake are poorly defined. The aim of this study was to determine if donor EtOH intake influenced pancreas allograft survival in SPK transplantation.

Methods: UK registry data was used to assess graft survival in SPK recipients between 2006-2012. Core donor data forms were analysed and (where quantified) EtOH intake was calculated. Variables were stratified by donor EtOH intake: group I – quantified high recent EtOH intake (>21 units/week in males; >14 units/week in females) or a history of EtOH abuse; group II – no (or unknown) history of EtOH abuse and a recent intake less than the above thresholds. Continuous variables are expressed as median (IQR).

Results: Seven hundred and seventy SPK transplants were performed (group I, n=120; group II, n=650). In group I, 51 donors had high quantified recent EtOH intake only, 34 had a history of EtOH abuse but recent intake wasn't documented, 33 had a history of abuse with a high recent intake documented, and 2 had a history of abuse with a recent intake less than threshold. As expected, quantified current EtOH intake was higher in group I than group II (39 (24-59) vs 10 (5-13) units/week; $p<0.001$). Donors in group I were more likely to be male (61% vs 49%; $p=0.02$), and older (42 (32-48) vs 38 (26-46) years; $p<0.001$); however, there were no differences in the proportions of DCD donors, median donor BMI, or median recipient age between the two groups. Cold ischaemic time was shorter in group I (660 (539-839) vs 733 (613-900) mins; $p<0.001$). There was no difference in subsequent graft survival between groups I and II ($p=0.95$, log rank test), or between group II and the sub-group of 33 donors with both a history of EtOH abuse and a high recent intake ($p=0.17$).

Conclusions: Pancreas donors with past EtOH abuse or recent high intake are common, and graft outcomes appear to be good. This analysis suggests that excessive donor EtOH intake, by itself, should not exclude pancreas utilisation.

O048

Peri-operative goal-directed haemodynamic optimisation improves short-term outcomes following simultaneous pancreas and kidney transplantation: a randomised clinical trial

Hussein Khambalia^{1,2}, Mahesh Nirmalan^{1,2}, David van Dellen^{1,2}, Angela Summers^{1,2}, Zia Moinuddin^{1,2}, Giuseppe Giuffrida¹, Insiya Susnerwala³, Simon Varley², Yvonne Alexander⁴, Titus Augustine^{1,2}

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Introduction: Simultaneous pancreas and kidney transplantation (SPKT) is associated with significant peri-operative morbidity in patients with pre-existing co-morbidities. Protocolised, peri-operative optimisation is known to improve outcomes in high-risk individuals following major surgery. This study aimed to investigate the benefits of such optimisation techniques in the peri-operative period post-SPKT.

Methods: Recipients were randomly allocated to either Goal-Directed (GDT) or Standard Therapy (ST) cohorts. The GDT cohort underwent peri-operative optimisation, guided by lithium indicator dilution, to attain an indexed oxygen delivery of 600ml/min/m². The ST cohort was managed according to current unit protocols.

Results: Thirty patients were randomised to each group (Mean age 39.96 ± 7.35 and 44.27 ± 6.83, male 13 (44.8%) and 21 (70.0%), mean BMI 25.02kg/m² ± 3.43 and 25.39kg/m² ± 2.91 and DBD 22 (73.3%) and 23 (76.7%) in the GDT and ST cohorts respectively). The GDT cohort (n= 29) had significantly lower critical care unit length of stays when compared to the ST cohort (n= 30; 4 days (IQR 3- 5.5) and 8 days (IQR 6.0- 9.3) respectively, p<0.001, MWU). They also had shorter time to mobilisation (2.0 days (IQR 1.0- 3.0) and 4.0 days (IQR 3.0- 6.25) respectively; p<0.001, MWU) and shorter time to tolerating oral diet (5.0 days (IQR 4.0- 8.0) and 8.0 days (IQR 6.75- 10.0) respectively; p<0.001, MWU).

Conclusions: For the first time in a study investigating peri-operative supra-physiological optimisation in pancreas transplantation, we have demonstrated significantly improved short-term outcomes. This approach highlights the positive impact of peri-operative optimisation and should serve to streamline and focus management of these patients. (NCT01619904)

Thursday 12th March
Tregonwell Seminar Suite – 16:00
Organ Perfusion
Chairs: Prof Chris Watson and Dr Frank Dor

O049

MicroRNA profiles in perfusate during *ex situ* normothermic machine perfusion of human donor livers are predictive biomarkers for graft viability

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Introduction: *Ex situ* oxygenated normothermic machine perfusion (NMP, 37°C) can potentially be used to assess viability of donor livers prior to transplantation. The identification of suitable predictive biomarkers for graft viability and bile duct injury is necessary to aid in the selection process. Here, we investigated whether the release of hepatocyte- and cholangiocyte-derived microRNAs (HDmiRs and CDmiRs, respectively) during NMP of human donor livers is predictive for graft and bile duct viability.

Methods: After a median cold preservation time of 7.8 hrs, 11 human donor livers that were declined for transplantation were subjected to 6 hrs of NMP. Perfusion solution was based on red blood cells, fresh frozen plasma, and nutrients. Using previously published criteria for graft viability based on cumulative bile production, livers were classified as well- or poor-functioning. Perfusate samples were taken at baseline, after 3 and 6 hrs of NMP for quantification of miRNA by qRT-PCR assays for the HDmiRs 122 and 148a, and for the CD-miRs 30e and 222. Ct values were used to calculate relative expression levels (2^{-Ct}).

Results: Seven livers were classified as well-functioning, 5 as poor-functioning. In poor-functioning livers the level of CDmiR-222 was significantly higher at 3 hrs ($p=0.043$) and 6 hrs of NMP ($p=0.021$), compared to well-functioning livers. The ratio between HDmiRs and CDmiRs was significantly higher in well-functioning livers compared to poor-functioning livers at both 3 hrs (HDmiR-148a/CDmiR-30e, $p=0.008$) and 6 hrs of NMP ($p=0.008$). Also the ratio of HDmiR-148a/CDmiR-222 was higher at 3 hrs ($p=0.023$) and 6 hrs of NMP ($p=0.059$).

Discussion: This study indicates that profiles of hepatocyte- and cholangiocyte-derived miRs in perfusate during *ex situ* NMP of human donor livers can be used as biomarkers of graft function. This finding is clinically relevant as it may aid in optimizing the selection of suitable donor livers prior to transplantation and expanding the donor pool.

O050

Ex-vivo normothermic perfusion - an innovative technology for quality assessment of marginal donor kidney transplants

Sarah Hosgood, Adam Barlow, James Hunter, Michael Nicholson

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Introduction: A significant proportion of kidneys are discarded due to concerns about their suitability for transplantation. In this study we have used *ex-vivo* normothermic perfusion (EVNP), a novel technique that restores renal circulation and function, as a quality assessment device in renal transplantation.

Methods: Seventy four human kidneys deemed unsuitable for transplantation underwent 60 minutes of EVNP with an oxygenated red cell based solution at 36°C. Receiver operating characteristic curves were used to identify thresholds of renal blood flow and urine output. These thresholds and the graded macroscopic appearance were incorporated into a quality assessment score (QAS; highest quality = 1, lowest = 5). This was applied to a series of 36 EVNP transplanted kidneys.

Results: In the discarded series, 60 kidneys (81%) had QAS = 1 - 4 and 14 kidneys (19%) had QAS = 5. In the 36 transplanted kidneys, the QAS ranged between 1 and 3. All kidneys were transplanted without any complications or primary non function. QAS predicted early graft function [QAS 1 - 2 (n = 28) vs QAS 3 (n = 8) eGFR Day 7, 46 ± 19ml vs 23 ± 17; P=0.049]. The delayed graft function rate was 3.6% in kidneys scoring 1 - 2 and 37.5% in those scoring 3 (P=0.028). eGFR at 12 months was (QAS 1-2) 56 ± 16 vs (QAS 3) 38 ± 21ml; P = 0.017.

Conclusion: EVNP combined with a simple scoring system is an innovative technology for pre-transplant assessment of kidney quality. This study suggests that a high percentage of kidneys are being unnecessarily discarded.

O051

End-ischemic oxygenated machine perfusion of rat livers from donation after circulatory death donors results in better preservation of the bile ducts compared to static cold storage alone, independent from the temperature during perfusion

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Background: A short period of oxygenated machine perfusion (MP) after traditional static cold storage (SCS) might reduce biliary injury, especially in donation after circulatory death (DCD) donors. However, the optimal temperature at which perfusion should be performed is unknown.

Methods: End-ischemic oxygenated MP was performed with three different temperature protocols and compared with a reference DCD rat liver model for bile duct injury consisting of 30 minutes donor warm ischemia, followed by 6 hr SCS, 60 minutes of mimicked anastomosis time, and 2 hr of *ex-situ* normothermic blood reperfusion (37°C) to mimic transplantation. In three MP study groups, one hour of end-ischemic oxygenated MP was performed between the period of SCS and mimicked anastomosis time at either hypothermia (8°C HMP), subnormothermia (20°C SNP), or with controlled oxygenated rewarming (COR; 8-20°C). After 2 hr of reperfusion, graft and bile duct viability were assessed by perfusate and bile analysis. Hepatic mitochondrial oxygen consumption was measured with a Clark electrode. Injury of the extrahepatic bile ducts was assessed with light microscopy using H&E staining.

Results: Analysis of perfusate samples revealed lower levels of hepatocyte injury markers (AST, ALT and, LDH) in the three MP study groups, compared to SCS ($p < 0.05$). In parallel, mitochondrial oxygen consumption was significantly better in the MP groups. Markers of biliary function, including bile production, biliary bicarbonate concentration, and biliary pH were significantly higher in the MP groups, compared to SCS, whereas markers of biliary epithelial injury (biliary gamma-GT and LDH) were significantly lower in MP preserved livers. Histological analysis revealed less injury of extrahepatic bile duct epithelium in the three MP study groups, compared to SCS.

Discussion: Compared to conventional SCS, end-ischemic oxygenated MP of DCD livers provides better preservation of biliary epithelial function and morphology, independent from the temperature at which MP is performed. End-ischemic oxygenated MP could reduce biliary injury and improve outcome after DCD liver transplantation.

O052

Hypothermic oxygenated dual machine perfusion after cold preservation improves viability and hepatobiliary function of human donor livers by restoring ATP content

Negin Karimian, Andrie C. Westerkamp, Alix P.M. Matton, Rianne van Rijn, Paria Mahboub, Janneke Wiersma-Buist, Sanna op den Dries, Henri G.D. Leuvenink, Ton Lisman, Robert J. Porte

University Medical Center Groningen, Groningen, the Netherlands

Background: Machine perfusion (MP) is a promising method to reduce donor liver injury and improve viability prior to transplantation. Although animal studies have suggested that MP is particularly beneficial in livers from extended criteria donors (ECD), data on human livers is still sparse. Aim of this study was to assess the efficacy and safety of a short period of end-ischemic hypothermic oxygenated dual (arterial and portal) perfusion (HODP) after traditional static cold storage (SCS) of human ECD livers.

Methods: Twenty-two ECD livers that were declined for transplantation were procured in a conventional manner using rapid cold flush out and subsequent transportation in cold (0-4°C) UW preservation fluid. Upon arrival at our center after a mean period of 6 hr SCS, hepatobiliary viability was assessed during 6 hr of *ex-situ* normothermic (37°C) machine perfusion (NMP) using a pressure-controlled system (Liver Assist, Organ Assist). Prior to NMP, 6 livers first underwent 2 hr HODP (12°C). The remaining sixteen control livers underwent NMP without prior HODP treatment.

Results: The hepatic ATP content was 10-fold higher after 2 hr of HODP compared to NMP alone ($p= 0.004$). Livers that underwent HODP displayed significantly less injury and better function during *ex-situ* assessment using NMP, compared to controls. Vascular resistance (portal and arterial) during NMP was lower in livers that first underwent HODP. After 6 hr of NMP, hepatic injury markers (AST, ALT, and LDH) and lactate levels in perfusion fluid were significantly lower in the HODP group compared to controls. In parallel, cumulative bile production during NMP was significantly higher in the HODP group (46 versus 14 mL bile/kg liver; $p=0.015$).

Discussion: A short period of 2 hr of end-ischemic dual oxygenated perfusion of donor livers at 12°C after traditional SCS restores cellular energy levels, resulting in less injury and better hepatobiliary function during subsequent *ex-situ* NMP. This study is the first to indicate that end-ischemic HODP is a safe and effective novel method to improve the quality of human ECD livers.

O053

Normothermic machine liver perfusion can be used for the ex-vivo assessment of viability in discarded human donor livers

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Introduction: Demand for donor livers in transplantation far exceeds supply. There is increasing reliance on marginal donors, including livers donated after circulatory death (DCD). Despite this, 63% of DCD livers are untransplantable. Normothermic machine liver perfusion (NMLP) might allow for viability testing of marginal donor organs that would otherwise be discarded. The aim of this study was to test the feasibility of NMLP on human livers discarded for transplantation.

Methods: Between July 2013 and September 2014, six discarded human livers, transported from the donor on static cold storage, were subjected to NMLP using the CE-marked Liver Assist device (Organ Assist, The Netherlands). Livers were perfused with a packed red cell based fluid at 37°C. Hepatic arterial and portal venous flow parameters, blood gas analysis and bile output were recorded. Liver biopsies were performed at the start and every 3 hours of NMLP.

Results: Two groups of livers, viable and non-viable, were observed (n=3 each). Donor ages were similar (Median viable 63.3yrs IQR 46.2-66.3yrs, non-viable 59.9yrs IQR 52.8-68.2yrs). Half were male (Viable 2/3, non-viable 1/3) and the majority DCD (2/3 for each). Steatosis was similar in both groups. Cold ischaemic times were shorter in the viable group (Median viable 7:06hrs, non-viable 7:52hrs). NMLP time was longer in the non-viable group (Median viable 4:37hrs, non-viable 12:59hrs). Hepatic arterial flow increased more in the viable group (Median viable end flow 551ml/min, non-viable end flow 355ml/min) as did portal venous flow (Median viable end flow 1.07L/min change +860ml/min, non-viable end flow 1.04L/min change +460ml/min). More marked decreases in lactate were observed in the viable group (Median viable end 3.2mmol/L, non-viable end 18.7mmol/L). Glucose was utilised by the liver in both groups without exogenous insulin. Oxygen extraction was more stable in the viable group. Cumulative bile production was higher in the viable group after 6 hours (Median viable 12.3g, non-viable 2.6g).

Conclusion: NMLP is technically feasible and may distinguish between viable and non-viable discarded donor livers.

O054

Reconditioning of kidneys after inadequate *in-situ* perfusion using ex-vivo normothermic perfusion

Sarah Hosgood, Adam Barlow, James Hunter, Michael Nicholson

University of Leicester, Leicester, UK

Introduction: Inadequate *in-situ* perfusion during organ retrieval is a significant problem in renal transplantation. Many of these kidneys are rejected for transplantation due to a high risk of additional ischaemic injury and microvasculature thrombosis. This study describes the resuscitation of discarded kidneys after inadequate *in-situ* perfusion using *ex-vivo* normothermic perfusion (EVNP).

Methods: Twenty-one human kidneys were retrieved but then deemed unsuitable for transplantation due to inadequate *in-situ* perfusion. After a period of static cold storage, kidneys were perfused for 60 minutes with an oxygenated red cell based solution at 36°C. Renal function was measured throughout perfusion and a visual assessment of each kidney made at the end of EVNP.

Results: Nineteen out of 21 kidneys (90%) were from donation after circulatory death (DCD) donors. The mean donor age was 55 ± 15.7 y (range 31-77y) and warm ischaemic time 12.2 ± 2.2 minutes. The mean cold ischaemic time was 24.7 ± 14.3 h (range 7-71h). During EVNP, 3 kidneys had a poor renal blood flow (Mean 41.8 ± 17.6 ml/min/100g) combined with a low urine output (7 ± 3 ml). They appeared mottled and purple at the end of EVNP and were considered non-recoverable. The remaining 18 kidneys had a mean renal blood flow of 70.1 ± 28.0 ml/min/100g and total urine output of 101 ± 72 ml. These EVNP parameters were within the range of kidneys in a successful clinical series. On visual inspection they all appeared perfused and suitable for transplantation.

Conclusion: Kidneys declined due to inadequate *in-situ* perfusion may be reconditioned by restoring circulation and function *ex-vivo*.

O055

Hypothermic machine perfusion improves the quality of marginal donor pancreata

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Introduction: Pancreas or islet transplantation is considered the most effective treatment for patients with type 1 diabetes mellitus. Due to the persistent organ shortage, pancreata from marginal donors are more frequently used for transplantation or islet isolation. These grafts are more vulnerable to ischemic damage. The traditional preservation method, cold storage (CS), might not be sufficient to completely prevent this damage. It is hypothesized that hypothermic machine perfusion (HMP) can improve the quality of the donor pancreas by an increase in viability and a reduction in injury compared to CS.

Methods: In this study, 8 human pancreata (4 DCD and 4 DBD) were preserved by HMP and 8 (4 DCD and 4 DBD) by CS. HMP was performed for 6 hours with oxygenated Belzer UW-MPS® with dual perfusion of the mesenteric superior artery and the splenic artery. Tissue biopsies and samples of the preservation fluid were collected at baseline and after 6 hours of preservation by either HMP or CS.

Results: At baseline, the ATP content in the DCD group (8,2 ± 5,6 µmol/gram protein) was significantly lower than in the DBD group (43,5 ± 16,2 µmol/gram protein). After 6 hours of CS, the ATP content decreased to 4, ± 1,7 (DCD) and 25,6 ± 8,6 (DBD) µmol/gram protein. In the HMP preserved pancreata, the ATP content increased to 47,9 ± 25 (DCD) and 136,4 ± 144 (DBD) µmol/gram protein. In the DCD group, the ATP content after HMP was significantly higher compared to CS and it was equivalent to the ATP content at baseline in the DBD group. During HMP, amylase, lipase and LDH levels in the preservation fluid increased. Lipase and LDH levels reached a plateau after 5 hours of HMP.

Conclusion: HMP seems to improve donor pancreata quality, demonstrated by the increased levels of ATP and potentially by washing out degrading enzymes. Therefore, we propose that DCD pancreata preserved by HMP could reach the quality of DBD pancreata and could be considered transplantable.

O056

Post-conditioning reduces renal warm ischaemia-reperfusion injury in an experimental large animal model

James Hunter¹, Sarah Hosgood¹, Adam Barlow², Michael Nicholson¹

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

Methods: Pigs (45-50kg) underwent laparotomy and 60 minutes occlusion of the left renal pedicle. Animals were randomised into three groups; untreated controls (n=7); direct post-conditioning 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 peri-conditioning 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 7 days.

Results: The direct post-conditioning group had lower area under the serum creatinine curve (1071±136 vs. 1722±973µmol/L.day respectively; P=0.025) and peak creatinine levels (312±49 vs. 519±268µmol/L respectively; P=0.008) compared to control. There was a significant increase in serum levels of TNFα on day 1 in control animals but not in the conditioning groups (P=0.013). There was no increase in urinary levels of NGAL from pre-operative to day 7 (NGAL/Cr ratio) in the direct group (P=0.176). However, there was an increase in levels over the study period in both the control and remote groups (P=0.0008 and P=0.0004) respectively). There was no difference in serum Endothelin-1, nitric oxide or superoxide dismutase levels between the groups although levels in the direct group were numerically lower. There was no mortality and no complications related to either conditioning technique.

Conclusions: In this *in vivo* large animal model direct renal artery ischaemic post-conditioning protected kidneys against warm ischaemic injury. This straightforward technique could readily be translated into clinical practice.

Thursday 12th March
Bayview – 16:00
Antibodies
Chairs: Dr Dave Roelen and Dr Martin Howell

O057

Course of anti-HLA antibodies after induction therapy with rituximab in renal transplantation

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Introduction: The presence of pre-existing or de novo donor-specific antibodies against HLA (DSA) is associated with a worse graft outcome after renal transplantation. B-cell depletion protocols have shown to reduce DSA and chronic antibody mediated rejection. We aimed to study the effects of rituximab as a single-agent induction therapy on the titers of pre-existent or *de novo* DSA and non-DSA after renal transplantation and relate this to rejection free and overall graft survival.

Methods: We collected sera in participants of a prospective double-blind randomized study on the efficacy and safety of the prophylactic use of rituximab, added to standard immunosuppressive treatment (prednisolone, tacrolimus and mycophenolate mofetil) in comparison with standard immunosuppressive treatment alone in renal transplantation (www.clinicaltrials.gov, NCT00565331). 280 patients were included (142 received placebo, 138 rituximab). Anti-HLA antibodies were determined in serum taken pre-transplant and 12 and 24 months after transplantation. Serum was available pre-transplant and at 12 months from 124 placebo and 118 rituximab treated patients.

Results: Pre-existent anti- HLA antibodies were present in 48/124 (39%) patients in the placebo group and in 29/118 (25%) patients in the rituximab group ($P < 0.05$). In 33/77 (43%) patients pre-existent HLA antibodies disappeared after transplantation: 19/48 (39.6%) in the placebo group and 9/29 (31%) in the rituximab group. At 12 months, 30/242 (12.3%) developed *de novo* HLA antibodies, 18 (14.5%) placebo treated patients and 12 (10.2%) rituximab treated patients (NS). 14/242 (5.8%) had *de novo* HLA class I antibodies: 6 (4.8%) and 8 (6.8%) in the placebo and rituximab treated patients, respectively (NS). 16/242 (6.6%) had *de novo* HLA class II antibodies: 12 (9.8%) in the placebo group and 4 (3.4%) in the rituximab group ($P < 0.05$). The results of antibody screening at 24 months and of luminex single antigen analysis (including complement binding) will be available in March 2015.

Conclusion: Induction therapy with rituximab compared to placebo inhibits the formation of *de novo* class II anti-HLA antibodies, but does not affect the levels of pre-existent anti-HLA antibodies nor the formation of *de novo* class I anti-HLA antibodies at 12 months after transplantation.

O058

Both preformed and de novo Cw donor specific antibodies are clinically significant in renal transplantation

Alexander Gueret-Wardle, Michelle Willicombe, Vinnod Dibbur, Paul Brookes, Adam McLean, David Taube

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Introduction: Preformed [PF] and de novo [DN] anti-HLA A, B, DR and DQ donor specific antibodies [DSAbs] are associated with poorer allograft outcomes secondary to antibody mediated injury. Although PF Cw DSABs occurring in isolation are associated with rejection, the significance of DN Cw DSABs is uncertain. In this study we describe the clinical importance of both PF and DN isolated Cw DSABs.

Methods: 1273 CDC/FCXM negative renal transplant recipients [mean follow up 4.46 ± 2.50 yrs] receiving a steroid sparing, tacrolimus based maintenance regimen with monoclonal antibody induction were studied. Patients were screened for DSAB pre-transplant and post transplant at months 1, 3, 6, 12 and then yearly and at times of allograft dysfunction.

Results: 67/1273[5.3%] patients had a Cw DSAB of which 28/67[41.8%] occurred in isolation [13 PF, 15 DN]. Compared with the sensitised [S][HLA+,DSAb-] and non-sensitised [NS] groups, patients with PF Cw DSAB [Cw] were more likely to develop rejection and transplant glomerulopathy [TG] as shown below. The development of DN Cw DSABs was associated with inferior allograft survival, AMR free survival and TG free survival.

Survival (%)	Preformed group				De novo		
	NS	S	Cw	p value	No DSA	Cw	p value
Allograft	79.5	85.8	90.0	0.95	85.2	76.2	0.029
Rejection	74.2	72.9	31.3	0.0021	80.2	80.0	0.55
ACR	80.9	78.9	55.9	0.03	81.8	93.3	0.45
AMR	91.1	89.1	76.4	0.11	98.2	86.7	0.0003
TG	92.9	91.3	0	0.0003	97.1	85.6	0.0003

Conclusion: This study shows that both PN and DN Cw DSABs are clinically significant. Patients with these antibodies may benefit from increased surveillance and immunosuppression. To conclude, patients with isolated Cw DSA, whether preformed or dn are at increased risk of alloimmune injury, as such their presence should be considered a poor prognostic indicator and highlights an at risk group which may benefit from optimisation or augmented immunotherapy.

O059

DQB1 epitope matching predicts the development of de novo DSA and antibody mediated rejection

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Introduction: HLA DQ antibodies are the commonest de novo [DN] DSA specificity seen post renal transplantation. Their presence is associated with antibody mediated injury and allograft loss. However it is known that allorecognition is epitope rather than antigen dependent and that epitopes may be shared between two or more HLA antigens.

Methods: The aim of this study is determine the significance of DQ epitope mismatching in the development of DN DQ DSA. We retrospectively identified patients transplanted at our centre who had a single DQ antigen mismatch (MM) by low resolution typing. Epitopes were determined using Tersaki defined epitopes (TerEp). DSA were detected at times of allograft dysfunction and routine screening. 50/485[10.3%] of patients mismatched [MM] at a single DQ antigen developed a DQ DSA. The median TerEp MM was higher in the DSA+ [median 4(IQR:3-6)] compared with DSA- [median 3(IQR: 2-4)] patients, p<0.0001. By ROC analysis, patients MM at ≥4 epitopes were at risk of developing a DSA. DSA free survival was 87.1% and 66.1% in patients MM at ≤3 and ≥4 epitopes respectively, p<0.001. AMR risk was also increased in the ≥4 MM group but TG and allograft loss were not significantly different between the ≤3 and ≥4 groups as shown in the table below.

Results:

Event free survival [%]	TerEp MM ≤3	TerEp MM ≥4	p value
De novo DQ DSA	87.1	66.1	<0.0001
Allograft loss	84.4	89.9	0.22
Rejection	69.6	67.9	0.26
AMR	90.9	82.9	0.041
TG	95.4	89.5	0.16

Conclusion: This study demonstrates that DQ epitope mismatching may predict the development of de novo DQ DSA and AMR in patients who have an equivalent mismatch by low resolution typing.

O060

Measuring affinity of polyclonal HLA-specific antibodies in highly sensitised cases can serve as an additional biomarker to guide direct transplantation

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Introduction: Significant numbers of patients on transplant waiting lists in the UK are sensitised (43%). Direct transplantation across these HLA-specific antibodies using risk stratification strategies is increasingly being used. However current solid phase assays cannot fully predict graft outcomes following transplantation. We have validated a biosensor platform that allows observation of real time binding of human mAbs and polyclonal IgG on HLA proteins.

Method: Serum samples from 32 highly sensitised cases were processed to enrich IgG and HLA-specificities were confirmed using Luminex single antigen beads. Binding experiments were performed against a range of HLA proteins corresponding to sample anti-HLA specificities. Binding kinetics were calculated using modified Langmuir mathematical models.

Results: 23/32 cases gave a detectable binding response. In nine cases showing no binding, the highest MFI was below 2500 in 8/9 cases. In 23 positive cases, the binding was observed against 38 HLA specificities studied. The binding kinetics and dissociation constant varied between cases. Dissociation constants (K_D) ranged between 10^{-5} to 10^{-11} M.

Discussions: This is the first description of affinity measurements in a clinical transplantation cohort using a real-time biosensor platform. Binding kinetics can be measured in clinical cases using surface plasmon resonance following a manageable antibody processing protocol. The observed dissociation constants had a wide range representing low (10^5 to 10^7 M), moderate (10^7 to 10^9 M) and high ($>10^9$ M) levels of affinity. HLA-specific antibodies of varying specificity and affinity were present in sera of highly sensitised cases. These data could potentially guide stratification in to three groups based on novel affinity parameters that may predict risk of antibody-mediated organ damage post-transplantation. Larger clinical studies are required to validate this hypothesis and approach.

O061

Histology and not donor specific antibody helps predict 5-year kidney transplant failure using 1 year post-transplant data

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Introduction: Using a multi-centre validation study, using RISK score (using recipient age, sex, and race; acute rejection; transplant function; serum albumin level and proteinuria) inform clinicians of at-risk transplant patients. The objective of this study was to validate these data in a different cohort and assess if protocol biopsy data and anti-donor HLA antibody improved this model to predict 5-year failure from 12month data.

Method: Using published methodology, negative crossmatch transplant recipients (n=2159) were assessed for death-censored and overall transplant failure 5 years post-transplantation. The resulting risk scores were evaluated for prognostic utility (discrimination, calibration, and risk reclassification). Weighted regression coefficients for baseline and 12-month demographic and clinical predictor characteristics were used.

Results: Multivariate analysis identified glomerulitis and interstitial fibrosis and only Class II DSA as associated with graft failure ('g' HR=2.5, 'ci' HR=1.66, DSA Class II MFI>800 HR= 4.34, p<0.001). Using histology (g and ci scores) improved discrimination for death censored transplant failure (excellent C statistics, 0.90 cf 0.84 without histology) whereas Class II DSA showed no improvement (C-statistic 0.83) Both scores demonstrated good calibration (Hosmer-Lemeshow P< 0.05 in with both histology and DSA variables). Compared with standard RISK scores, application of the histology resulted in statistically significant and clinically relevant risk reclassification for death-censored transplant failure (net reclassification improvement [NRI], 29.0%, p< 0.001), but using 1 year DSA Class II data NRI, 1.2%, p=0.90)

Conclusions: These validated risk scores may be of prognostic utility in kidney transplantation, accurately identifying at-risk transplants, and the addition of 1 year protocol biopsy data improves the assessment of risk – improving the classification in 30% of patients into high or low risk populations. The addition of DSA data did not improve this model.

O062

Differences in reactivity of HLA-specific antibodies may be explained by differences in their affinities for selected epitopes on HLA proteins

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Introduction: Affinity of IgG immunoglobulins for antigen varies and matures within the evolution of immune responses. Affinity is likely to be different for different epitope-antibody interactions and it also has been hypothesised that it could be different for the same epitope on different HLA antigens. We have utilised a biosensor platform to study the binding kinetics of HLA-specific antibodies.

Methods: Biotinylated HLA proteins were immobilised on sensor chips and binding kinetics were studied using the XPR ProteOn (BioRad) surface plasmon resonance instrument. The mouse monoclonal antibody W6/32 and five human monoclonal HLA-specific antibodies were studied. Binding kinetics were compared between sensitizing antigen and other cross-reactive antigens sharing epitopes for human monoclonal antibodies. The bivalent analyte mathematical model was used to calculate interaction kinetics. We compared relative MFI values derived from Luminex assay and calculated affinities for the same concentration of the panel of monoclonal HLA-specific antibodies.

Results: Calculated antibody affinities were different for different HLA antigens despite the presence of the same epitopes. Dissociation constants (K_D) values were between 10^{-8} to 10^{-10} M for the human monoclonal HLA-specific antibodies. In every case, higher affinity and slower dissociation rates were observed with the original sensitizing antigen compared to the same epitope(s) on other HLA antigens. The difference between the calculated dissociation constants ranged from two- to ten-fold. Luminex MFI values for the same concentration of each monoclonal antibody on different HLA specificities differed, the rank order being similar to the affinities.

Discussions: Kinetic analysis of antibody binding to HLA antigens in real time using multi-channel surface plasmon resonance has been carried out successfully and allows for the study of additional parameters such as association and dissociation rates that are not measurable in current solid phase platforms such as Luminex.

O063

HLA matching and cornea transplantation outcome in the Netherlands

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Introduction: In the Netherlands, some patients need a corneal graft which is HLA-A, -B and -DR matched on broad level. Clinical criteria for matching include prior transplantations and deep stromal vascularisation. We questioned which HLA mismatches affect cornea transplant outcome.

Methods: We evaluated 490 HLA matched cornea transplants performed in 2000-2013 and registered by the Dutch Organ Transplantation Registration. We analyzed the impact of HLA matching and other variables possibly influencing the immune response on 5 year graft survival. We used univariate and backward selection multivariate Cox regression analyses.

Results: Univariate analysis on five year graft survival, shows that the sum of HLA-A and -B mismatches (Hazard Ratio (HR): 1.681 ; $p = 0.007$), transplant sequence of that eye (HR = 2.162; $p = 0.001$), and pre-transplant deep stromal vascularisation (HR = 1.340; $p < 0.001$) are associated with graft failure. Of the primary diagnoses for transplantation, prior graft failure (HR = 2.649; $p = 0.003$), and trauma (HR = 5.844; $p < 0.001$) are associated with worse graft survival. Recipient and donor age, HLA-DR mismatches, and the sum of HLA-A, -B and -DR mismatches appear not to affect graft survival ($P > 0.05$). In multivariate analysis, including all variables mentioned above, HLA-A and -B mismatches (HR = 1.981; $p = 0.001$), transplant sequence (HR = 1.919; $p = 0.002$), pre-transplant deep stromal vascularisation (HR = 1.330; $p = 0.003$), and trauma as cause of corneal dysfunction (HR = 3.952; $p = 0.006$) remain significant risk factors.

Discussion: HLA-A and -B matching appears to have more influence on cornea transplant outcome than HLA-DR matching. Matching for only HLA-A and -B should increase the chance on receiving a graft for these patients.

O064

Transfer of HLA-specific allosensitisation from a highly sensitised organ donor to both kidney recipients

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Introduction: The presence of donor passenger lymphocytes in transplanted organs has been associated with the transfer of donor immune responses to the recipient and can clinically manifest as graft-versus-host disease, haemolytic anaemia, severe idiopathic thrombocytopenia, vitiligo and peanut allergy. We report for the first time the transfer of donor HLA class I and class II specific allosensitisation in two recipients following deceased donor kidney transplantation from a highly HLA-allosensitised donor.

Methods and results: Kidney transplantation was undertaken from a single donation after circulatory death (DCD) donor in two non-transfused males receiving their first transplant with no detectable HLA antibodies. Both patients experienced ATN associated delayed graft function and on day seven clinically indicated HLA-specific antibody screening was undertaken. Surprisingly, high level de novo IgG HLA class I and class II specific antibodies were detected in both recipients, with largely overlapping antibody profile ($P < 0.00001$), that differed only by the absence of reactivity against the respective recipient self HLA; there were no antibodies to donor HLA. The unusual rapid kinetics of antibody development in immunosuppressed non-sensitised recipients and the absence of donor HLA-specific antibody (DSA) prompted testing of stored kidney donor serum that revealed high level HLA-specific antibodies with almost identical specificity profile to that seen in both recipients ($P < 0.001$ and $P = 0.006$ respectively), but differed by the presence of strong recipient specific HLA-class I and class II antibodies (RSA). Antibodies persisted beyond two months, but with slowly declining antibody levels.

Discussion: We attribute the post-transplant de novo HLA-specific alloantibodies to the transfer of donor alloreactive passenger B-cells/plasma cells present within the transplanted kidney and the systemic absorption of RSA, thereby leaving circulating third party HLA-specific antibodies.

Friday 13th March
Tregonwell Auditorium – 10:00
Organ Allocation
Chairs: Mr Gabriel Oniscu and Dr Michiel Erasmus

O065

National paired donation programmes in the UK and the Netherlands: which is most effective?

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Background: National kidney paired donation (KPD) programmes have been established in The Netherlands for 10 years and the UK for 7 years. While more recent, the UK scheme serves a population almost four times as great (64m cf 17). This study compares the relative effectiveness of the schemes.

Methods: We analysed data for each quarterly matching run Jan 2010 - Dec 2013 (16 runs) from both programmes. Domino pairs were excluded.

Results:

2010-2013	UK	NL
Mean pool size (per million pop)	179 (2.8 pmp)	52 (3.1 pmp)
% new pairs in each run	22%	29%
No. matches identified	299	108
Matches per average pool size	1.7	2.1
No. transplants (% of matches)	185 (64%)	80 (74%)
Transplants per year pmp	0.8 pmp	1.2 pmp

The UK pool for each run is over 3 times greater than in the Netherlands, but both represent approx. 3 patients pmp. This has led to a higher number of matches and transplants in the UK, despite a lower proceeding transplant rate (64% cf 74%). The programme in the Netherlands is more efficient with a higher transplant rate per average pool size. Highly sensitised patients (95-100% PRA) are a problem in the UK (50% of the pool cf 18%). Also, in the Netherlands a second run identifies further transplants if a match cannot proceed within two months of the run.

Conclusion: KPD in the UK yields numerically more transplants because of the larger pool of patients registering. The programme in the Netherlands is more efficient at achieving transplants for registered pairs and yields 1.2 transplants pmp compared with 0.8 in the UK. In the UK consideration is being given to extending the identification of antibody incompatible transplants in the programme to help highly sensitised patients and to moving to six matching runs per year instead of four.

O066

Costs of liver transplantation with extended criteria donor grafts: a prospective cost-analysis study

Rianne van Rijn¹, Christian S. van der Hilst¹, Herold J. Metselaar², Bart van Hoek³, Jan T. Bottema¹, Maarten J.H. Slooff¹, Robert J. Porte¹

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Background: The shortage of available donor livers causes the transplant community to push its limits for criteria for donor selection allowing more suboptimal or compromised grafts to be used. These donors are termed 'extended criteria donors (ECD) and it is unknown to which extent livers from high risk donor are associated with higher costs. Aim of this study was to assess the costs and outcome of liver transplantation with liver grafts from donation after brain death (DBD) donors with different quality.

Methods: A prospective observational national, multicenter study was performed including all DBD liver transplantations followed during the first year after transplantation. Patients were divided in four groups based on graft quality determined by the donor risk index (DRI). Primary outcome parameter was cumulative 1-year cost. Secondary outcome parameters were patient and graft survival, patient level costs for transplantation, ICU and hospital stay, clinical and out-patient complications.

Results: A total of 268 adult patients undergoing primary DBD liver transplantation were included between 2004 and 2009, excluding 66 patients listed as high urgency, 40 split or reduced liver grafts, and 7 patients with missing data. Median DRI of the four groups was 1.01 (interquartile range [IQR] 0.94-1.12), 1.30 (IQR 1.25-1.35), 1.48 (IQR 1.44-1.53), and 1.75 (IQR 1.66-1.86). Cumulative 1-year costs were similar with a median of € 68,695 (IQR 49,166-90,915), € 65,301 (IQR 54,567-91,673), € 63,701 (IQR 52,117-89,783), and € 64,822 (54,041-93,756) in groups of increasing DRI ($p = 0.91$). One-year graft and patient survival rates were equivalent between groups of increasing DRI (82%, 79%, 85%, and 84% [$p=0.83$] and 85%, 88%, 90%, 88% [$p=0.58$] respectively). The costs for transplantation, ICU and hospital stay, clinical and out-patient complications were similar between the four groups.

Discussion: This prospective observational study based on a large population demonstrates that patient and graft survival is not affected by the quality of DBD liver graft. Moreover, the costs of liver transplantations in both clinical and out-patient setting are not affected by the quality of the graft.

O067

The impact of duration of brain death on outcomes in abdominal organ transplantation: rush and retrieve or rather relax and repair?

Catherine Boffa¹, Elinor Curnow², Kate Martin², Rachel Johnson², Rutger Ploeg¹

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Background: Brain death (BD) induces a progressive systemic pro-inflammatory and coagulatory response affecting function of the grafts-to-be and survival. With longer BD duration more injury in donor organs becomes evident, but also up-regulation of defence mechanisms occurs initiating repair. This creates the dilemma whether to retrieve organs asap after consent to minimise the effects of hostile environment or optimise in-situ enhancing repair? Limited data are available with regards to this issue, and uncertainty increases, with the higher risk donors, when deciding which organ to accept or not for transplantation. We assessed the effect of BD duration on outcomes after kidney, liver and pancreas transplantation in the UK.

Methods: In a retrospective analysis, UK DBD donors during 2008-2012 were evaluated. Cox regression was used to investigate the relationship between BD duration and graft survival (GS) at 90d, 1 and 3y.

Results: Kidneys from 1881 donors used in adult-to-adult first kidney-only transplants were analysed. Median BD duration was 33h (IQR 25-48) in 2008 increasing to 36h (IQR 27-51) in 2012 (p=0.03). Longer BD did not have a detrimental effect on GS, in fact, prolonged BD duration led to increased GS following first kidney-only transplantation. Risk-adjusted Cox regression analyses of GS at 90d, 1 and 3y after kidney transplant suggest a significant interaction between BD duration and CIT (p=0.06, 0.02, 0.09 respectively). When CIT is 18-24h there is significant evidence that chance of graft failure decreases for every hourly increase in BD duration. There was a significant interaction between BD duration and year of donation (p=0.01, <0.005, 0.04, respectively) at 90d, 1 and 3y post pancreas transplant, but no association with GS for liver (p>0.6 in each case).

Discussion: Our study demonstrates that prolonged BD is not detrimental to outcomes in abdominal organ transplantation and actually beneficial to GS. This finding supports that time is required to adequately optimise organ donors and suggests a window of opportunity for in-situ organ conditioning with targeted intervention. This analysis renounces the need for a 'Rush and Retrieve' policy.

O068

Longer duration of donor brain death does not harm transplantation outcome of abdominal organs

Willemijn Nijboer, Jan IJzermans, Jeroen De Jonge

Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands

Introduction: Donor brain death is a known risk factor for organ quality in transplantation. However, little is known about the influence of brain death duration. As a result, organ procurement is often rushed and transplantation procedures scheduled outside office hours. This increases chances of fatigue and mistakes in the procuring and transplanting teams. Earlier, slightly better kidney transplantation results were reported after longer brain death duration using data from the US Organ Procurement and Transplantation Network (OPTN). However, US donor characteristics differ from European donors, therefore for this analysis we included data from both OPTN and Eurotransplant (ET).

Methods: Databases from both OPTN (2006-2012) and Eurotransplant (2002-2012) were used. We included all transplanted abdominal organs where brain death duration was available. Brain death duration was divided in 12h cohorts (up to 12h, 12-24h etc) and compared. Graft and patient survival were studied using Kaplan Meier curves and multivariate analyses were performed using Cox regression.

Results: Average donor brain death duration was 10h (liver), 12h (kidney) to 20h (pancreas) longer in the OPTN cohort compared with the ET cohort, without a negative effect on graft and patient survival. For kidney transplantation, duration of brain death did not influence outcome in the ET cohort. For liver transplantation, survival was better after longer brain death duration in the OPTN cohort (KM graft survival $P=0.007$ and patient survival $P=0.016$); in the ET cohort the same trend was not statistically significant. In multivariate analysis, brain death duration was not an independent risk factor. For pancreas transplantation, duration of brain death did not influence outcome in both OPTN and ET cohorts.

Discussion: A prolonged duration of brain death does not negatively affect graft and recipient survival after abdominal organ transplantation. Although heart and lung transplant results are not yet included, we feel that procurement procedures for abdominal organs may be safely scheduled at daytime.

O069

Integrating desensitisation with the National Living Donor Kidney Sharing Scheme

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Introduction: The National Living Donor Kidney Sharing Scheme (NLDKSS) has increased the opportunity for HLA sensitised recipients to receive a compatible transplant. However, for those with a cRF > 95%, the chance of finding a match is low.

Methods: The unacceptable HLA antigen profile of 5 sensitised patients entered in the NLDKSS was modified to remove non-cytotoxic antibodies with a luminex MFI <5000. This profile was used in anticipation of achieving a cytotoxic negative, flow cytometry positive cross match that would be amenable to desensitisation by antibody removal. The desensitisation regimen comprised Rituximab 4 weeks prior to transplantation, double filtration plasmapheresis (DFPP), induction with Alemtuzumab and triple oral immunosuppression.

Results: Potential matches leading to transplantation were identified for all 5 recipients in runs 1 (n=1), 2 (n=3) and 3 (n=1). Four recipients had positive cytotoxic cross matches with their original donors. Cross matches with NLDKSS donors were all cytotoxic negative, four were flow cytometry positive. Median cRF prior to de-listing antibodies was 99% (range 72 – 100%), and after delisting 87% (range 64 – 96%). All grafts functioned immediately. Two recipients received DFPP post-transplant in response to a rise in donor specific antibodies. The recipients are now 5 – 29 months post transplant. One patient had two episodes of borderline cellular rejection and none had antibody mediated rejection. The mean eGFR at last follow up was 69±17 ml/minute, and no recipients have proteinuria.

Discussion: Transplantation of selected highly sensitised recipients can be facilitated using a combination of desensitisation and the NLDKSS.

Friday 13th March
Purbeck Lounge – 10:00
Clinical Outcomes
Chairs: Dr Erik Verschuren and Prof Michael Nicholson

O070

Acute kidney injury and outcome after cardiac transplantation

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Background: Chronic kidney disease (CKD) is a frequently seen complication after cardiac transplantation and is partly explained by the prolonged use of calcineurin inhibitors. However, few data are present on the consequences of acute kidney injury (AKI) in the post-operative period. In the present study, incidence and impact of AKI on mortality and renal function was studied.

Methods: We conducted a retrospective cohort study evaluating all cardiac transplant recipients ≥ 18 years, between 1984-2012. The primary outcome was the incidence of AKI in the post-operative period. Secondary outcome parameters were renal function and overall survival at 1 year after transplantation. AKI and its severity was defined by de Kidney Disease Improving Global Outcome (KDIGO) criteria.

Results: The study population included 531 patients; median age was 51 years and 78% of male gender. Median estimated glomerular filtration rate (GFR) at baseline was 60 ml/min/1.73m². 405(76%) met the AKI criteria. 211(40%) had AKI stage 1, 119(22%) stage 2 and 75(14%) stage 3. 25 patients (5%) required renal replacement therapy (RRT) after transplantation and at hospital discharge 3 (0.5%) patients were chronic dependent on dialysis. Independent risk factors for AKI and increase in AKI stage: body-mass index (BMI), postoperative right ventricle (RV) failure and renal function at baseline. In contrast, a higher age and the postoperative use of induction therapy were associated with better outcome. One-year overall survival was 88% and 1-year renal survival censored for death was 99%. Survival rates in patients without AKI, stage 1, 2 and 3 were 95%, 92%, 88% and 85%, respectively (log-rank test $p=0.065$). In patients that required RRT 1-year survival was 72% (log-rank test $p=0.001$). Independent risk factors for mortality: age, postoperative overall graft failure and time on mechanical ventilation. A trend was observed for the association between AKI requiring RRT and 1-year mortality. After 1 year, 8 (2%) patients had CKD0-1 (eGFR >90), 94(20%) CKD-2 (eGFR:61-90), 323(69%) CKD-3 (eGFR:31-60), 42(9%) CKD-4 (eGFR:16-30) and 4(1%) CKD-5 (eGFR ≤ 15). Median eGFR at 1 year in patients without AKI, stage 1, 2 or 3 were 50, 45, 46 and 44, respectively. Independent risk factors for a lower eGFR 1 year after transplantation: age, BMI, AKI stage, preoperative use of ECMO and renal function at baseline. In contrast male gender and a longer time on mechanical ventilation were associated with better outcome.

Discussion: AKI is highly frequent after cardiac transplantation and a significant determinant of higher mortality and lower renal function 1 year after transplantation. Renal function during the perioperative phase should be monitored intensively and protected as much as possible to avoid future adverse effects.

O071

Ex-vivo lung perfusion reduces graft immunogenicity via mitochondrial salvage and induction of anti-apoptosis

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Introduction: Inflammation in the early post-operative period following lung transplantation has well reported negative consequences on clinical outcome. Reducing inflammation and graft immunogenicity via ex-vivo lung perfusion could be of therapeutic benefit.

Methods: 12 female recipient pigs were randomised to receive either i) a left male lung following 2 hours of EVLP or ii) a left male lung retrieved using standard protocols. To examine changes within the donor lung we profiled 29 phosphokinases and 35 apoptosis related molecules. We then quantified circulating mitochondrial, donor and recipient DNA as a marker of cell death.

Results: A global profile of mitochondrial salvage and cell survival was observed in the EVLP lung compared to standard transplantation. This included upregulated AMPKa and EGFR pathways with increases in associated downstream pro-survival signaling molecules ERK1/2, FAK and Akt. Src kinase family members including Src, Hck, Fgr and Lck, were markedly increased in EVLP relative to standard lung transplantation. An upregulation of the anti-apoptotic proteins BCL-2, HSP-70, LIVIN and PON2 with downregulation of the apoptosis inducing mitochondrial associated molecules clusterin, cytochrome C and HTRA2/Omi also occurred within EVLP treated lung tissue. Importantly there was no detectable change in cleaved caspase 3, despite the increase in pro-caspase-3 expression. Pigs receiving EVLP treated lungs had a significantly lower concentration of circulating mtDNA ($p=0.008$) in the early post-operative period (immediately following completion of the transplant procedure) than those in the standard cohort. Genomic DNA did not differ between groups in the 24 hour period ($p=0.483$).

Conclusions: EVLP alters the inflammatory signaling profile of the donor lung prior to transplantation. This includes a relative downregulation in mitochondrial cell death molecules, upregulation of mitochondrial salvage and a global anti-apoptotic signature.

O072

The role of the incretin effect after pancreas transplantation

Shruti Mittal^{1,3}, Rachel Franklin^{2,5}, Agata Juszczak^{2,4}, Filip Knop⁶, Edward Sharples^{1,4}, Jens Holst⁶, Peter Friend^{1,3}, Stephen Gough^{2,4}

¹Oxford Transplant Centre, Oxford, UK, ²Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, UK, ³Nuffield Department of Surgical Sciences, Oxford, UK, ⁴Radcliffe Department of Medicine, Oxford, UK, ⁵Biomedical Research Centre, Oxford, UK, ⁶University of Copenhagen, Copenhagen, Denmark

Introduction: The ability to generate a greater insulin response to an oral compared to an intravenous glucose load is the result of pancreatic stimulation by gut hormones and is known as the incretin effect (IE). A diminished IE is seen in diabetes and is associated with abnormal glucose tolerance (GT). We have recently reported that 30% of pancreas transplant subjects have abnormal glucose tolerance post-operatively, despite insulin independence and that this is associated with later graft failure. The incretin effect is thought to be mediated via a neuroendocrine axis and the role of the incretin effect in people receiving a denervated pancreas transplant is unknown. This study aimed to assess the incretin effect after pancreas transplantation

Method: The incretin effect was measured with extended frequently-sampled oral glucose tolerance tests and matched isoglycaemic intravenous glucose infusions in 10 pancreas transplant recipients and 10 kidney transplant recipients at 2 weeks and 3 months post-transplant, and in 10 healthy controls.

Results: The groups were comparable for demographics. Isoglycaemia was achieved in each group. The pancreas transplant group at 2 weeks post-transplant showed lower glucose disposal compared to the kidney only transplant group and healthy controls (26.2% vs 42% vs 56.4%), with a significantly diminished incretin effect (7.5% vs 36.9% vs 46.5%, $p < 0.01$) respectively. However, by 3 months, glucose disposal and the incretin effect had improved (26.2%-51.4% and 7.5%-27.4% respectively).

Conclusion: The present data suggest, for the first time, that pancreas transplantation may also be associated with a delay in establishing a full incretin effect. Whilst we cannot attribute a causal role, improvement at 3 months may represent re-innervation and future studies including an incretin therapy intervention trial are needed to determine whether incretin based therapies can improve long term pancreas transplant outcomes.

O073

Socioeconomic deprivation is a strong independent factor for pancreas graft survival in England

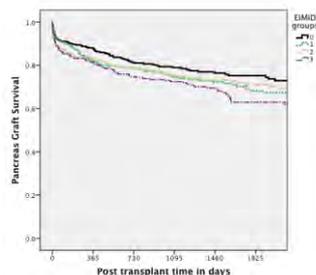
Argiris Asderakis¹, Usman Khalid¹, Susanna Madden²

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Introduction: Socioeconomic deprivation is associated with higher prevalence of chronic diseases including diabetes and renal failure, with poorer outcomes. By using the Welsh Index of Multiple Deprivation we have not demonstrated differences in outcomes following pancreas transplantation in Wales in relation to socioeconomic deprivation. Therefore we set to study the influence of deprivation on outcomes following pancreas transplantation in a larger scale.

Methods: We included all English pancreas recipients transplanted between 1 December 2004 and 31 December 2012. We used the English Index of Multiple Indices of Deprivation (EIMID) to assess the influence of socio-economic deprivation on patient and pancreas graft survival. Higher scores mean higher overall deprivation status.

Results: 1270 patients were analysed. The EIMID was the same in patients who received SPK (18.8) compared to patients who received PAK (17.7) or PTA (18.1). The Pancreas graft survival is dependent on the donor age ($p=0.08$), CIT ($p=0.0001$), the type of Pancreas graft (SPK vs. PAK or PTA, $p=0.0001$), and the social deprivation as expressed by the EIMID ($p=0.016$).



When patients were separated to quartiles according to their EIMID score the 3 years pancreas survival in the 25% most deprived was 72% compared to 79% among the 25% coming from the least deprived areas. The difference was mainly evident in the SPK group. EIMID was strongly correlated with patient survival too.

Conclusion: Social deprivation, as expressed by the EIMID is an independent factor of pancreas graft and patient survival. Given most PAKs followed a living donor kidney; a previous LD kidney was not more common in less deprived patients. Targeted approaches to more deprived population might reduce the significant penalty of graft survival seen in patients from the most deprived areas.

O074

The role of the pre-autoantibodies in predicting pancreas graft outcome

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Introduction: Anti-islet cell and anti-glutamic acid decarboxylase (GAD) autoantibodies are associated with beta-cell destruction and are known to emerge prior to the development of diabetes. Autoantibodies usually decrease following diabetes development but may persist in some individuals. The aim of this study was to examine the significance of autoantibody positivity in the context of pancreas transplantation.

Method: Pretransplant anti-islet cell and anti-GAD autoantibody results and graft outcomes were retrieved for all pancreas transplants performed at a single centre from 2002- 2011. Graft failure was defined as a return to exogenous insulin. Kaplan Meier analysis was performed to assess associations between autoantibody positivity and graft outcomes.

Results: 485 pancreas transplant recipients were included (364 SPK, 113 isolated pancreas (IP) transplants, 8 retransplants). Pretransplant anti-GAD autoantibody titres were available for 395/485 (81.4%) and were positive in 124/395 (31.4%). Anti-islet autoantibody titres were available for 394/485 (81.2%) and were positive in 24/394 (6.1%). Anti-GAD autoantibody positivity was not associated with graft survival in Kaplan-Meier analyses in either the SPK (p=0.65) or IP group (p=0.54). Anti-islet autoantibody positivity was not associated with graft survival in the SPK group (p=0.59). In the IP group lower graft survival was observed at 1, 3 and 5 years post-transplant in those with anti-islet antibody positivity (66.7%, 44.4% and 29.6% vs 80%, 72.3% and 59.9%) but this did not reach statistical significance (p=0.06).

Conclusion: The presence of pretransplant anti-GAD and anti-islet autoantibodies do not appear to be significant in relation to pancreas graft survival in SPK transplantation. However, a small proportion of IP recipients display anti-islet positivity pre-transplant and may be at higher risk of graft loss. These recipients may benefit from targeted immunosuppression therapies.

Friday 13th March
Tregonwell Seminar Suite – 10:00
Immunosuppression
Chairs: Dr Hanneke de Kort and Dr Richard Borrow

O075

Effect of inpatient variability and mean tacrolimus levels in renal transplant patients

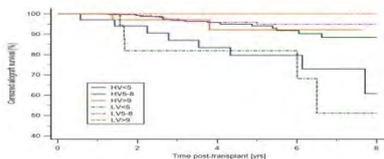
Dawn Goodall, Michelle Willicombe, Adam Mclean, David Taube

Imperial College Renal and Transplant Centre, London, UK

Introduction: Nonadherence to immunosuppressive (IS) medication and adherence to IS protocols is a potent risk factor for rejection and graft loss which can be patient and/or physician led. We have previously shown that inpatient variability (IPV) of tacrolimus (FK) levels can predict rejection and graft loss. In this study, we link IPV with the maintenance of sub, therapeutic and suprathreshold FK levels.

Method: We retrospectively analysed 668 patients who received a kidney transplant between 11/2005 and 09/2013. All patients received alemtuzumab induction and FK monotherapy with a steroid sparing protocol; target FK level 5-8ng/ml. Coefficient of variance (COV) was defined as SD/mean of all outpatient FK levels taken between 6-12 months post-transplant. High variability (HV) was defined as a COV>median of the overall cohort and low variability (LV) was defined as a COV≤median of the overall cohort.

Results: 5983 FK levels were included in the analysis. The mean number of samples analysed per patient was 8.96 ± 3.78 . The median COV of FK levels was 18.15%. Graft survival was 51.2% and 94.9% in the LV<5ng/ml and LV 5-8ng/ml group respectively $p<0.0001$. AMR free survival was 80% and 97.5% in the LV<5ng/ml and LV 5-8ng/ml group respectively $p<0.0001$. TG free survival was 74.8% and 98% in the LV<5ng/ml and LV 5-8ng/ml group respectively $p<0.0001$.



Conclusion: This study shows that patients maintained on an FK monotherapy regimen are most at risk of developing AMR, TG and graft loss if their FK levels are <5ng/ml, especially if the FK COV is low. Raising the FK dose to maintain levels between 5-8ng/ml is very important unless there are good mitigating clinical reasons.

O076

Inpatient variability (IPV) of tacrolimus levels and outpatient non-attendance rates predict poor renal allograft survival

Dawn Goodall, Michelle Willicombe, Adam McLean, David Taube

Imperial College Renal and Transplant Centre, London, UK

Introduction: Nonadherence to immunosuppressive medication post-renal transplant is an important risk factor for rejection and graft loss. In this study we assess the association between IPV of tacrolimus [FK] levels and the patient's rate of outpatient [OP] clinic non-attendance and the impact on renal allograft outcomes.

Method: We retrospectively analysed 668 patients who received a kidney transplant between 11/2005 and 09/2013. All patients received alemtuzumab induction and FK monotherapy with a steroid sparing protocol with a target FK level of 5-8ng/ml. Coefficient of variance (COV) was defined as SD/mean of all OP FK levels taken 6-12 months post-transplant. High variability (HV) was defined as a COV>median of the overall cohort and low variability (LV) was defined as a COV ≤ median.

Results: 5983 FK levels were included in the analysis. The mean number of samples analysed per patient was 8.96 ± 3.78 (range 2-23). The median COV of FK levels was 18.15%. Patients with a HV of FK levels were significantly more likely not to attend their OP appointments; the median number of non-attendances was 4 (range 0-22) in the HV group and 2 (range 0-17) in the LV group (p<0.0001). Patients who developed rejection, a DSA or lost their graft had a significantly higher number of OP non-attendances than those patients who did not develop rejection, a DSA or lose their graft.

DNAs and cancellations	Graft Loss	No Graft Loss	Rejection	No rejection	DSA	No DSA
Range	0-13	0-22	0-17	0-22	0-17	0-22
Median	5	3	4	3	4	3
P value	0.0004		0.0001		0.0138	

Conclusion: This study shows that patients with a HV of FK levels are more likely not to attend OP clinic appointments and a high nonattendance is associated with a significantly increased risk of development of DSA, rejection and graft loss. This analysis supports the need for a prospective study to assess strategies which minimise nonadherence and reduce the risk of development of rejection and graft loss.

O077

Post transplant focal segmental glomerulosclerosis: successful management with plasma exchange and rituximab

Konstantinos Koutroutsos¹, Rawya Charif¹, Candice Roufousse², Georgios Spanos¹, Jack Galliford¹, David Taube¹, Marina Loucaidou¹

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Background: Post-transplant Focal Segmental Glomerulosclerosis (FSGS) is associated with renal allograft loss. Currently, optimal treatment remains controversial. We propose a management protocol that includes treatment of recurrent or de novo FSGS with Plasma Exchange (PEX) and Rituximab (RTX).

Methods: This was a prospective study, aiming to examine the efficacy and safety of PEX and RTX in the management of post-transplant FSGS. All patients received a steroid sparing immunosuppressive regime with Alemtuzumab induction and tacrolimus monotherapy. Steroids and MMF were only introduced to treat rejection. The post transplant FSGS treatment protocol consisted of RTX (total of 2gr over 2 infusions, 2 weeks apart) and monthly cycles of 5 PEX over 7 days for 6 months. Partial remission was defined as 50% reduction of proteinuria, while complete remission as proteinuria <1g/day or uPCR<100. A post treatment biopsy was performed in 7 patients.

Results: We treated 10 transplant recipients (9 male, mean age 52,6 +/-10,7 years) with biopsy proven post-transplant FSGS. 7/10 patients had late (> 3 months) and 3/10 early (< 3 months) post-transplant FSGS. The mean time to diagnosis post transplant was 7.6 (1.3 – 34.6) months. On histology, 2 patients' biopsies showed collapsing, 3 tip lesion and 5 NOS variants of FSGS. All patients received treatment with 2gr of RTX in total and remained B-cell deplete for 6.6+/-3.4 months. 9 patients completed 6 cycles of PEX as intended, while 1 patient had only one cycle of PEX, as he did not tolerate further treatment. Mean follow up after FSGS diagnosis was 16.7+7.2 months. 8 out of 10 patients achieved remission upon completion of PEX (5 complete and 3 partial). During the follow up period, one patient relapsed, and ended up requiring dialysis and one patient died from unrelated complications, at 11 and 16 months post diagnosis, respectively. There was a significant reduction in mean uPCR between diagnosis (281.2+/-149 mg/mmol) and last follow up (44.8+/-40 mg/mmol) in the patients with complete remission (p=0.02). There was no significant decline in eGFR in the 7 relapse-free responders at the end of follow up (53.3+/-6.8 from 54.7+/-16.3ml/min) (p=0.1).

Conclusion: Post-transplant FSGS treatment with RTX and PEX appears to be safe, well tolerated and achieves an increased rate of remission. Further studies are needed to determine to define the optimal timing, dose, and duration of treatment.

Plasma 4 β -hydroxycholesterol measurement as a potential biomarker for CYP3A5 activity in informing tacrolimus dosing

Toqa Elnahas^{1,2}, Evert de Jonge⁴, Terry Lee², Bertrand van Zelst⁴, Joyce Popoola³, Rajeshwar Ramkhelawon³, Ron van Schaik⁴, Atholl Johnston^{1,2}, Iain MacPhee³

¹Clinical Pharmacology, William Harvey Research Institute, Barts and the London, Queen Mary University of London, London, UK, ²Analytical Services International, St. George's, University of London, London, UK, ³Institute of Medical and Biomedical Education-Renal Medicine, St. George's, University of London, London, UK, ⁴Department of Clinical Chemistry, Erasmus MC Rotterdam, Rotterdam, the Netherlands

Background: Recently, 4 β -hydroxycholesterol (4 β -OHC) has been shown to be an endogenous marker of P450 3A activity in clinical practice (Diczfalusy et al, 2011). 4 β -OHC concentration increases with the number of active CYP3A5*1 alleles.

Objectives: The aim of this study was to investigate the relationship between genetically determined variation in CYP3A expression in comparison to the phenotypic marker 4 β -OHC and tacrolimus pharmacokinetics in adult renal transplantation recipients.

Methods: Fifty nine patients aged between 21 to 76 years were included in this study. CYP3A5 genotype was determined using a Roche LightCycler®. Plasma 4 β -OHC and tacrolimus blood concentrations were measured by liquid chromatography/tandem mass spectrometry. To correct 4 β -hydroxycholesterol concentrations, total cholesterol was measured on Roche Modular P800 analyser. The data were analysed using analysis of variance (ANOVA). Correlation between variables was analysed by Pearson's product-moment correlation coefficient.

Results: The mean 4 β -OHC/C for CYP3A5*1/*1 (n=12), *1/*3 (n=16) and *3/*3 (n=31) genotypes were 7.64 ± 2.3 , 7.09 ± 4.1 and 5.03 ± 2.0 , respectively ($P < 0.01$). The mean plasma concentrations of 4 β -OHC in White, Asian and Black patients were 22.7 ± 1.4 , 21.5 ± 2.6 and 36.9 ± 6.2 ng/ml, respectively. Black subjects had significantly higher 4 β -OHC concentrations in comparison to Whites ($P = 0.001$) and Asian ($P = 0.011$) and there was no significant difference between White and Asian subjects. The association with CYP3A5 genotype was preserved after exclusion of Black subjects. A significant correlation was observed between 4 β -OHC/C and tacrolimus normalized C_{max} ($r = -0.29$, $p = 0.025$), normalized AUC_{0-24} ($r = -0.32$, $p = 0.014$), normalized C0 ($r = -0.29$, $p = 0.024$) and normalized dose ($r = 0.46$, $p > 0.001$).

Conclusion: Plasma concentration of 4 β -OHC was greater in CYP3A5 expressers. The 4 β -OHC/C ratio was significantly correlated with tacrolimus exposure and dose requirement. We concluded that 4 β -OHC/C ratio may be a useful biomarker for tacrolimus dosing in renal transplanted patients although it remains to be determined whether it would enhance predictions over CYP3A5 genotyping alone.

References: Diczfalusy, U., H. Nylén, P. Elander, and L. Bertilsson. "4 β -Hydroxycholesterol, an Endogenous Marker of CYP3A4/5 Activity in Humans." *Br J Clin Pharmacol* 71, no. 2 (Feb 2011): 183-9.

Influence of *CYP3A5* and *ABCB1* genotypes on pharmacokinetics of immediate and prolonged release tacrolimus preparations

Toqa El-Nahhas^{1,2}, Terry Lee², Michelle Moreton², Denise McKeown², Joyce Popoola³, Rajeshwar Ramkhelawon³, Atholl Johnston^{1,2}, Iain MacPhee³

¹Clinical Pharmacology, William Harvey Research Institute, Barts and the London, Queen Mary University of London, London, UK, ²Analytical Services International, St. George's, University of London, London, UK, ³Institute of Medical and Biomedical Education-Renal Medicine, St. George's, University of London, London, UK

Background: Tacrolimus is available in two formulations, immediate-release, (Prograf®) and prolonged -release formulation of tacrolimus (Advagraf®). Tacrolimus has a narrow therapeutic index with wide variation between- and within individuals. Tacrolimus is mainly metabolized in liver and intestinal mucosa by CYP3A4/5 and is transported by P-glycoprotein (P-gp). Expression of CYP3A decreases and expression of P-gp increases along the length of the gut.

Objective: The aim of this study was to determine whether the *CYP3A5**3 and *ABCB1* genotypes influence the pharmacokinetics of prolonged-release tacrolimus in the same way as is well established for the immediate release preparation, in stable renal transplant recipients.

Methods: A total of Sixty-four stable renal transplant recipients treated with twice daily tacrolimus (Prograf®) were switched to the same total daily dose of Advagraf® with 24 hour pharmacokinetic profiles before and two weeks after the change. Genotyping for *CYP3A5**3 and *ABCB1* was performed using a Roche LightCycler®. Patients were divided into 4 genotype categories based on expression of *CYP3A5* (*1/*1 or *1/*3), *CYP3A5* non-expressers (*3/*3), high expressers of P-gp (*ABCB1*; CC) or low expressers of P-gp (*ABCB1*; CT or TT). Pharmacokinetic data were analysed using analysis of variance (ANOVA).

Results: *ABCB1* polymorphisms contributed to significant changes in tacrolimus pharmacokinetic parameters and dose requirements only in *CYP3A5**1 allele carriers. Dose-adjusted pharmacokinetic parameters 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		n	Twice daily tacrolimus				Advagraf®			
<i>CYP3A5</i>	<i>ABCB1</i>		AUC ₀₋₂₄	C _{max}	CO	Dose	AUC ₀₋₂₄	C _{max}	CO	Dose
Expressers	High	12	179	17.2	5.2	9.2	166	14.1	4.7	9.3
Expressers	Low	18	254	22.0	8.5	7.0	261	20.8	8.0	6.9
Non-expressers	High	4	536	41.8	17.7	3.5	419	31.6	11.7	3.5
Non-expressers	Low	30	471	35.0	16.4	3.7	440	31.1	13.9	3.6

Conclusion: Pharmacogenetic dosing strategies based on these genotypes are likely to be equally applicable to prescribing the once daily tacrolimus formulation, Advagraf®, as to twice daily formulations.

Friday 13th March
Bayview 1 – 10:00
Ethics/Psychology
Chairs: Ms Anya Adair and Ms Emma Massey

O080

Priority organ allocation for renal transplantation based on clinical need: The role of an “urgent” kidney waiting list

Emma Aitken¹, Ann-Margaret Little², Colin Geddes¹, David Kingsmore¹, Enric Murio¹, John Asher¹, Vladyslav Shumeyko¹, Marc Clancy⁰

¹*Department of Renal Transplantation, Western Infirmary, Glasgow, UK,* ²*Department of Histocompatibility and Immunogenetics, Gartnavel General Hospital, Glasgow, UK*

Background: In the UK, most deceased donor kidneys are allocated to specific patients via the NHS-BT Organ Allocation Policy. This complex matching algorithm attempts to provide both optimal utilisation and equity of access by prioritising based on factors such as waiting time, HLA-match and age similarity. Unlike heart, lung and liver transplantation, however, the current system takes no consideration of clinical need. There are a small, but significant, number of patients with end-stage vascular access (ESVA), with high rates of death or removal from the list who cannot wait 3 or 4 years for their “turn” on the waiting list.

Methodology: DCD kidneys from donors >50 may be allocated via locally determined policy. At our centre we have established an “expedited” list of patients with ESVA (bilateral central vein occlusion, failed PD and mortality risk, deemed by the MDT, to be >50% at 1 year on dialysis). It has been regionally agreed that kidneys from DCD donors aged >50 years old will first be allocated to these patients if compatibility exists. We describe our 3 year results.

Results: 21 patients with ESVA were identified. 18 have been transplanted during the study period (9 via the “expedited” list, 6 via the national allocation policy, 3 live donors). The three patients with ESVA who have not been transplanted yet all have cRF ≥99%. Half of those who were transplanted had cRF >90%. Mean age and waiting time for “expedited” transplants (n=9) was comparable to the general transplant population (n=420) (46.3+/-10 vs 48.8+/-12.9 years; p=0.56 and 1305.4+/-925.5 days). 1-year patient and graft survival was 88.9%. 44.4% had DGF. Mean eGFR at 1 year was comparable to the general transplant cohort (62.0+/-13.4 vs 58.4+/-20.9ml/min/1.73m²; p=0.71). In all but one case, the patient who would have been allocated the kidney according to the national algorithm, was transplanted within the subsequent year.

Conclusions: Priority allocation of DCD kidneys to ESVA patients has proven effective with acceptable outcomes and minimal negative impact on the global transplant population.

O081

Integrating mental and physical healthcare in long-term kidney transplant patients

Sharon Frame¹, Anna Simpson², Faith Matcham², Joseph Taylor², Amy Carroll¹, David Goldsmith¹, Matthew Hotopf², Antonia Cronin^{1,2}

¹Guy's and St. Thomas' NHS Foundation Trust, London, UK, ²King's College, London, London, UK

Background: In the UK integrating physical and mental healthcare is a key national priority. IMPARTS (Integrating Mental and Physical healthcare in Research Training and Service) is a package developed to facilitate integration through the collection of patient reported data via tablets and offering guidance on referral pathways. An increased prevalence of psychological illness, in particular anxiety and depression, in long-term kidney transplant patients (LKT) has been documented and this has been associated with poor outcomes, such as graft failure. We embedded the IMPARTS package into our Annual Transplant Review Clinic (ATR) for LKT to help address this.

Methods: We screened 99% (n=299) of LKT attending our ATR between 1 July 2013 and 6 November 2014. Measures included: depression (Patient Health Questionnaire - PHQ-9), anxiety (Generalised Anxiety Disorder Assessment GAD-7), medication adherence, and functional impairment scores. Information was recorded on a tablet prior to clinical consultation and uploaded live to the Electronic Patient Record.

Results: The mean age of the LKT screened was 53.0 years. 36.8% of LKT screened were female. We identified probable Major Depressive Disorder in 4% (11/299) and probable Generalised Anxiety Disorder in 5% (16/299) of LKT screened. Patients with mood difficulties or significant worry were referred to the team clinical psychologist for further assessment and management. Medication Adherence data showed 39.2% forget to take medication; 8.2% intentionally do not take medication.

	N (%)
Mental health	
Probable Major Depressive Disorder (MDD) (/299)	11 (3.7)
Severe depression	2 (0.7)
Suicidal ideation	1 (0.3)
Suicidal ideation and severe depression	1 (0.3)
Probable Generalised Anxiety Disorder (GAD) (/299)	16 (5.4)
Severe anxiety	8 (2.7)
MDD OR GAD	22 (7.4)
MDD AND GAD	5 (1.7)
Adherence	
Forget to take medication (/291)	114 (39.2)
Do not take medication as instructed (/291)	24 (8.2)

Discussion: IMPARTS has been well established within our ATR. 99% of all LKT attending the clinic have been screened. This preliminary data has been used to focus consultations and provide detailed information for the clinical psychologist where appropriate. It has also identified areas for service development including the set up of an adherence clinic. Adherence is a well-known problem in this patient group, however these data will allow for referral into the clinic and provide specific intervention targets. Further analyses to identify associations between physical (e.g. Glomerular filtration rate and Haemoglobin) and mental health parameters are underway, the results of which we anticipate will, in time, inform targeted treatment and management to improve clinical outcomes.

O082

Predicting mental health after living kidney donation: the importance of the medical process of donors and recipients

Lotte Timmerman, Mirjam Laging, Reinier Timman, Willij Zuidema, Denise Beck, Jan IJzermans, Michiel Betjes, Jan van Busschbach, Willem Weimar, Emma Massey

Erasmus Medical Center, Rotterdam, the Netherlands

Introduction: A minority of living kidney donors have poor psychological outcomes after donation. There is mixed evidence as to the influence of the medical process on these outcomes. We examined whether the medical process experienced by donors and recipients influenced donors' mental health up to one year post-donation.

Methods: One-hundred forty-five donors completed validated questionnaires on wellbeing (Positive and Negative Affect Schedule, Mental Health Continuum Short Form) and psychological symptoms (Brief Symptom Inventory) a median of 2.4 months before donation, and 3 and 12 months after donation. Indicators of the medical process were severity of donor complications (none; light; severe) and number of recipient re-hospitalizations at 3 and 12 months after the operation. Multilevel regression analyses were used to examine whether these indicators were related to donors' mental health over time.

Results: More severe donor complications and more recipient re-hospitalizations were both related to a greater number of donors' psychological symptoms over time, e.g. depressive symptoms. However, indicators of the medical process were not related to donors' wellbeing, e.g. life satisfaction.

Discussion: Clinicians should be aware that donors who experience complications themselves and/or recipient re-hospitalizations are at greater risk for poorer psychological outcomes after donation and should evaluate their need for support. In such cases when needed, psychological support should be offered that focus on preventing psychological symptoms rather than on increasing wellbeing.

O083

Telephone advice by (neuro-) psychologists (TAP) is successful in increasing consent rate for organ and tissue donation: A Dutch study

Sohal Ismail, Evelien Kums, Bernadette Haase-Kromwijk, Andries Hoitsma, Nichon Jansen

Dutch Transplantation Foundation, Leiden, the Netherlands

Background: A high percentage of family refusal is found for several outcomes in the Donor Register. Misconceptions and concerns regarding donation impede next of kin from making a well-considered decision. The donation request is the moment in which such concerns should be addressed by the requester. The Communication regarding Donation (CrD) – Telephone Advice Psychologist (TAP) is a direct telephone support for physicians who are just about to request the relatives for donation. Thus the aim of this study is to improve physician's communication skills regarding the donation request and thereby increase the consent rate for organ and tissue donation.

Method: The study started on the 1st of April and will last until 31st of December 2014. To determine the effects, the consent rates were compared between physicians who received the TAP intervention and those who did not.

Results: The following preliminary results are based on interventions that took place between 1st of April 2014 until 31st of August 2014. The physicians who received the CrD-TAP intervention (N=68) had a significant ($p=0.008$) higher consent rate (50%) compared to the group who did not receive the intervention (33.5%). No significant difference was found in the intervention effect with regard to type of donation, time or day. Furthermore, the physician's confidence in requesting for donation increased by the intervention ($p<0.001$). The intervention is unanimously experienced as positive and valuable by physicians.

Discussion: Based on these preliminary results the intervention is effective in increasing the consent rate for organ and tissue donation. The final results will be presented at the congress.

O084

The myth of psychological benefit after living kidney donation

Hannah Maple¹, Joseph Chilcot², John Weinman², Nizam Mamode¹

¹*Guy's and St Thomas' NHS Foundation Trust, London, UK*, ²*King's College London, London, UK*

Introduction: Living kidney donation is partially justified on the basis that the donor experiences a psychological benefit after donation; however, there are no studies that prove this to be the case. The aims of this study were to determine whether living kidney donors benefited from donation and whether this was quantifiable. We hypothesised that wellbeing, life satisfaction, self-esteem and social comparison scores would increase, that distress, depression, stress and anxiety scores would decrease and that social support and optimism would not change.

Methods: 100 living kidney donors completed 11 validated psychological questionnaires at 3 time points: pre-operatively and 3 and 12 months after donation.

Results: 55 men and 45 women participated. The average age was 45yrs (s.d. 12.98; range 18-70yrs). Our results demonstrated that there was neither a clinically nor statistically significant difference in scores for wellbeing (29.5 vs. 29.5 vs. 29.5; $p=0.81$), distress (10.2 vs. 9.4 vs. 10.7; $p=0.09$), mood (0 vs. 0 vs. 0; $p=0.15$), stress (4.5 vs. 4.5 vs. 5.2; $p=0.074$), life satisfaction (27.5 vs. 27.0 vs. 26.0; $p=0.92$), self-esteem (22.7 vs. 21.8 vs. 21.8; $p=0.37$), anxiety (10.0 vs. 10.0 vs. 11.0; $p=0.36$), optimism (21.2 vs. 20.7 vs. 20.2; $p=0.72$) and social comparison (68.6 vs. 66.8 vs. 66.7; $p=0.89$). Social support was the only measure that demonstrated a statistically significant change across the 3 time points and this was found to decrease (72.0 vs. 71.0 vs. 67.5; $X^2(2, 70) = 10.29$, $p=0.006$).

Discussion: This study has failed to demonstrate psychological benefit from living kidney donation across a range of validated psychosocial measures within the first year after donation. This calls into question whether donors really do experience a psychological benefit after donation; which in turn raises questions about the moral and ethical justifiability of living donation. Donors experience lower social support after donation and this is likely to represent an assumption by their social network that less support is needed following transplantation.

Friday 13th March
Bayview 2 – 10:00
Surgical
Chairs: Mr Keith Rigg and Dr Frank Dor

O085

Living kidney donation in the elderly: the UK experience

Zubir Ahmed¹, Riccardo Tamburrini¹, Pankaj Chandak¹, Laura Pankhurst², Nicos Kessar¹, Nizam Mamode¹

¹*Guy's and St Thomas NHS Foundation Trust, London, UK,* ²*NHS Blood and Transplant, Bristol, UK*

Introduction: The increasing demand for organs has led many institutions to accept elderly patients onto their living donor programmes. However no large UK based datasets exist to assess the scope of the practice and patient outcomes. It is therefore unclear if an upper age limit to donation should exist.

Methods: Details of all 10,900 patients undergoing living kidney donation (LDN) in the UK from 2000 – 2013 were obtained. Patients were stratified into under 65 and 65+ years populations. Baseline demographics, co morbidity burden, nature and incidence of complications and their severity, renal function and proteinuria were all analysed using univariate tests of association.

Results: 586 (5.8%) over 65s underwent LDN during the 13 year period. Elderly LDN increased from 2.29% in 2000 to 11.08% of the total cohort in 2013 (p=0.000). Older donors were more likely to be white (96 v 86% p=0.00) have a lower deprivation score (mean IMD14.9 v 21.3 p=0.001) and be hypertensive (15.8% v 7.12% p=0.000), but had an otherwise lower comorbidity burden (ASA 2+) (8.19% v 13.32% p=0.00). BMI, sex and operative factors were similar in both groups. The occurrence of minor (Clavien 1/2:8.9 v 10.1% p=0.353) and major (Clavien 3+: 2.39 v 1.76% p=0.263) complications were also similar. Mean hospital stay was equivalent (mean 4.63 v 4.42 days, p=0.12). Incremental rises in systolic blood pressure (3.62 v 1.56mmHg p=0.02) and creatinine (36.7 v 30.4 μ mol p=0.000) 1 year post donation were all greater in the over 65s. Incidence of new onset proteinuria at 1 year was similar (3.41 v 3.51% p=0.433).

Discussion: Elderly donors comprise a significant and increasing proportion of the kidney organ donor pool. Older donors are being chosen based on more conservative parameters of co-morbidity and come from more affluent backgrounds. Perioperative morbidity is similar to their younger counterparts. Postoperative measures of cardiovascular risk are also within acceptable limits. Continued and increasing use of elderly donors is acceptable, however further data on recipient outcomes assessing the impact on graft function is required.

O086

Incisional herniation following hand assisted laparoscopic donor nephrectomy

Zubir Ahmed, Irene Mosca, Marie Dirix, Riccardo Tamburrini, Nicos Kessarlis, Nizam Mamode

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

Introduction: Living kidney donor demographics, perioperative outcomes and data on renal function is recorded by national mandate. However other longer term and potentially significant surgical outcomes such as incisional herniation remain unquantified in the donor population.

Methods: A retrospective review of a database of 800 patients undergoing hand assisted laparoscopic donor nephrectomy (HALDN) and who had also undergone a minimum of one year follow up was undertaken. Episodes of incisional herniation were recorded from patient records and also from operative records held in the unit database. Incidence, time to herniation and potential patient (sex, age, BMI, smoking status) and surgical risk factors (retro v intraperitoneal, site of hand port, Clavien 3+ postoperative complications, wound infections, operative time, use of a surgical drain, open conversion) were identified and entered into a univariate and then multivariate logistic regression model.

Results: 43 (5.4%) patients developed an incisional hernia following HALDN. The median time to hernia diagnosis was 8 months. 42/43 were at the site of the hand port. 41/43 underwent operative mesh repair (32 open 9 laparoscopic). Recurrence occurred in 2 patients (1 lap 1 open). The mean hospital stay post repair was 3.1 (SD 1.32) days. A higher BMI, presence of postoperative chest infection, clavien 3+ complications, and a supraumbilical hand port position were associated with incisional hernia on univariate analysis. On multivariate analysis only handport position (supra v infraumbilical) was a significant predictive factor for incisional herniation (OR 3.8 95% CI 1.33 – 10.8)

Discussion: Incisional herniation (IH) is common following HALDN and is of an equivalent incidence to traditional open methods of nephrectomy. Post HALDN IH requires corrective surgery resulting in a postoperative hospital stay equivalent to the original operation. The data presented - in addition to highlighting IH as significant source of morbidity – has identified an opportunity to reduce IH incidence through the more judicious use of supraumbilical fascial incisions.

O087

Donor and recipient outcomes following right versus left laparoscopic living donor nephrectomy; does side matter?

Scot Robertson¹, Lucy Garrard¹, Shahid Farid¹, Richard Feltblower², Richard Baker¹, Lutz Hostert¹, Jon Cartledge¹, Niaz Ahmad¹, Magdy Attia¹

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Introduction: Reservations continue to exist in the procurement of the right donor kidney for the purposes of live related transplantation. We present the largest national study to date comparing donor and recipient outcomes following right or left laparoscopic donor nephrectomy.

Methods: A total of 5393 patients undergoing laparoscopic donor nephrectomy (LDN) and their transplant recipients between Jan 2003 and Dec 2013 were included in the study from 24 centres across UK. Donor outcomes for analysis: hospital stay, intra/post-operative complications, use of anti-hypertensive drugs, 1-year serum creatinine, eGFR, and creatinine clearance. Recipient outcomes for analysis: Delayed graft function (DGF), primary non function (PNF), 1-year serum creatinine, eGFR and graft survival.

Results: Of the 5393 donors, 4568(84.7%) were left-LDN and 825(15.3%) right-LDN. No significant difference was observed in all donors outcomes between right and left LDN, except in the incidence of post-operative wound infection (0.038% vs 0.012%, $p < 0.001$). In transplant recipients there was no difference in DGF (5.7% vs. 4.3%), PNF (1.8% vs 1%), 1 year serum creatinine, eGFR and graft survival in recipients receiving kidneys from right or left LDN respectively.

Conclusion: We present the largest study to date comparing the donor and transplant outcomes following right or left LDN and have shown no significant differences in terms of safety and function. Preference of kidney for LDN based on side should be abandoned for more objective criteria to optimise selection of donor graft and facilitate optimal transplant outcomes.

O088

Outcomes of deceased donor kidney transplants offered through the Kidney Fast Track Scheme: a single-centre analysis

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Introduction: The Kidney Fast Track Scheme (KFTS) was introduced in 2012 to optimise the utilisation of 'hard to place' deceased donor kidneys. However, only 12 UK transplant units currently participate in the scheme. Concerns regarding outcomes may account for the slow uptake of the scheme nationally. We undertook a review of KFTS activity and post-transplant outcomes at a large single-centre user of these organs.

Methods: A retrospective analysis of transplants from kidneys offered through the KFTS at our centre between November 2012 and July 2014 was undertaken. Donor, recipient, intra-operative, and post-transplant outcomes were collected. The 4-variable MDRD equation was used to calculate eGFR. Time-zero or pre-implantation kidney biopsies were done routinely to determine the Karpinski (Remuzzi) score (0-12).

Results: 58 patients underwent renal transplantation from KFTS donors (37 DBD, 21 DCD). Of these, 12 patients (20.7%) underwent dual kidney transplantation. The mean (range) donor age was 57.5 (20-81) years; mean (range) final paraffin Karpinski score was 4 (1-7). The mean age of the recipients was 58.2 years (range 32-77). The median (IQR) CIT was 15.7 (13.1-20.4) hours with a DGF rate of 59.6%. The median in-patient stay was nine days (IQR 7-14). Six-month patient and graft survival were 98.3% and 89.3%, respectively. The median (IQR) recipient eGFR at six months was 37.5 (24.5-49) mL/min/1.73m². One-year patient and graft survivals were 98.3% and 86.4%, respectively, with a median (IQR) eGFR of 38 (21.5-51.5) mL/min/1.73m².

Conclusions: Kidneys transplanted at our centre after offering through the KFTS provide acceptable early function and graft survival. At present, KFTS kidneys make up 21% of our deceased donor kidney programme. However, the volume of offers received through the scheme, and the 45 minute window within which offers must be accepted, place significant strains on participating teams. It is unlikely that all UK kidney transplant centres will opt to be included in this scheme.

O089

Determinants of postoperative hospital stay in kidney donors in the laparoscopic era

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Background: Postoperative hospital stay is a ubiquitous indicator of early postoperative recovery and is thus a useful surgical quality outcome in laparoscopic surgery. Laparoscopic donor nephrectomy is a relatively new procedure and robust outcome data regarding trends in hospital stay and its determinants is lacking outwith clinical trial settings.

Methods: A retrospective analysis of 900 patients undergoing hand assisted laparoscopic donor nephrectomy (HALDN) at one institution was carried out. Postoperative hospital stay was recorded and stratified by 4 caseload quartiles. Associative patient and surgical factors were investigated. Factors associated with a short hospital stay (2 days or less) were also elucidated and a logistic regression model developed: (age, sex, bmi, smoking status, comorbidity, deprivation score, number of arteries, location of hand incision, day of the week effect, postoperative complications and ethnicity).

Results: The median hospital stay was 4 days (IQR 3 -5) and this remained unchanged through all four caseload quartiles ($p=0.12$). Only 11.2% were discharged within 2 days or less. Presence of co-morbidity ($p=0.001$), operating on a later day of the week ($p=0.035$), presence of postoperative complications ($p=0.002$), an increasing number of donor arteries (0.032) and operating surgeon ($p=0.02$) were all associated with a longer hospital stay. Co morbidity (OR 0.5, 95% CI 0.36 – 0.64) and postoperative infection (OR 0.29 95% CI 0.086 – 0.6) was predictive of a >2 day hospital stay on multivariate analysis.

Discussion: Despite the employment of minimally invasive techniques, postoperative hospital stay following HALDN remains high without any obvious surgical risk factors. This is in contrast to published data in the United States where quoted mean postoperative hospital stay ranges from 1.0 – 2.7 days. Apart from reducing postoperative infection rates, further reductions in hospital stay will likely require a paradigm shift in the perioperative management of kidney donors (enhanced recovery principles) rather than focusing on one specific factor.

Posters

Moderated Poster Session: Wednesday 11 March, 18:30
Purbeck Hall

Category: T-Cell Subsets

P001

DNA methylation of the *IFN* γ promoter in CD8⁺ T cell subsets is modulated by CMV infection but not by alloreactivity in kidney transplantation patients

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Introduction: DNA methylation plays a critical role in the function of cells, including cells of the immune system. Little is known about the methylation status of immune related genes in relation to viral infections and alloreactivity. Here we studied the methylation status of the pro-inflammatory cytokine *IFN* γ in relation to CMV infection and rejection in kidney transplantation patients.

Methods: The DNA methylation status of two regulatory CpGs (CpG-186 and CpG-54) in the *IFN* γ promoter was determined by pyrosequencing in FACS sorted naïve, central memory (CM), effector memory (EM) and EMRA CD8⁺ T cells of CMV-seropositive and CMV-seronegative donors and before, 3 months and 12 months after transplantation in CMV-seronegative patients. Both patients who developed a biopsy proven acute rejection (rejectors) and patients who remained free from rejection (non-rejectors) were included.

Results: A clear-cut difference was seen between the *IFN* γ methylation in naïve CD8⁺ T cells (CMV-seronegative donors, CpG-186 and CpG-54, median with range: 65% (53-71) and 79% (65-83)) and the memory CD8⁺ T cell subsets (CM: 13% (8-17) and 17% (10-21); EM: 6% (5-13) and 8% (7-20); EMRA: 2% (2-6) and 2% (2-9)). The *IFN* γ methylation status inversely correlated with the % of *IFN* γ producing cells. Before transplantation the *IFN* γ methylation was comparable to the methylation status in CMV-seronegative donors and did not significantly change during the first year after transplantation. Comparing rejectors and non-rejectors did not demonstrate significant differences. In contrast to alloreactivity, CMV infection significantly ($p < 0.05$) decreased the % of methylation of both CpGs in the naïve, CM and EM CD8⁺ T cells.

Conclusion: Chronic kidney disease, the transplantation procedure itself and subsequent alloreactivity does not modulate the methylation status of *IFN* γ , while CMV infection significantly decreases the methylation status of *IFN* γ in CD8⁺ T cells.

P002

Elderly ESRD patients have a significantly narrowed T-cell receptor repertoire diversity

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Introduction: A diverse T-cell receptor (TCR) repertoire is central to effective T-cell mediated immune responses. Advanced T-cell ageing is observed in elderly ESRD patients. However, little is known whether uraemia affects TCR repertoire diversity. The aim of this study is to assess the effects of uraemia on TCR repertoire diversity and relate this to T-cell ageing parameters.

Methods: Twenty ESRD patients (65—73 years) and 20 healthy individuals (HI; 64—72 years) matched for age, total number of circulating T cells and CMV-serostatus were enrolled. The TCR beta (TCRB) repertoire was measured by DNA-based multiplex TCRB gene PCR. Ageing parameters included thymic output (the number of CD31⁺ naïve T cells), T cell differentiation status and relative telomere length (RTL).

Results: Eighty percent of the elderly ESRD patients had a narrowed TCRB repertoire (oligoclonal) versus only 40% of the HI (P=0.02). More specifically, within the CMV-seronegative group, 5 out of 9 ESRD patients had an oligoclonal TCRB repertoire versus none of the 7 HI (P=0.03); In the CMV-seropositive group, all 11 ESRD patients had an oligoclonal TCRB repertoire versus 8 of the 13 HI (P=0.04). In addition, ESRD patients with an oligoclonal TCRB repertoire tended to have lower numbers of CD4⁺ CD31⁺ naïve (P=0.08) and higher numbers of CD8⁺ EMRA (P=0.08) T cells than those with a more polyclonal repertoire. Moreover, the RTL of CD8⁺ T cells tended to be shorter in patients with an oligoclonal TCRB repertoire than those with a more polyclonal repertoire (P=0.06).

Conclusion: Uraemia decreases TCRB repertoire diversity in elderly ESRD patients and this reduction may relate to lower thymic output, increased numbers of highly differentiated CD8⁺ T cells and shorter telomeres within CD8⁺ T cells. Assessment of TCRB repertoire diversity of elderly ESRD patients on the kidney transplant waiting list may be useful for evaluating the risk of infection and rejection after transplantation.

P003

Not only CD28null but also CD28pos T cells contribute to rejection during belatacept treatment

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Introduction: Treatment with belatacept, an inhibitor of the co-stimulatory CD28-CD80/86-pathway, leads to higher rejection rates after kidney transplantation than standard therapy. Here we report on the phenotypical and functional characteristics of graft infiltrating lymphocytes during rejection under belatacept.

Methods: A 61-year old female received her first, cross-match negative, 1-2-2-mismatched kidney-transplant. Fifty-six days after transplantation she was admitted because of fever, graft tenderness and acute kidney failure. Consequently she was treated with pulse glucocorticoids. Renal biopsy demonstrated a severe Banff grade II vascular rejection with T – and B cell infiltrates, large vessel thrombosis and massive necrosis. Because of absent transplant-perfusion, a nephrectomy was performed and graft infiltrating lymphocytes were isolated. We also conducted 16 mixed lymphocyte reactions (MLRs) in the presence of belatacept as comparison.

Results: CD86 on peripheral CD14+ monocytes was completely blocked by belatacept before and during rejection. 60-70% of the graft infiltrating T-lymphocytes were CCR7+CD45RO+ effector-memory CD4 and CD8 T-lymphocytes. 5% of the CD4+ and 51% of the CD8+ T-lymphocytes did not express CD28. Ex vivo, 50% of the CD8+CD28null T-lymphocytes expressed granzyme B, an important component of the lytic machinery of cytotoxic cells. In addition a high IFN γ -production capacity (64%) was measured by these CD8+CD28null T-lymphocytes. However, also 47% of the CD8+CD28pos T-lymphocytes expressed granzyme B and had a great IFN γ -production capacity (66%). CD4+ lymphocytes did not express granzyme B, but 39% produced IFN γ upon stimulation. In the MLRs the highest IFN γ production was measured in induced CD28null T cells, but also CD28pos T cells produced allogeneic IFN γ .

Conclusion: From this combination of in vivo and in vitro data can be concluded both IFN γ and granzyme B-producing CD28null and CD28pos T-lymphocytes contributed to rejection under belatacept treatment.

P004

Metabolic syndrome in morbid obese patients is associated with T-cell telomere shortening

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Introduction: Obesity (Body Mass Index (BMI) ≥ 30) and especially morbid obesity (BMI ≥ 40) adversely affect health. Recently it has been shown that higher BMI is not related to worse outcome in kidney donors but it is in kidney transplant recipients. A possible explanation is the link to obesity and inflammation, which may negatively influence the outcome. Production of inflammatory (adipo) cytokines by adipose tissue results in a state of chronic subclinical inflammation, which in turn increases the risk of developing metabolic co-morbidities. This phenotype is possibly also linked to accelerated ageing of the immune system. A key marker for cellular and biological ageing is telomere length. Telomeres are the end structures of chromosomes which protect and stabilize integrity, but shorten with each cell division. Recently it has been shown that T-cells of patients with end-stage renal disease have shorter relative telomere length compared to healthy live kidney donors. To examine the effects of obesity on T-cell ageing, we measured telomere lengths in circulating T-cells in morbidly obese patients with and without the metabolic syndrome.

Methods: Forty patients with morbid obesity were included of which 30 had no comorbidities, and 10 suffered from metabolic syndrome. Relative telomere length was measured in CD4- and CD8 T-lymphocytes via flowcytometric fluorescent in situ hybridization (FL-FISH). Relative telomere length (RTL) was assessed by relating the median fluorescence intensity of the PNA probe (specific for telomeres) to that of a control cell-line with very long telomeres (CCRF-CEM subline 1301 human T-cell leukemia cell-line). A comparison of the RTL was made between age groups <30 and >50 years and with and without the presence of metabolic syndrome. Overall RTL was compared to age-matched healthy controls (both healthy volunteers and live kidney donors). As the presence of cytomegalovirus (CMV) is known to affect RTL, CMV-status of the patients was determined.

Results: Relative telomere length (%) in CD4- and CD8- T-cells between the age groups did not differ significantly (CD4:22.7vs.19.7, $p=0.29$; CD8:21.9vs.18.3, $p=0.18$). The presence of CMV caused a decrease in CD4- but not CD8 RTL compared to CMV-negative patients (CD4:17.5vs.22.6; $p=0.04$; CD8:18.4vs.21.5, $p=0.19$). The presence of metabolic syndrome led to a significant decrease in RTL (CD4:15.0vs.21.8, $p=0.03$; CD8:13.0vs.21.9, $p=0.001$). Both metabolic syndrome and CMV-seropositivity accelerated this decline (CD4:12.1vs.23.5, $p=0.01$; CD8:10.3vs.22.7, $p=0.003$). When age-matched to healthy controls, the RTL of morbid obese patients without metabolic syndrome did not differ from those of the healthy controls (CD4:20.5vs 20.9, $p=0.91$; CD8:17.7vs.20.5, $p=0.40$).

Conclusions: Relative telomere length did not differ between morbid obese patients without comorbidities and healthy controls, suggesting that obesity alone does not lead to accelerated ageing. However, the presence of the metabolic syndrome decreases relative telomere length, which is amplified by the presence of CMV. These data suggests that the metabolic syndrome is a risk factor for accelerated ageing of the immune system in morbidly obese patients which could be related to the worse outcome in obese kidney transplant recipients.

P005

Increased CD8⁺CD28^{null} cell frequencies as a robust marker of “immunosenescence” are associated with neutrophil dysfunction and increased risk of infection following kidney transplantation

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Introduction: Kidney transplantation is associated with increased risk of infection and rejection. In a prospective study of 85 kidney transplant recipients we determined the most relevant markers of immunosenescence and the mechanism behind increased risk of infection. Clinical, immunological and biochemical information were serially evaluated from the time of transplantation to 5 years.

Methods: Detailed immunophenotyping of peripheral blood mononuclear cells (PBMCs) isolated prior to transplantation and then 14 days, 3 months, and 12 months post-transplantation was undertaken using multicolour flow cytometry. Cluster analysis was used to identify the most robust marker of immunosenescence. Neutrophil function was assessed by in vitro studies of bactericidal and phagocytic function (phagotest and phagoburst), and NET production. Neutrophil migration was quantified by isolating neutrophils from whole blood, incubating with interleukin 8 using an Insall chamber and video microscopy. The parameters of neutrophil migration (chemokinesis, chemotaxis, chemotactic index, persistence) were assessed by Java software ImageJ.

Results: Cluster analysis of candidate T- and B-cell phenotype characteristics revealed CD8⁺CD28^{null} cell frequency as the most robust marker of immune senescence. Recipient CMV seropositivity was associated with frequencies of these cells (p=0.02). On multivariate analysis (Cox model with time-dependent modelling), higher CD8⁺CD28^{null} frequencies were independently associated with increased risk of infection (p=0.005). Higher CD8⁺CD28^{null} cell frequencies were associated with impairment of the four neutrophil migration parameters (p<0.005 for all), but not with bactericidal or phagocytic function.

Conclusion: CD8⁺CD28^{null} cell frequency is a robust marker of “immune senescence”, which is likely driven by latent CMV. As defined, immune senescence is associated with increased risk of infection and impaired neutrophil migration following kidney transplant. This study suggests immune senescence as a biomarker of infection risk and offers insight into the associated mechanism.

P006

Murine cytomegalovirus infection dysregulates regulatory T cell suppressive function preventing allograft survival

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Introduction: Infection with cytomegalovirus (CMV) has been persistently associated with increased rejection rates in transplantation. Moreover, heterologous immunity and bystander activation of alloreactive T cells have been implicated in the increased transplant rejection rates following infection. However, the direct impact of CMV infection on alloreactive T cell responses, and specifically on regulatory T cells (Treg), has not been fully elucidated.

Methods: We used a fully mismatched BALB/c (H2K^d) skin graft into C57Bl/6 (H2K^b) mouse model. At the time of transplantation, animals were infected with 10⁶ pfu mCMV and T cell responses were measured using flow cytometry based assays.

Results: We show that mCMV-primed CD8⁺ T cells can crossreact at low levels to alloantigens, resulting in the production of TNF and IFN- γ inflammatory cytokines. Surprisingly, the accumulation of alloreactive CD8⁺ T cells is significantly decreased in the draining lymph nodes (dLN) of transplanted animals following mCMV infection. However, we observed an augmented migration of alloreactive effector CD8⁺ T cells into the allograft. Accumulation of CD4⁺CD25⁺Foxp3⁺ T cells was also significantly reduced in the dLN of infected animals compared to uninfected controls. In contrast, Treg migration into the graft was not impaired and yet rejection is accelerated. Assessment of mCMV infection on the suppressive capacity of CD4⁺CD25⁺Foxp3⁺ T cells *in vivo* established that Treg isolated from mCMV-infected animals had a significantly hampered ability to protect the allograft from rejection in a Treg cell intrinsic manner.

Discussion: This is the first incidence of a direct impact of mCMV on Treg function *in vivo*. Deciphering the molecular mechanisms behind Treg functional impairment upon infection could help improve clinical protocols to generate Treg, to better time Treg transfusions, and possibly to provide an advantage in the development of allospecific Treg.

P007

Successful expansion of functional and stable regulatory T cells for immunotherapy in renal and liver transplantation

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Strategies to prevent transplant rejection whilst minimizing long-term immunosuppression are currently under investigation with regulatory T cells (Tregs) at the cutting-edge of research. Trials in bone marrow transplantation and type I diabetes have demonstrated the clinical safety of these cells, encouraging their broader application. Two clinical trials, the One Study and ThRIL, have recently commenced centered on the concept of Treg cell therapy in the treatment of renal and liver transplant recipients, respectively.

To date, clinical grade autologous Tregs from healthy controls and prospective renal and liver transplant recipients have been expanded in the Clinical Research Facility at Guy's Hospital using anti-CD3/CD28 beads, IL-2 and rapamycin.

Here we demonstrate the large-scale expansion of patient-derived Tregs to numbers suitable for their clinical application. By employing our rapamycin-based protocol we not only show the expansion of a functionally superior Treg population, as compared to freshly isolated cells, but also report their abrogated conversion to Th17 cells under pro-inflammatory conditions. Furthermore, we report the successful cryopreservation of the final product, demonstrating the maintenance of phenotype and function post thaw.

As such, four patients, enrolled as part of the ONE study, have received the final Treg product, manufactured in accordance with our clinical protocol, with a further three Treg lines in preparation for injection by March 2015. In parallel, recruitment for the ThRIL trial is ongoing, with the first patient transplanted and Treg manufacture nearing completion.

The much-anticipated results of the One Study and ThRIL will undoubtedly provide insight into the safety and potential efficacy of this treatment, directing the future of Treg cell therapy in solid organ transplantation.

P008

CD44 antibody generates extremely potent, stable alloantigen-reactive Treg *in vitro* that can prolong allograft survival in an immunocompetent host

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Background: It is unclear which regulatory T cell (Treg) population would best suit clinical use in transplantation. Few direct comparisons have been made between alloantigen reactive Treg (allo-Treg) and activated naturally-occurring Treg (nTreg), partly because it is difficult to generate large numbers of phenotypically stable allo-Treg *in vitro*.

Hypothesis and aim: The presence of memory T cells may be detrimental to allo-Treg generation and CD44 blockade may offer a relevant way to generate alloreactive regulatory T cells *in vitro*.

Methods and results: To examine whether the presence of CD4⁺CD44^{hi} memory T cells impairs allo-Treg generation, flow-sorted CD44^{hi} T cells were added to naïve CD4⁺ T cells in an established Treg protocol in which the phosphodiesterase 3 inhibitor, cilostamide is used to promote Treg expansion. Surprisingly, an increased proportion of CD44^{hi} T cells did not impair Treg generation in this protocol, suggesting that CD44 blockade by αCD44 antibody might inhibit Tm effects. To test this possibility, CD4⁺ T cells were stimulated with alloantigen in the presence of αCD44 antibody. Remarkably, this approach yielded 3-fold higher Tregs than the cilostamide protocol. Pre-incubation of CD4⁺ T cells with αCD44 antibody reduced CD44^{hi} T cell IL-6 expression by 50%, suggesting that the reduced IL-6 enhances Treg yield. Importantly, adoptive transfer of 1x10⁶ CD44 allo-Tregs into CBA (H2k) mice led to a moderate but significant increase in survival of fully mismatched heart allografts (H2b). Significantly, the same dose of allo-Tregs in combination with a suboptimal dosing regimen of Rapamycin, led to long term survival of the heart grafts in the majority of recipients.

Conclusions: CD44 antibody in combination with alloantigen stimulation generates large numbers of highly suppressive, phenotypically stable allo-Tregs that can prolong the survival of an allograft in an immunocompetent recipient.

P009

Excretory-secretory products from the helminth parasite, *heligmosomoides polygyrus*, ameliorate allograft rejection by expansion of foxp3+ regulatory T cells

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Introduction: 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. We have recently reported extended survival of fully-allogeneic skin grafts in mice infected with the intestinal parasite, *Heligmosomoides polygyrus*. The purpose of this study was to determine whether helminth infection is required for allograft protection, or if the same effect can be achieved by treatment with soluble mediators secreted by the parasite.

Methods: Adult *H. polygyrus* larvae were maintained in culture for 21 days with twice-weekly collections of culture media containing excretory-secretory (ES) products. ES-containing media was then concentrated by ultrafiltration under nitrogen pressure and delivered to C57BL/6 skin graft recipients by continuous infusion via an intraperitoneal osmotic mini-pump. Full-thickness BALBc (fully-allogeneic) skin grafts were performed on the same day as mini-pump insertion. Skin grafts were monitored daily (complete rejection was defined as >95% necrosis of the graft surface area) and lymphocyte populations were analysed by flow cytometry at day 28.

Results: In mice receiving an infusion of *H. polygyrus* ES, allograft survival was prolonged by 40% (p=0.0001). A similar reduction in histological features of allograft rejection was observed at day 7 following transplantation. Flow cytometric analysis of lymphocytes isolated from the allograft-draining lymph node revealed a 31.34% increase in the mean percentage of CD4⁺CD25⁺Foxp3⁺ regulatory T cells (of total CD4⁺ cells) in treated vs. untreated mice (p=0.014) and persistent elevation (16.25% more Treg in treated mice) at day 28 (p=0.034).

Discussion: For the first time, we have shown that *H. polygyrus*-derived protection of allografts from rejection does not require live infection. Identification of the specific mediators within ES that expand CD4⁺CD25⁺Foxp3⁺ regulatory T cells may lead to a safe and effective novel alternative to current immunosuppression strategies.

Category: Stem cells/DCs/B-cells

P010

Inverse monocytic subset profile in blood and tissue during heart transplant rejection

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Introduction: Increased monocytic infiltration of heart transplant tissue is documented during acute rejection. It is still unclear how changes in circulating monocyte pool relate to counterpart alterations of monocyte-macrophage infiltrates on tissue level. We aimed to establish blood and tissue monocyte/macrophage profiles using serial blood samples and endomyocardial biopsies in 10 heart transplant recipients experiencing rejection in comparison to time points prior to rejection intra-individually. Blood profiles of heart transplant recipients were compared with 33 healthy individuals using a cross-sectional approach.

Method: Flow cytometric expression of co-stimulatory and migration-related molecules; HLA-DR, CD40, CD80, and CD54 were studied on different monocyte subsets. TNF- α , IFN- γ , IL-1 β , IL-6, IL-10, IL-12 production capacity of monocytes were measured after LPS stimulation. Using immunohistochemistry we studied expression of CD14, CD16, CD56, CD68, CD80, CD163 in endomyocardial biopsies.

Results: Increased classical CD14⁺⁺CD16⁻ monocytes and simultaneously decreased fractions of intermediate CD14⁺⁺CD16⁺ and non-classical CD14⁺CD16⁺⁺ monocytes signify the subset composition of circulating monocytes in heart transplant recipients compared to healthy individuals. However, rejection was reflected by significantly increased expression of CD54 and HLA-DR within the CD16⁺ monocyte pool indicative of a higher antigen presentation potential and migration capacity. Cytokine production potential was consistently high and independent of rejection. Significantly more CD16⁺ monocytes were found in rejecting endomyocardial biopsies compared to non-rejection. Significantly more CD68⁺CD163⁺ M2 macrophages were documented during rejection parallel to this increase in intra-graft CD16⁺ monocyte infiltration.

Conclusions: Our data show inverse monocytic subset profile in blood and tissue during human heart transplant rejection with a simultaneous predominance of M2 anti-inflammatory macrophages.

P011

Monocytic profiles in kidney transplant recipients: stable grafts vs rejection

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Introduction: Monocytes compose a neglected immune cell type in transplantation despite their contribution to antibody mediated rejection. Here, we aimed to define the phenotypic and functional profiles of circulating monocytes in kidney transplant recipients during rejection and non-rejection stable status.

Methods: Using flowcytometry, immunophenotype, activation status and cytokine production capacity of monocytes were determined in a cohort of 33 healthy individuals and in 30 stable patients over time. Moreover, we performed a case-control study comparing 8 recipients who developed rejection to 8 non-rejecting stable control patients using timely matched blood samples prior to and at rejection or non-rejection in both groups.

Results: We documented high frequencies of CD16+ monocytes at all-time points in stable recipients compared to healthy individuals. Monocytes retain their high potential to produce the pro-inflammatory cytokines TNF- α , IFN- γ , IL-1 β and IL-6 post-transplant despite immunosuppressive drugs and recovered kidney function. Importantly, the percentage of IL10 producing monocytes was even significantly increased post-transplant suggestive of a different monocyte polarization in stable patients. At rejection, the balance in the monocyte subset composition was skewed towards a significant decrease in the percentage of circulating CD14++CD16+ monocytes, while the percentage of CD14++CD16- monocytes was increased. Significantly increased expression of HLA-DR, CD40, ICAM-I and CCR2 by CD16+ monocytes was found at the time of rejection pointing towards enhanced antigen presentation and migration capacity.

Conclusion: Altogether, our data refer to the monocyte as an active immune cell type interfering with alloimmune response towards the graft.

P012

Mesenchymal stem cell treatment in a mouse model of combined liver ischemia reperfusion injury and regeneration

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Background: Liver ischemia reperfusion injury (IRI) is inevitable during transplantation and extended resections. Hepatic IRI is characterized by hepatocellular injury and hepatocyte loss and may compromise regeneration. At present there is no therapy to treat IRI. Therefore, potential therapeutic strategies to reduce hepatic IRI and accelerate liver regeneration could offer major benefits in both liver transplantation and resection. Mesenchymal stem cells (MSC) are reported to have anti-inflammatory and regeneration promoting properties in models of isolated ischemia or resection. Whether they are of benefit in a more clinically relevant model where IRI is combined with resection induced need for rapid regeneration is currently unknown. Therefore we investigated the effect of MSC administration in a mouse model of combined IRI and partial resection.

Methods: IRI was induced by occlusion of the blood flow to the left lateral and median liver lobes for 60 minutes followed by partial hepatectomy of 40% of the liver volume (PH) in C57Bl/6 mice. Animals were treated intravenously with 2×10^5 , or 3×10^5 mouse syngeneic MSC or PBS control, 2 hours before-, or 1 hour after IRI. Six hours, and 2- and 5 days after combined ischemia and resection mice were sacrificed. Liver damage was evaluated by measuring liver enzymes, histological damage, and inflammatory markers IL-6 and TNF- α . Liver regeneration was determined by measuring liver/body weight ratio and numbers of proliferating hepatocytes at 2 and 5 days after combined IRI and PH.

Results: Liver damage in mice treated with 3×10^5 MSC was increased compared to controls. 2×10^5 MSC 2 hours before or 1 hour after IRI and PH was not significantly different from PBS treated control mice. Liver regeneration was also not different from control animals.

Conclusion: In contrast to what is generally assumed, intravenous administration of high numbers of MSC increase liver damage, whereas lower numbers have no beneficial effect on liver IRI or regeneration in a clinically relevant model of combined IRI and resection.

P013

Assaying the bone marrow for antibody production and B cell memory

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Introduction: HLA antibodies may harm transplanted organs by binding to graft vascular endothelium and thereby leading to graft thrombosis. Antibodies in the serum of transplant recipients are mainly produced by bone-marrow residing plasma cells. However, some immunized patients may harbour HLA-specific memory B cells in the absence of long-lived plasma cells and therefore have undetectable HLA antibodies. Since long-lived antibody producing plasma cells and memory B cells are the two main mediators of the humoral immune protection, studying these cell types may aid in better understanding of the development of the humoral alloimmune response.

Method: To this aim, we first set out to determine whether we could use bone marrow as a source of long-lived plasma cells as well as memory B cells. Therefore, we measured the presence and distribution of IgG, IgM, IgA and tetanus toxoid (TT)-specific antibody secreting plasma and memory B cells by ELISPOT in bone marrow samples from hematologically healthy donors.

Results: We detected IgM spots to a lesser extent compared to IgG and IgA in the plasma cell fraction. When we stimulated the non-plasma cell fraction of the same bone marrow sample with activation cocktail that selectively activates memory B cells, we found comparable number of IgM and IgG spots whereas IgA spot formation was scarce. Moreover, we were able to detect both TT-specific memory B cells as well as TT-specific plasma cells in the bone marrow. We have previously shown the existence of HLA-specific memory B cells in the peripheral blood of immunized individuals in the presence, but also in the absence of detectable serum HLA antibodies.

Conclusion: Here, our results suggest the existence of memory B cells capable of antibody secretion upon activation in the bone marrow. Assaying the bone marrow and peripheral memory B cell compartment with HLA-specific ELISPOT assays together with serum HLA antibody specificities may provide an additional screening tool for the potential risk of donor-specific HLA antibody-producing plasma cells and HLA-specific memory B cells after organ transplantation.

P014

Plasmacytoid dendritic cells (pDC) are primed by virus-infected renal epithelial cells for efficient phagocytosis

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Introduction: pDC are important in the clearance of viral infection and are characterized as antigen presenting cells (APC), capable of activating CD4⁺ and CD8⁺ T cells. We recently demonstrated a strong influx of pDC in the **tubulointerstitium of renal** biopsies with acute rejection. However, pDC are thought to have poor phagocytic capacities, and the role of pDC in rejection has not been studied extensively.

Methods: Human pDC were isolated from buffy coats, and cocultured with CFSE-labelled apoptotic human renal epithelial HK2 cells (AC). Cocultures were performed in the presence of conditioned medium (CM) from non-infected HK2 cells (HCM) or with CM from HK2 infected with CMV (HCCM).

Results: pDC showed a limited capacity to ingest AC when cultured without CM (5%) or HCM (10%, ns). Importantly, addition of HCCM increased the uptake to 49% (mean, range 21% – 64%, $p < 0.0001$, $n=10$). This activity was not explained by the presence of CMV, since direct addition of CMV did not increase the uptake (11%). Moreover, HCCM induced IFN α production (mean 498 p/ml) and increased the expression of pDC maturation markers (CD83, CD86, and HLA-DR), the latter was further increased following phagocytosis of AC.

Conclusion: Our data point to a role of CMV-infected epithelial cells in priming / activating pDC. Through a still undefined factor, pDC can become potent phagocytic cells, thereby contributing not only to anti-viral immunity, but also an increased alloimmunity.

P015

Repopulation and revascularization of human liver matrix scaffolds for graft engineering

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Introduction: Increasing numbers of patients facing end-stage liver disease demand development of novel techniques in tissue engineering and regenerative medicine to overcome organ donor shortage. Evidence from rodent and porcine models, suggests that decellularization of whole liver organs is feasible and provides a non-immunogenic scaffold for reseeding liver cells for graft engineering. This aims to recellularize human liver matrix with vascular endothelial cells and stem cell-derived hepatocytes and cholangiocytes.

Methods: Whole human liver grafts unused for transplantation (n=10), were de-cellularized by perfusion of 4% Triton X-100 + 1% NH₄OH for up to 96 hrs. Sections of the extracellular matrix (dECM) was used for recellularization of human umbilical vein endothelial cells (HUVEC) and LGR5⁺ stem cell-derived liver organoids.

Results: The dECM was analyzed for the absence of cells, RNA and DNA content and for the presence of (matrix) proteins by mass spectrometry (LC-MS). Histo-logical analysis (H&E stain) showed that virtually all nuclei were removed and that the elastin and collagen fibers was not affected by the decellularization process. Glycosaminoglycans were not affected by the procedure. Obviously, the most abundant proteins were related to extra-cellular matrix, some fragments of liver-specific proteins (related to fatty acid and ATP metabolism and complement) were found. No proteins related to MHC molecules were found, indicating that the dECM is not immunogenic when used for transplantation. The vascular integrity was demonstrated by CT scanning of the biliary tree and the vascular tree. Results of re-seeding the dECM with HUVEC and human liver organoids indicate that the matrix is not toxic for (stem) cells as they adhere to the matrix and remain alive for several days in culture.

Conclusion: We established a method to make a-cellular ECM from human livers and showed proof of concept to seed several cell types, including liver-specific LGR5⁺-organoids. This can be explored for future bio-engineered liver tissue.

P016

Role of syndecan-1 in DC- T cell interaction and allograft rejection

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Introduction: Syndecan-1 is a heparan sulphate proteoglycan capable of binding chemokines, and growth factors by its heparan sulphate chains. Both T cells and dendritic cells (DCs) express syndecan-1. We previously demonstrated an immunomodulatory role of syndecan-1 in an experimental model of glomerulonephritis. A possible role of syndecan-1 in DC – T cell interaction has not been studied yet. In this study we aimed to investigate the role of syndecan-1 in DC - T cell interaction and allograft rejection.

Methods: The role of syndecan-1 on T cells was studied *in vitro* by co-culture of mouse syndecan-1^{-/-} C57Bl/6 or wild type (WT; C57Bl/6) CFSE labelled splenocytes, and bone marrow-derived (Balb/c) DCs. Proliferation was evaluated by dilution of CFSE signal. Co-culture supernatants were analyzed for cytokine levels to evaluate T cell differentiation. Effect on allograft survival was investigated *in vivo* in a fully MHC-mismatched heterotopic heart transplant model; Balb/c hearts were transplanted into either WT (n=8) or syndecan-1^{-/-} C57Bl/6 mice (n=8), and Balb/c mice received either a syndecan-1^{-/-} (n=9) or WT C57Bl/6 (n=8) heart.

Results: The proliferative response of syndecan-1^{-/-} splenocytes after stimulation by immature DCs was less as compared to WT splenocytes. Moreover, syndecan-1^{-/-} splenocytes produced significantly less IL17 upon stimulation by mature DCs. Levels of interferon- γ , IL10, and IL4 were comparable in supernatants of syndecan-1^{-/-} and WT splenocytes. Syndecan-1 deficiency in donor or recipient had no effect on heart allograft survival.

Conclusion: Syndecan-1 appears to be involved in DC – T cell interaction, illustrated by diminished proliferation and IL17 production by syndecan1^{-/-} compared to WT splenocytes *in vitro*. Nevertheless, *in vivo*, syndecan-1 deficiency in graft or recipient does not affect allograft survival in a fully mismatched heterotopic heart transplant model.

P017

Human *in vitro* - generated myeloid-derived suppressor cells (MDSC) inhibit T cell-mediated immune responses

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Introduction: Myeloid-derived suppressor cells (MDSC) have been described as a heterogeneous population of immature myeloid cells that display immunoregulatory properties and play a role in cancer, infections and transplantation. In rodent transplant models MDSC were shown to accumulate in the allograft and mediate graft survival, suggesting a possible role for human MDSC as a tolerance-promoting cell population. In this study, we developed a protocol to generate highly functional human MDSC and tested their ability to regulate T cell responses.

Methods: CD14⁺ and CD33⁺ myeloid cells were isolated from peripheral blood mononuclear cells (PBMC) and incubated in the presence of recombinant cytokines. We compared the effect of starting population, cytokine combination and length of culture on effectiveness of MDSC generation and suppressive capacity *in vitro*. Next, we tested the effect of PBMC and MDSC co-transfer in immunodeficient, humanized mice.

Results: CD33⁺ cells cultured in the presence of GM-CSF and IL-6 or IL1 β generate highly suppressive CD11b⁺HLA-DR^{-/lo}CD14⁺ MDSC able to suppress CD4⁺ and CD8⁺ T cell proliferation and IFN γ , IL-17 and IL-13 production *in vitro*. In the short-term *in vivo* experiments, MDSC co-injection inhibited CD8⁺ T cell activation and enhanced FoxP3⁺CD127^{lo}CD4⁺ Treg frequency.

Conclusions: We have developed a reproducible and effective protocol for *in vitro* generation of human MDSC and tested their suppressive capacity. These results highlight the potential offered by human myeloid-derived suppressor cells and provide an essential tool to study their role in transplantation.

Category: Donation - Living Donor

P018

Ten-year follow-up after live kidney donation – a prospective cohort study

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Background: Previously reported short-term results after live kidney donation, show no negative consequences for the donor. The occurrence of e.g. cardiovascular diseases takes years to emerge, making it highly likely that this will be missed during a short-term follow-up. Therefore evidence on long-term outcome is essential.

Methods: A ten-year follow-up on renal function, (new onset) hypertension, quality of life (QOL), fatigue scores, and survival was done of a cohort of 100 donors of a single blind, randomised controlled trial.

Results: After a median follow-up time of ten years, clinical data was available for 97 donors and QOL data was available for 74 donors. Nine donors died during follow-up of unrelated causes to donation, and one donor was lost to follow-up. There was a significant decrease in kidney function after ten years of follow-up of 12.9 ml/min ($p < 0.001$), however there was no significant decrease compared to the kidney function after one year post donation ($p = 0.858$). Physical fatigue score demonstrated a significant decrease at ten-year follow-up ($p < 0.001$), which was also seen in QOL dimension score of physical function ($p < 0.001$). Donors with pre-existing hypertension have a well regulated blood pressure without compromising their kidney function. New onset hypertension was present in 25.6% of the donors after ten years of follow-up (818 person-years). Their kidney function was not significantly different from non-hypertensive donors ($p = 0.109$), however they were significantly older, mean age of 57 versus 45 years respectively ($p = 0.001$). Donor and graft survival were 91% and 66% respectively.

Conclusion: Donor outcomes are excellent ten years after donor nephrectomy. Kidney function appears stable and hypertension does not seem to occur more frequently compared to the general population.

P019

Long-term follow-up after live kidney donation – a systematic review and meta-analysis

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Background: Annually, thousands of living individuals donate their kidney and accept the risks associated with major surgery and living with one kidney. Recently, contradictory results were reported on long-term outcomes for live kidney donors. To assess potential long-term risks a systematic review was performed.

Methods: A systematic review and meta-analysis were performed in accordance with the Cochrane Handbook for Interventional Systematic Reviews and written by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Comprehensive searches were performed in MEDLINE, Embase, CENTRAL, OVIDSP and Google Scholar. Articles that reported on long-term outcomes (e.g. kidney function, incidence of morbidity and mortality) with an average follow-up of ten years or more after donation among adults were included.

Results: Out of 5,305 identified articles, 24 were included for analysis: 21 cohort follow up studies, and 9 studies comparing donors with non-donors,. Reported outcomes were kidney function, hypertension and diabetes, quality of life, and mortality. The cohort follow up studies included 9,459 donors, pooled into two groups (i.e., less than 20 years and over 20 years of follow-up) A meta-analysis revealed significant differences on all outcomes, except for proteinuria; data suggest that morbidity increases with longer follow-up. The studies comparing donors with non-donors included 4,782 donors; analysis of different studies shows contradictory results on the long-term outcome. Overall quality of life was found to be better among donors. The main limitation of this analysis is caused by the heterogeneity of the different donor and non-donor cohorts and the design of studies.

Conclusion: The current literature is inconclusive concerning possible negative consequences of live kidney donation. The lack of uniformity makes it hazardous to make a final statement on the long-term health status after living kidney donation. Therefore, new studies addressing this important question are necessary to guarantee the safety of living kidney donors.

P020

South Asian donor/recipient gender disparity in a living-donor kidney transplant program – a retrospective analysis

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Introduction: There is a paucity of information relating to South Asian gender disparity in living kidney donation between donors and recipients. The aim of this study was to explore this within the setting of a multi-cultural region.

Methods: This was a retrospective cohort study of all living-donor kidney transplant procedures performed at a single transplant centre. Data was obtained from the United Kingdom National Transplant Database and hospital IT systems. Donor/recipient demographics were collected including gender, age, ethnicity, religious belief (where stated) and relationship.

Results: We analysed data from 713 living donor kidney transplant procedures performed (between 1987 and July 2014). 54.6% of donors were female and 45.4% male. Mean age of donors versus recipients was 45 versus 40 respectively ($p < 0.001$). 18.7% of organ donors were from Black, Asian or Minority Ethnic backgrounds. No religious affiliation was documented in 68.3% of kidney donors, limiting analysis of religion as a variable. Females donated more to males (70.2%) than females (29.8%), while male-to-female (50.9%) and male-to-male (49.1%) donations were similar ($p < 0.001$). South Asian partner-to-partner transplants ($n=22$) were more likely to be female-to-male versus male-to-female (90.9% versus 9.1% respectively, $p=0.003$). Male donations were more common to paediatric recipients compared to females (10.2% versus 6.4% respectively, $p=0.046$). There was no difference in South Asian male versus female donations to paediatric recipients (16.7% versus 16.0% respectively, $p=0.586$), but male donations were noted to be exclusively to boys (5/5) compared to a more equal split for female donations (3/5) to boys.

Conclusion: South Asian gender disparity exists in living kidney donor/recipient exchanges. This requires targeted counselling and further research to understand.

P021

Age should not be considered a contraindication for living kidney donation

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Introduction: The increasing numbers of patients with ESRD on the transplant waiting list has been the main driving force for expanding the donor pool. Acceptance of elderly living donors remains controversial because of the higher incidence of comorbidities. We undertook living kidney donor transplantation from elderly donors after reports that short-term outcomes are safe. We report 5-yr data and compare these with the outcomes of younger donors.

Methods: Data was prospectively collected on 553 consecutive live donors from 2000-2012. Donors were categorized in two age groups: <60 years (younger) and ≥60 years (elderly). We analysed 5-yr follow-up data for kidney function [Creatinine Clearance (CrCl)] and protein excretion as well as blood pressure control.

Results: 83 donors were ≥60 years and 470 were <60 years. 62 (74.7%) in the group of elderly donors were Caucasians. Overall, in the total donor population, 18.4% of the Caucasians were elderly, while 10.6% of SA and 2% of AC were elderly. There was no difference regarding gender (60.2% female in elderly vs 55.5% in younger, $p=0.425$). There were more Caucasians ($p=0.008$) and more hypertensive in the elderly group (19.3% versus 7.4%, $p=0.001$). Elderly group had lower CrCl pre-donation (98.6 ± 22 vs 112 ± 33 , $p<0.001$). There was no difference in BMI or proteinuria. The CrCl at 5 years was 78.7 ± 16 in elderly and 91.6 ± 27 mls/min in younger donors ($p=0.067$). Decline of CrCl was similar in both groups [figure1]. There was no significant proteinuria at 5 years (Elderly= 0.12 ± 0.1 , Younger= 0.12 ± 0.6 g/24hrs, $p=0.872$). Blood pressure remained well-controlled at 5 years at 133/77 (elderly) vs 136/82 (younger) ($p=0.384$ and 0.07). 13 (15.7%) elderly and 30 (6.4%) younger donors developed post-donation HTN ($p=0.001$).

Discussion: We conclude that donor nephrectomy in carefully selected elderly donors seems to be safe. There was no difference in Creatinine Clearance trends among elderly and younger donors and proteinuria was minimal over 5 years. Long-term follow up of donors remains important enabling identification of patients at risk of declining renal function or hypertensive complications

P022

Kidneys from living donors with high body mass index do not have inferior outcomes

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Introduction: The disparity between donor kidney availability and demand has increased utilization of kidneys from marginal living donors. Data regarding outcome of transplantation from living donors with high Body Mass Index (BMI) and elderly donors is limited. Our aim was to compare outcomes from elderly living donors and donors with high BMI.

Methods: Data was prospectively collected on consecutive recipients from live donors in 2002-2012. We excluded donors with hypertension. Donors were categorized as elderly (≥ 60 years) or younger and with high (≥ 30) or normal BMI.

Results: We included 449 patients and follow up was 74 months (median, range 3-145). 64 patients lost their grafts and 34 patients died. Recipients with Afro-Caribbean (AC) donors were more likely to lose their grafts ($p=0.019$). Receiving a kidney from an elderly donor ($p=0.724$) or a donor with high BMI ($p=0.410$) was not associated with graft loss. Median eGFR at 3 and 5 years for kidneys from younger donors was 55 (range 14-93) and 50 ml/min (range 17-73), respectively and from elderly donors it was 42 (range 19-66) and 34 ml/min (range 24-51), respectively ($p=0.001$ for both). Median eGFR at 3 and 5 years was similar between recipients from donors with normal BMI (53, range 14-93 and 48.5 ml/min, range 17-90, respectively) and high BMI (48, range 33-90 and 48 ml/min, range 38-83, respectively) ($p=0.966$ and $p=0.546$, respectively). Death-censored graft survival was similar regarding kidneys from elderly and younger donors (log rank $p=0.639$) and from donors with normal or high BMI (log rank $p=0.350$). Patient survival was similar in recipients with donors with high or normal BMI (log rank $p=0.159$) and with elderly or younger donors (log rank $p=0.588$). In Cox-regression, receiving a kidney from an AC donor ($p=0.02$) and rejection ($p<0.001$) increased the risk of graft loss, whereas a kidney from an elderly donor ($p=0.632$) or a donor with a high BMI ($p=0.359$) did not.

Discussion: A graft from a donor with high BMI was not associated with inferior graft outcome or increased risk of graft loss. Kidneys from elderly donors did not have increased risk of graft loss, but had inferior function.

P023

A single centre experience with the living donor kidney sharing scheme: more is better!

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Introduction: The living donor kidney sharing scheme was introduced in the UK to expand the donor pool. In this study we have reviewed our experience since its inception in 2009.

Methods: Data were collected from a prospectively maintained database and review of case notes.

Results: 98 pairs have been registered since 2009. 24 pairs (24.5%) were successful to find a match. The mean age of the recipients was 57 y (SD±10) and 71% were female. The donors' mean age was 55 y (SD±12) and 46% were female. 79% of the donors were unrelated to the recipient, of which the majority were either spouse or partner. All donors from our centre had an uncomplicated laparoscopic donor nephrectomy. 22/24 (92%) of the successful pairs were equally split between blood group & HLA incompatibility. One donor was both HLA and blood group incompatible and in one pair the HLA match was poor. 13/24 (54%) of recipients found a match after a single matching run and 17/24 (71%) were matched after two runs. The mean number of runs per recipient is 2.5; two recipients required nine runs to match.

All patients received basiliximab induction with maintenance immunosuppression with tacrolimus and an antimetabolite. 20/24 (83%) patients experienced immediate graft function. Three patients had delayed graft function with early rejection confirmed on biopsy. One patient was re-explored for anuria on the same day and had a clot blocking the transplant ureter. The average length of inpatient stay was 7.5 days. All patients were discharged with a functioning graft and a mean creatinine of 116 (SD ±52).

Discussion: A quarter of our incompatible pairs have benefitted. The majority of pairs required two runs to match successfully. The outcome of the transplanted kidneys has been good. The scheme would benefit with more frequent matching runs and the inclusion of non-directed donors and pairs with a poor HLA match.

P024

Renal tubular dysfunction following donor nephrectomy and its impact on residual kidney function

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Background: Recent publications have described an increasing incidence of end stage renal disease amongst kidney donors. This highlights the paucity of knowledge which exists in the understanding of postoperative renal physiology and thus the determinants of residual renal function. We investigated the impact of donor nephrectomy on the physiology of the residual kidney through the measurement of validated markers of ATP depletion / tubular dysfunction, glomerular filtration rate (GFR), and hyperfiltration.

Methods: 48 patients undergoing hand assisted laparoscopic donor nephrectomy consented to the collection of urine and plasma samples pre and postoperatively (immediate, day1, day2, day3, day30). Urinary retinol binding protein (RBP: a marker of ATP depletion and mitochondrial stress), urinary albumin creatinine ratio (UAC) and plasma cystatin C calculated GFR were measured with colorimetric nephelometry.

Results: The cohort mean age was 46yrs (SD11.7) and 31 patients were female. RBP levels were normal preoperatively (mean 9.5 mg/mol SD 5) and peaked on day 3 (mean 2969mg/mol, min 31 max 12004) on day 3 before normalising again at day 30 (mean 14.1, SD 5). UAC was normal preoperatively (mean2.2 g/mol SD 5) and peaked postoperatively (20g/mol SD 4) before reaching a steady state at Day 3 5.6g/mol (SD13). Peak RBP levels demonstrated a positive correlation with post/preoperative Cystatin C ratio ($r=0.56$ $p=0.04$) and UAC ($r=0.44$ $p=0.04$) ratio. In a linear regression model $\{F(4,34) = 13.10, R^2 0.61$ $p=0.00\}$ adjusted for preoperative GFR, day 3 GFR, age and sex); day3 RBP was an independent negative predictor ($\beta = -2.39$ $p=0.022$) of Day 30 GFR.

Discussion: Our results indicate the existence of a mitochondrial stress environment with a lasting negative impact on residual kidney function at 30 days postoperatively. This likely reflects renal tubular dysfunction in the remaining kidney following donor nephrectomy. Further biochemical analyses are ongoing to confirm the nature of this dysfunction. This will allow the targeting of timely interventions to mitigate the effect of such dysfunction and thus optimise residual renal function.

P025

National Living Donor Kidney Sharing Scheme: no travel sickness?

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Background: Paired/pooled living kidney donation provides an excellent alternative for incompatible donor-recipient pairs and results in increased living donor (LD) transplant rates. Engagement with the National Living Donor Kidney Sharing Scheme (NLDKSS) varies between UK transplant centres, potentially due to concern regarding outcomes of shared kidneys compared to locally implanted direct LD kidney transplants. We compared the short-term outcomes of both cohorts in our centre.

Methods: Matching run reports for our centre were reviewed and all donor-recipient pairs entered into the NLDKSS from October 2009 to October 2014 recorded. Patient demographics, degree of sensitization, transplantation rates and clinical outcomes were analysed through review of patients electronic care records. These were compared to all the direct living donor transplants that took place in the same time period.

Results: 78 donor-recipient pairs have been entered into the NLDKSS in our centre and the first transplant took place in January 2010. Thirty (38%) of those entered have been transplanted via the pooled scheme, in 8 (27%) this was pre-emptive. 3 (10%) transplanted were very highly sensitized with a calculated reaction frequency of >95%. 32 patients (41%) have subsequently been transplanted by other means (22 alternative direct LD, 1 altruistic LD, 9 deceased donors). There were 204 direct LD transplants in the same time period, 65 (32%) were pre-emptive and 11 (6%) were very highly sensitized recipients. Average total ischaemic time for those transplanted via the pool was 312 minutes, compared to 246 minutes for direct LD. 3 (10%) patients in the NLDKSS had delayed graft function compared to 7 (3%) of local LD kidney transplants. Length of hospital stay was comparable between the two cohorts (10 v. 12days,) as was the discharge creatinine (144 v. 123umol/L.)

Conclusions: NLDKSS has contributed to the expansion of the living donor programme at our centre with almost 40% of patients entered being successfully transplanted. The short-term outcomes are good and comparable to direct LD transplants.

P026

A single centre's five year experience with altruistic kidney donation

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Introduction: Since 2008 there have been a growing number of non-directed (altruistic) kidney donors in the UK, with 259 to date. This study focuses on 26 non-directed donors and 16 recipients of kidneys from non-directed donors at our centre over 5 years.

Method: A retrospective review of a prospectively kept database was done; donor demographics, pre and post donation renal function was noted using serum creatinine levels (sCr); and reasons underlying altruistic donation were assessed. The outcome in recipients receiving an altruistic kidney was also analysed.

Results: 15/26 (58%) of donors were female. Ages ranged from 22 to 81 and the average age was 55 years. 19/26 (73%) underwent left-sided nephrectomy. All grafts had primary function with 1 kidney removed on day 1, due to renal vein thrombosis. After donation, at a median 13 month follow up (range 6-26 months) mean sCr rose from 70 to 103 (47%). In recent donors at a median 1 month follow up (range 1-3 months) mean sCr increased from 60 to 95 (58%). There is no evidence of correlation between age and increase in creatinine levels although there is correlation between increasing age and higher final creatinine level. Four themes motivating donation are emphasised: the desire to help, personal exposure to renal disease / transplants, media coverage and regular blood donation. All 16 recipients had primary function post-transplant and are dialysis independent. The mean sCr measured at a median 11.5 months (range 6-24 months) decreased from 696 to 122 (82%). For more recent transplants at a median 1 month follow up (range 1-3 months) the mean sCr decreased from 697 to 101 (86%).

Discussion: Altruistic kidney donation greatly benefits transplant recipients. Donors retain satisfactory renal function and age does not appear to be a risk factor for donors. To maximise the benefits, non-directed donors should be encouraged to participate in the living donor sharing scheme.

P027

A large single-centre analysis of living kidney donation and reasons for non-donation between 2004 and 2014

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Introduction: Kidney transplantation is the treatment of choice for patients with end-stage kidney disease. Living donation offers optimum graft survival and has helped to fill the disparity between the shortage of deceased donor kidneys and the growing waiting list of potential recipients. Comprehensive evaluation of each donor should take into account medical, ethical and psycho-social aspects of live donation. The aim of this study was to determine the magnitude of workload generated by potential living donors (LD) and reasons for not proceeding to donation.

Method: Data was prospectively collected on all potential LD who were evaluated at our centre between January 2004 and December 2013 in accordance with the British Transplant Society Guidelines. Each donor underwent step-wise work up following self-referral to the live donor transplant coordinator.

Results: There were 574 (48% males) prospective LD of which 248 (43%) went on to donation. Of those who donated, 138 were related and 108 unrelated (11 altruistic). The most common reasons for non-donation (ND) were inadequate glomerular filtration rate (20%), medical contraindications (19%) and donor withdrawal from process (17%). There was a higher rate of ND in the altruistic LD (84%) compared to other LD (43.5 and 55.6%) and the former were more likely to withdraw (20%). Of the 62 patients unable to donate for medical reasons, cardiovascular disease accounted for 16 (26%) cases followed by diabetes 15 (24%), malignancy 11 (17%) & BMI > 32.6 (10%). A new medical diagnosis was made during the donor work up in 31 of the 62 patients.

Discussion: This is the largest cohort of patients in such a study in the UK with some differences compared to earlier published UK studies. The study shows differences in rates & reasons for ND between different types of LD. The data can be used to counsel potential LD when they start the evaluation process and ensure appropriate support is available. It can be used for cost analysis to help in allocating resources and funding to the donation process

Category: Donation - Deceased

P028

RAG scoring for deceased donor kidney offers – does it reliably predict outcomes?

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Introduction: Disparity between organ supply and demand has necessitated increasing use of Expanded Criteria Donor (ECD) kidneys. However, concerns over higher rates of delayed graft function, rejection and inferior graft survival associated with ECD kidneys results in significant variation in acceptance of such organ offers. To facilitate standardisation of organ acceptance, our unit introduced a RAG scoring system to enable risk stratification of potential organ offers. We present evaluation of the scoring system at 30 months since introduction.

Method: All deceased donor kidney offers that were accepted and transplanted in our unit or rejected by our unit but subsequently transplanted elsewhere between September 2011 and February 2014 were coded according to our RAG scoring system. Based on donor characteristics, offers were coded as red (unconditional rejection), amber (ECD requiring consultant decision) or green (mainly unconditional acceptance). Outcomes included graft and patient survival, delayed graft function (DGF) and the 3 month estimated glomerular filtration rate (eGFR).

Results: 186 deceased donor kidneys were accepted and transplanted at our renal unit. 205 kidneys rejected by our unit, were transplanted elsewhere. There was a significant difference in eGFR between the different colour coded groups (Green: eGFR 56 ml/min/1.73m²; amber: eGFR 43 ml/min/1.73m²; red: eGFR 33 ml/min/1.73m²). DGF rates also correlated with the RAG score (green 15%, amber 34%, red 48%, p<0.001). When looking specifically at the amber donors, although there was a trend towards higher DGF rates in the rejected group (29.3% vs 39%, p=0.11), there was no difference in 3 month eGFR between the two groups (45.0 vs 42.6 ml/min/1.73m², p=0.711).

Conclusion: Our RAG scoring system reliably predicts outcomes of interest and appropriately risk stratifies deceased donor kidney offers. The analysis also indicates amber kidneys turned down by our unit but accepted elsewhere have reasonable 3 month outcomes. Further sub-group evaluation is necessary to provide the information needed for clinicians to strike the right balance between accepting & rejecting amber category offers.

P029

Regional sharing of DCD kidneys leads to a reduction in cold ischaemia time

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Introduction: Following the recent introduction of regional sharing of DCD kidneys in the UK, concerns have been raised about the possible impact of this on cold ischaemia time (CIT). We examined the impact on CIT of transplanting paired DCD kidneys in one centre versus sharing the second kidney regionally. We also sought to determine the percentage of patients that were transplanted using a virtual crossmatch in the two groups. Data was prospectively collected over a 14-month period from June 2011 and July 2012 from 16 of the 22 transplant centres and all 19 Histocompatibility and Immunogenetics (H&I) laboratories. For the purpose of this study we examined CIT and crossmatch type (virtual crossmatch vXM or pre-transplant crossmatch pXM) in 267 pairs of DCD kidneys. 201 pairs were transplanted in the same centre during the period of the study.

Results: The median CIT was significantly shorter for the first kidney than the second (10.8 hours v. 16.1 hours, $p < 0.0001$), with a median difference of just over 5 hours. If the second kidney was transplanted at a second centre, either in an agreed regional sharing scheme or nationally, the difference in CIT was only 3 hours (66 pairs). CIT for the first kidney was 9.8 hours, and for the second kidney was 13.4 hours, $p < 0.0001$. Median CIT for a second kidney transplanted at a different centre was significantly shorter than if both kidneys were transplanted at the same centre ($p < 0.0001$). We went on to examine the % kidneys performed by vXM. Overall 42% DCD kidneys were transplanted using vXM. In paired DCD kidneys transplanted in the same centre, 54% of first kidneys were transplanted using vXM and 23.3% of second kidneys. If the second kidney was transplanted in a different centre from the first, 65% of first kidneys were transplanted using vXM, and 40.6% of second kidneys.

Conclusion: Regional sharing has a beneficial effect on CIT compared to transplanting both kidneys locally. A higher % of first kidneys than second were transplanted using vXM, and regional sharing may disadvantage the more highly sensitised patients. In order to interrogate the data further, modelling of CIT will examine the confounding effects of sharing, sequential transplantation and type of crossmatch.

P030

Single centre experience of en bloc kidney transplantation from donors less than three years of age

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Introduction: Despite increases in organ donation seen over recent years, there still remains a significant disparity between the supply of and demand for donor kidneys. Historically, there has been a reluctance to use en bloc kidneys from young paediatric donors because of concerns over technical issues and early failure. There is thus a high decline rate for these donors. We report a single centre experience of utilising en bloc kidneys from donors less than 3 years of age.

Methods: We reviewed the outcomes of all en bloc kidney transplants undertaken in our unit from donors under the age of 3 years. Donor and recipient characteristics in addition to post-transplant outcomes were reviewed.

Results: We undertook our first en bloc renal transplant from a paediatric donor in January 2011 and have since undertaken a further 3 en bloc transplants. The mean age of the donors was 20.25 months (range 16 – 29 months) with an average weight of 11.5kg (range 8.9 – 13kgs). En bloc transplants were performed in recipients with mean age of 25 years (range 19 – 30 years) and mean weight of 76.3kgs (range 50 – 111.3kgs). Recipients have been followed up for a mean of 27 months (range 9 – 46 months) with excellent one year serum creatinine results (mean 82, range 71 – 90, creatinine 59 for single recipient currently at 9 month follow up). To date, no perioperative or longer term complications have arisen in this group of patients.

Conclusion: Excellent graft and patient outcomes can be achieved from en bloc kidney transplants with graft function continuing to improve with time out from transplantation, even in those recipients with the greatest donor-recipient weight mismatch. We would encourage that greater consideration is given to this small but important group of potential kidney donors as a means of maximising the potential donor pool.

P031

Influence of donor organ type upon outcome of renal transplantation in the UK and Europe

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Introduction: Outcome data from patients receiving second kidney grafts in 2001-12 in the UK were examined to investigate whether the order of transplantation of a living donor (LD) or deceased donor (DD) organ influenced long term outcome.

Results: Patient survival following second transplantation by donor organ type (univariate analysis):

		No at risk on day 0	% Patient survival (95% confidence interval)		
			One year	Three year	Five Year
DD	then DD	1441	9 (94,97) 6	9 (90,93) 1	8 (83,87) 5
DD	then LD	503	9 (95,98) 7	9 (90,95) 3	9 (89,94) 2
LD	then DD	277	9 (93,98) 6	9 (87,95) 2	8 (81,91) 7
LD	then LD	201	9 (96,100) 9	9 (93,99) 8	9 (87,98) 5

These data suggest that patient survival is affected by the type and the order of organ transplantation, with poorer outcomes when the second kidney is transplanted from a DD. Data from the Collaborative Transplant Study (CTS) yielded similar results. However, bias may have resulted from the median age of the DD then DD cohort being significantly higher than the other patient groups.

When graft survival in the UK was examined, recipients of first and second kidneys from deceased donors exhibited worse graft survival than those receiving other combinations of donor organs (log rank $p < 0.0002$). These data were confirmed by data from the CTS where five year graft survival was 89% for DD/LD and LD/LD combinations, compared to 80% for LD/DD and DD/DD transplants.

Conclusion: These data help inform transplant strategies where options for both DD and LD transplantation are available. Both patient and graft survival are improved when LD transplantation is first line therapy.

P032

Local expansion in DCD kidney transplant activity improves waiting list outcomes and addresses inequities of access to transplantation

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Introduction: Following expansion in our circulatory death (DCD) transplant program, our centre now performs twice as many DCD as brain-death (DBD) kidney transplants. Here, we investigate how a large pool of locally-allocated DCD kidneys influences outcomes for waiting list populations of different ages.

Methods: A retrospective observational cohort study comparing outcomes for adults listed for renal transplantation between 2002 and 2012 according to age at listing: under 45 years (Grp A); 45 to 65 years (Grp B); and over 65 years (Grp C). DCD and DBD kidneys were allocated according to a similar algorithm, but as DCD kidneys were not shared nationally, it was possible to employ additional constraints, typically recipient age, in their allocation. Data on UK transplant activity was obtained from NHSBT and cross-referenced locally.

Results: Compared to UK data, listed patients of all ages in our centre waited significantly less time for a transplant. Consequently, overall transplantation rates were higher for our patients and waiting-list deaths lower. This effect was most apparent for Grp C patients, whose median time to transplant of 730 days was much shorter than the national average (1357 days) and notably, comparable to waiting times for our Grp A and B patients (681 and 624 days, respectively).

Proportions of living-donor, DBD and DCD kidneys were strikingly different between the recipient groups in our centre, with Grp A patients receiving an approximately equivalent proportion of each, whereas two-thirds of the kidneys transplanted to Grp C patients were from DCD donors ($p < 0.001$). The majority of DCD kidneys were, however, still transplanted to younger recipients ($n = 131, 244, 46$ for Grps A to C, respectively), because much fewer elderly patients are listed. Transplantation was associated with a survival benefit from listing for Grps A and B, whereas survival for listed and transplanted patients in Grp C was similar.

Discussion: Local expansion in DCD kidney transplant activity improves survival outcomes from listing in younger patients, and although not conferring a survival advantage for older patients, may address inequity of access to transplantation.

P033

Have increases in organ donation had an impact on the types of donors we are offered – the Portsmouth perspective over the last 6 years

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Introduction: It is well documented that donation rates in the UK have increased in the last 5 years. Our aim was to see what impact this has had on our unit in terms of service provision and the types of donor kidneys we are being offered. The UNOS KDRI is a tool that can be used to help stratify the quality of the deceased donor kidneys using various donor criteria and linking this to graft outcomes.

Methods: Retrospective review of kidney offers 2008-2013 inclusive. The KDRI score was not used to help with the decision to accept a kidney but has been used retrospectively to help assess the quality of the kidneys offered. Graft outcome was assessed on function at 1 year (median MDRD GFR (ml/min)).

Results: We received 651 kidney offers in this time period. There was a 50% increase in offers from 2008-2013. 250 kidneys were declined during the study period. The percentage of offers declined annually increased each year from 2010-2013 (18%, 28%, 47%, 53% respectively). At the point of referral the most common reason for decline was a donor history of malignancy. The mean KDRI of offers declined has increased annually since 2010, from 1.27 in 2010 to 1.58 in 2013 whilst the mean KDRI score of kidneys transplanted has remained the same (1.37 in 2010 and 1.35 in 2013). We accepted 401 kidneys over the 6 years of which 279 proceeded to transplantation. The most common reason for not proceeding after accepting a kidney was the persistence of cardiac output in the donor after withdrawal of treatment. Despite the availability of more marginal organs for transplantation, the graft function at one year has improved from 45.6ml/min in 2008 to 49.9ml/min in 2013.

Conclusion: Donor rates have gone up over this time period whilst the workforce supporting this increase has not changed. Most of these offers occur out of office hours which has a major impact on the service that can be delivered by our consultants. Despite an increase in marginal donors being offered (by KDRI measurement) we have been consistent with our acceptance criteria and this has led to an improvement in 1 year graft function over this period.

P034

Cadaveric kidney allocation system: safely proceeding on a fast track

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Introduction: The implementation of the fast track kidney offer system (KFTS) was promoted to increase the number of kidneys available for transplantation. The aim of this study is to compare the outcome of kidney transplants allocated through the KFTS and of those offered through the National Allocation Scheme in terms of graft function and patient and graft survival in the first post operative course.

Methods: We conducted a retrospective audit of all the cadaveric kidneys offered through the KFTS and transplanted at this Center from 1-12-12 to 31-10-14. Data was collected on donor's characteristics, graft function, surgical complications, actuarial patient and graft survival.

Results: A total of 156 kidneys were transplanted. Of these 122 (78.2%) were allocated through the national allocation scheme while 34 (21.8%) through the kidney fast track system. 48.45% of the nationally allocated kidneys were DCD against 32.4% in the KFTS group. Delayed graft function (DGF) rates were 30.5% and 16.7% in the national allocation group and in the KFTS group. In the KFTS 80% of DGF was amongst the DBD kidneys. Primary non function (PNF) was observed in 2 cases (1.7%) in the first group and 1 case (3.3%) in the second. There were 3 deaths in the National Allocation Group, 2 with non working grafts, 1 with functioning graft. In the KFTS there were 2 deaths with a functioning graft and 1 nephrectomy due to thrombosis. Postoperative complications requiring relaparotomy were 6.7% in the first group and 6.6% in the KFTS group. Actuarial data from the KFTS group show that at current time the median eGFR and creatinine values are 42.3mL/min and 157.5 umol/L, with a patient survival rate of 93.5% and a graft survival rate of 96.7%.

Discussion: Preliminary data of kidney transplants from KFTS suggest that these organs can safely be transplanted and that the immediate post operative outcomes do not differ from those of kidneys allocated nationally.

P034.1

Increasing organ donation in the North West South Asian community through strategic intervention

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Background: A disproportionate number of South Asians (SA) are waiting for transplants because suitable matches are often found between people of same ethnic group. There is limited understanding on the reasons of scarcity of SA organ donor registrants (ODR) and deceased donors. This abstract seeks to explore, recognize and overcome the barriers to increase the number of SA ODR and actual donors and measuring the impact of different education approaches.

Method: Progressed in two sequential phases. *Phase One* used a sequential explanatory mixed-methods approach and applied Health Belief Model (HBM). Questionnaire survey (n=907), in-depth interviews (n=10) to understand beliefs, barriers, awareness and depth of organ donation shortage and to identify SA community suggestions/ interventions to overcome the barriers. *Phase Two:* Implementation of three different educational approaches: (1) Five GP practices with a high SA patient population recruited as educators/recruiters to ODR (2) Education and training for Specialist Nurses for Organ Donation (SNOD's) to develop skills/confidence to approach SA families (3) Peer education and media campaign supported by network of influential community/religious leaders.

Results: Out of 907 SA individuals (largest UK study, on organ donation among SA in the UK), 55% did not know about organ donor registration, people mistrusted health professionals, and misinformed regarding religious objections to organ donor registration despite 88% having higher education. More than 2,800 SA organ donors were recruited through peer education in 24 months.

Discussion: Provided an in depth understanding on reasons of scarcity of SA organ donors and informs policy to provide a comprehensive evidence base of best education approach and the pivotal role of a SA co-ordinator alongside religious leaders to increase SA organ donors. Draws on the HBM theory and uses the concepts throughout the education approaches which offer a concrete and simple framework to better understand the priorities for education on organ donation topic. Acknowledged the weakness of the current organ donation education programmes and recommends a different educational approach concentrating on public as well as primary and secondary health professionals in order to improve the organ donation rate in the future

Category: Donation - Living Donor Workup

P035

The successful launch of an interactive website dedicated to information on living kidney donor transplantation

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Introduction: The internet is increasingly used to find reliable information about living kidney donation (LKD) and transplantation (LKT). Therefore, an easily accessible, interactive website was developed with the aim of raising awareness of LKD and to inform and interact with potential donors and recipients (www.livingdonation.eu). The website includes general information on LKD, LKT and personal stories of donors and recipients. It is also possible to get in touch with a transplant professional to answer questions online or to indicate that donation of a kidney is considered. The website aimed to raise awareness of LKD, to inform potential recipients and donors, to interact with them and to get in touch with potential donors.

Methods: Data of all web-visitors between the launch of the website in March 2014 until November 2014 were included. Web-metrics were used to measure reach (unique/returning visitors, shared blogs). Interaction was measured by the number of questions asked to the transplant professionals. Donation intention was measured by the number of submitted donation forms. Actual kidney donation was measured by a follow-up of donors who submitted the donation form.

Results: On average, more than 500 unique visitors were recorded each month. From the total number of visitors, 38% visited the website frequently. Several blogs and personal stories were shared on facebook, which led to a greater reach (>2000 visits). There were 37 questions asked to the online panel of transplant professionals and 22 persons indicated they considered donation by submitting the donation form. Most of them were unspecified donors (N=17). This resulted in 1 donation so far. One person is on the waitlist for donor nephrectomy, and 5 potential donors are still in the evaluation process. Eight persons were referred to other Dutch transplant centres for geographical reasons. Four persons are still considering donation. Three persons decided not to donate.

Conclusion: The easily accessible website is well-used and has considerable reach. Potential donors and recipients gratefully use the possibility to interact with professionals. The website resulted in a substantial number of potential unspecified donors.

P036

Donor comprehension of provided information during informed consent process in live donor nephrectomy

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Introduction: Since living kidney donors are a unique group of “patients”, undergoing surgery for the benefit of someone other than themselves, safety and informed consent is even more important than in other surgical procedures. Current literature demonstrates great variations in informed consent practices. Donors report varying degrees of satisfaction with the information and preparation for live donor nephrectomy.

Methods: Thirty potential living kidney donors were observed during their preoperative surgical outpatient clinic visit. Provided information was scored using standardized checklists, and team members (two consultants, three fellows and two specialist nurses) received an “informer score” for each consult. Immediately after giving consent for donor nephrectomy, donors received a questionnaire testing their knowledge of the upcoming operation. In addition, demographic data and baseline donor characteristics were documented.

Results: There were marked variations between the information provided by different informers. Informers scored an average of 12 points out of 20 (range 7-20). Median donor score was 7 out of 20 (1.5-10). Donor comprehension of duration of hospital admission and convalescence was very good; 87% (N=26) had the maximum score. Comprehension of surgical technique (median 1 out of 4 points) and short term complications (median 3 out of 9 points) was mediocre. Only 11 donors (37%) understood there was a possibility of long term complications. Risk of death was mentioned 27 times (90%) by the surgical team but reproduced by only six donors (20%). No correlation between type of informer and donor comprehension could be demonstrated, nor did we find a correlation between donor characteristics and comprehension.

Discussion: Information provided to potential living kidney donors varies among different informers and relevant details are not always disclosed. Donors do not recall all provided information, not even immediately after the surgical consult. Standardizing the informed consent process is one way of further improving the care for living kidney donors. Further analysis of this process is necessary to achieve this goal.

P037

Caregiver burden in living kidney donors

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Introduction: Many living kidney donors are primary caregivers to their recipient. The psychological impact of primary caregiver status in living donation has not previously been investigated. The aims of this study were to quantify the proportion of donors with primary caregiver status and to determine whether primary caregivers demonstrated increased psychopathology. The hypothesis stated that primary caregivers would demonstrate a greater improvement in scores than non-primary caregivers due to the improvement in their own lives as a result of transplantation.

Methods: 100 living kidney donors completed questionnaires prior to surgery and at 3 and 12 months post-operatively. Questionnaires contained validated measures of wellbeing, mood, distress, stress and anxiety.

Results: 43 donors were primary caregivers. The majority were either parents (53.5%) or spouses (41.9%). Primary caregivers experienced worse pre-operative psychological scores; including lower personal wellbeing (31.2 vs. 27.1; $p < 0.001$) and mood (0.81 vs. 0.33; $p = 0.11$) 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; $p = 0.001$). At 3 months the 2 groups were no longer significantly different, principally due to improved scores in the primary caregiver group. By 12 months primary caregivers returned to having significantly higher distress, stress and anxiety and lower mood.

Discussion: This study has demonstrated that donor primary caregiver status is associated with inferior pre-operative psychological scores. Despite an improvement at 3 months, distress, anxiety, stress and mood remain significantly worse at 12 months. 3 months scores may reflect a post-transplant euphoria associated with the recipient being relatively well after transplantation. 12 month scores may represent a realisation that transplantation is associated with its own issues and complications, which in turn are a source of psychological distress. Pre-operative identification of primary caregiver status and interventions to improve psychological wellbeing prior to donation may be beneficial to donors.

P038

Incompatible living donor kidney transplantation and psychopathology in living donors

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Introduction: Incompatible living donor kidney transplantation is associated with increased peri-operative and post-operative risks to the recipient, including early graft loss and death. Very little research has been performed into the psychological impact of incompatible transplantation on living kidney donors. The aim of this study was to determine whether living kidney donors to incompatible recipients demonstrated psychopathological differences before donation.

Methods: 100 living kidney donors completed psychological questionnaires prior to surgery. Questionnaires contained validated measures of wellbeing, mood, distress, stress and anxiety and questions specific to donation and transplantation.

Results: 20 donors donated to incompatible recipients (15 blood group incompatible, 5 HLA incompatible). Donating to an incompatible recipient was associated with being asked to donate (rather than volunteering) ($p=0.002$). Incompatible donors had higher pre-operative distress (12.3 (SD 4.61) vs. 9.7 (SD 4.40); $t(92) = -2.18$, $p=0.032$) and higher pre-operative anxiety (13.5 (IQR=7) vs. 10.0 (IQR=5); $U = 1,047.0$, $p=0.009$) when compared to compatible donors. Incompatible donors thought about the process of donation more than compatible donors ($p=0.043$) and worried significantly more about something going wrong for their recipient ($p=0.007$).

Conclusions: This is the first study to show that living kidney donors donating to an incompatible recipient demonstrate increased distress and anxiety prior to donation. Incompatible donors worry more about the process of donation and adverse recipient outcomes. Whilst this provides reassurance that the increased risks of incompatible transplantation are registering with living donors (and therefore provides evidence in support of informed consent) it is important that donors are provided with an opportunity to discuss specific concerns with the transplant team and for additional support measures to be implemented where necessary.

P039

Evaluation of living kidney donors, is the split function isotope test useful?

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Introduction: Live Donor Kidney Transplantation (LDKT) remains the gold standard treatment for end stage renal failure (ESRF) due to excellent graft and patient survival. BTS guidelines stipulate that measurement of estimated glomerular filtration rate (eGFR) must be assessed prior to donation. In addition CT angiography, followed by isotope scanning are performed if there is a >2cm size difference between the kidneys to assess anatomy and differential function.

Aims: To investigate the role of isotope scanning in the decision making process in LDKT.

Methods: Retrospective analysis of live kidney donors (Jan 2012- Dec 2013) at a single centre was performed. All donors underwent medical assessment and CT angiogram and isotopic GFR split function test.

Results: The investigations for 119 patients (mean age 49 SD12 years; 54.6% female and the median isotope GFR 90 mls/min/1.73m² (range 64 – 116) were reviewed. CT angiography showed the median size of left and right kidneys were 10.8cm (range 8.4cm – 13.5cm) and 10.7cm (range 8.4cm – 13.4cm) respectively. The median split function was 50% bilaterally (range 41–59%). There was a significant correlation of kidney size with split function $r = 0.3$ ($p = <0.0001$) in the left kidney but a weaker correlation with the size of the right kidney $r = 0.15$ ($p = 0.05$). Seven cases demonstrated a >10% difference in split function, none of these cases had a size discrepancy >2cm. Of 119 donors, only one had >2cm size difference on CT angiogram (L9cm, R11cm), but the split function was <10% different. There was only one donor who required split function testing according to guidelines. Only 5.9% (n= 7) had differences in function of >10% indicating that few donors fall into this category.

Discussion: The results of this study confirm reports that a CT angiogram, which provides anatomical information as well as size, can be used to evaluate and predict the function in the majority of living donors without the isotope GFR split function test potentially generating both temporal and financial savings.

P040

Additional findings with CT and chest X-ray when assessing suitability for living kidney donation

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Objectives: To assess the incidence of additional findings with computed tomography (CT) and chest x-ray when assessing suitability for living renal donation and determine etiology and consequences

Methods: From 2011 to 2013 a total of 196 consecutive living renal donors were retrospective analyzed with regard to additional findings on the preoperative CT scan and chest X-ray. In addition, all patients who were rejected for donation were also analyzed.

Results: Additional findings were found in 49% of patients. The most common findings were benign cysts (55%), hemangioma (8%) and atypical findings of unknown origin (8%). The kidney and liver were the most common locations (41% and 38% respectively). About 50% patients who showed additional findings received further medical examination. Ultrasound, MRI and CT were performed most frequently as additional imaging study. In general <5% of all screened patients were rejected for donation based on additional findings.

Conclusions: Additional findings in potential living renal donors are very common and are usually located in kidney or liver. Due to improved radiological imaging techniques the incidence could become even higher and lead to over diagnosing and false positive results.

P041

Kidney paired donation programmes in the United Kingdom and the Netherlands

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Background: Living donor kidney exchange has become an efficient solution for recipients with a blood type or cross-match incompatible donor. A national kidney paired donation programme was established in The Netherlands (NL) in 2004 and in the UK in 2007. Here we describe the 10 years experiences of NL and the 7 years experiences of the UK. Methods: In the UK, with a population of 64 million inhabitants, 24 transplant centres participate in a national kidney paired donation programme. In NL with a population of 17 million inhabitants, eight centers agreed on a common protocol. Both programmes distinguish several steps; registration computerised matching, cross matching, and transplantation within or outside the programme. Both countries collected data of each step.

Results:

	UK 7 years	NL 10 years
Registered patients:	1043 (149 per year)	614 (61 per year)
- HLA incompatible	63%	42%
- ABO incompatible	36%	57%
- Compatible	1%	1%
Patients with PRA 95-100%	35%	8%
Outcomes of registrations:		
- transplanted in programme	29%	38%
- transplanted outside	39%	39%
- de-listed	9%	9%
- paired donation waitlist	23%	14%

Conclusion: In the 10 years of the Dutch programme 38% of the patients had received exchange kidneys compared to only 29% in the UK programme, resulting in 23% of the UK couples registered still waiting for the next run, compared with 14% in NL. One reason for this difference is that highly immunised patients are 35% of the UK programme compared with 8% in NL. Other possible explanations for the differences between countries might be the longer term experience in NL and/or the higher density of participating transplant centres per million inhabitants.

P042

Improving referral centre live kidney donor work up time cuts waiting time for donor surgery

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Introduction: Kidney transplantation from a living donor offers the best patient and graft survival for the majority of patients with end stage renal disease. Outcomes are optimal if the transplant is pre-emptive hence the importance of timely work up of donors.

Intervention: A dedicated live donor pathway and 'one stop' clinic with physician assessment, isotope renogram and CT angiography was set up in 2012 in our centre. The effect of this pathway on time taken to work up donors locally and on time taken from work up to donor surgery at the local transplant centre was evaluated.

Results

Year	Number of potential live donors completing medical work up	Mean time from start of specialist nurse assessment to completion of medical work up	Mean time from start of Specialist nurse assessment to transplantation at local transplant centre
2010-11	56 (over 2 years)	97 days	361 days
2012	43	38 days	268 days
2013	46	30 days	253 days
2014	41	27 days	184 days

Conclusion: Time taken to work up kidney donors locally has more than halved. This has significantly reduced waiting time for donor surgery and contributes towards improving rates of pre-emptive living donation.

Category: Donation - Extended Criteria Donors

P043

The effects of optimisation of the allocation time in kidneys from controlled donation after circulatory death

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Introduction: In the Netherlands allocation of DCD-kidneys was restricted until circulatory arrest. Since studies indicated that shorter Cold Ischemia Time (CIT) leads to a better transplant outcome, we intervened by starting the allocation process prior to circulatory arrest takes place. The purpose of this study was to evaluate the effects of this intervention.

Methods: We collected data from controlled DCD donors in the Netherlands from 1-3- 2013 until 1-9-2013 (control group with restriction) and 1-3- 2014 until 1-9- 2014 (intervention group). The main outcome was the mean CIT. Between the groups we also compared the time periods between the times of: registration, allocation, circulatory death and acceptance of the organ. And we collected the data on the number of rejected offers and rescue allocation (centre offer instead of patient offer in case of impending loss of the organ).

Results: After intervention the allocation started 3.8 h before the circulatory death and resulted in definitive acceptance of the kidney only 0.2 h after circulatory death vs. 3.9 h (control group). The CIT was 12.8 h in the intervention group and 14.5 h in the control group ($P < 0.05$). The part of registered kidney donors that were eventually used for transplantation was significantly lower than before intervention (62% vs. 80%). No differences were found in the duration of kidney allocation, number of rejected kidney offers or number of rescue allocations.

Discussion: It can be concluded that if kidneys are allocated before circulatory death, CIT can be kept significantly lower. However, at the time of ventilator switch-off it is hard to predict whether circulatory arrest will take place within 2 hours, so that the kidneys remain usable for transplantation. Therefore there is a trade off between the number of unsuccessful donor procedures and shorter CIT.

P044

Expanding the donor pool: a national survey and case series of dual kidney transplants (DKT)

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Introduction: Dual kidney transplantation (DKT) involves transplanting both kidneys from a single deceased donor into one recipient, where the kidneys are deemed 'unfavourable' for single kidney transplantation (SKT). The aims of this study were: 1) to explore acceptable donor and recipient criteria for DKT amongst UK transplant surgeons; 2) to review outcomes of DKT in a single centre.

Methods: An online survey (donor & recipient criteria) was distributed to consultant surgeons in all UK transplant centres. In addition a retrospective case series DKT study was completed at our centre from 04/2013 to 11/2014.

Results: Survey: 51 respondents; 89% worked in centres that perform DKT.

DONOR CRITERIA		RECIPIENT CRITERIA	
Variable: % would consider		Variable: % would consider	
Age < 55 years	49%	Age <55 years	44%
Age >80 years	51%	Age >75 years	47%
Anti-hypertensive : 3 or more	49%	BMI <20	55%
Type 1 Diabetes > 10 years	46%	BMI >40	3%
eGFR <40	24%	LVEF <30%	6%
Proteinuria + (30mg/dl)	70%	Previous PCI >2 vessels	47%
AKI	65%	PKD as cause of ESRD	70%
Requiring haemofiltration	58%	Pre-dialysis	28%
Haemofiltration for >48 hours	24%	< 1 year dialysis dependent	69%
No pre-transplant biopsy	43%	Any age, No dialysis options	76%

Case Series: 13 DKT's. Mean donor age was 71 years (63-79). 23% had diabetes. 77% were DCD donors, 62% had hypertension. Mean recipient age was 65 (49-75), mean serum creatinine at 1, 3 & 6 months was 198, 148 & 128 $\mu\text{mol/l}$. DGF occurred in 38%. One recipient developed a lymphocele. A single kidney was explanted due to renal vein thrombosis. No postoperative deaths or PNF occurred.

Conclusion: There are no internationally-agreed criteria for DKT. This national survey has demonstrated wide variation in national consensus as to acceptable donor and recipient criteria. Outcome from this small single-centre case series demonstrates that DKT is feasible and successful in expanding the donor pool.

P045

Early single centre results of dual kidney transplantation from marginal donors

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Background: With the increasing shortage of donor kidneys a constant review of organ quality and utilisation is required. Getting any positive result from a potential donor is superior to rejecting the organs outright. The major reason for rejection of potential kidney donors is age coupled with a positive past medical history, especially of Diabetes Mellitus (DM) and Hypertension (HTN). The results of graft survival and renal function from marginal donors with these characteristics has been demonstrated to be inferior to Standard Criteria Donors (SCD) in the past. The implantation of both kidneys from a marginal donor into the same recipient is gathering momentum.

Methods: A Dual Kidney Transplant (DKT) policy was developed at our centre. Selection criteria included a) DCD donors older than 70 years of age, b) DCD donors older than 65 with DM, HTN or both; and c) DBD donors older than 70 years of age with DM, HTN or both. Recipient exclusion factors were DM, Polycystic kidney disease, severe cardiovascular disease, treatment with Clopidogrel or Warfarin and BMI > 31. Both kidneys were implanted on the same side (ipsilateral). We compared outcomes of consecutive DKT between Feb 2011 and April 2014 with our historic single kidney transplant recipient group with identical donor criteria to the DKT group. Data was collected prospectively in the DKT group and retrospectively in the earlier single transplant group.

Results: Twenty Nine recipients received DKTs, of which 85.2% were from DCD donors. There was a higher incidence of HTN (77.8% vs 46.8%) and DM (18.5% vs 8.5%, $p=0.02$) among donors in the DKT group. Also, mean donor age was higher (76.5% vs 73%) though not significant. In contrast, the incidence of delayed graft function (DGF) was lower in the DKT group (74.1% vs 78.7%); and mean eGFR was superior at six months (58 vs 37), 12 months (66 vs 36) and 36 months (42 vs 36).

Conclusion: Results show that DKT delivers superior mid-term function compared to single kidney transplants from similar donors, which are still considered not suitable for transplantation by many centres. Longer term results are awaited and required for a nationwide policy.

P046

Outcome of expanded criteria (ECD) versus standard criteria donor (SCD) kidney transplants after practice change

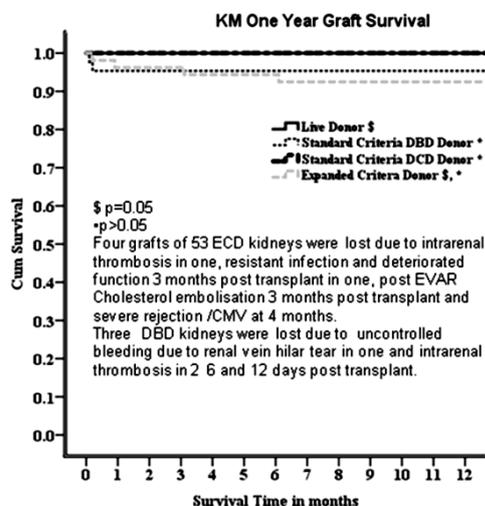
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Introduction: While ECD kidneys are considered a source of kidney grafts, they are considered suboptimal compared to SCD. We present the outcome of ECD compared with SCD and live donor kidney transplants.

Subjects and Methods: All kidney transplants performed between Jan 2013-Feb 2014 were reviewed. This period reflects expanding the deceased donor acceptance criteria. A total of 165 kidney transplants included 49 live donors (LD), 63 SCD (43 DBD and 20 DCD) and 53 ECD (32 DBD and 21 DCD). Six ECD kidney pairs were utilised as Dual. ECD is defined as a donor ≥ 60 or 50-59 years old with at least two co-morbidities including hypertension, cerebrovascular accident (CVA) as a cause of death, and pre-retrieval creatinine $>132.6 \mu\text{mol/L}$.

Results: There was no significant difference in gender, age and co-morbidities between the 4 groups' recipients. There was no significant difference in cold ischemia time between SCD (DBD, DCD) and ECD groups. There was significant difference in delayed graft function (DGF) between ECD (17%) and LD (6%), ECD and DBD (11.6%) and ECD and DCD (40%) group ($P < 0.05$). There was no significant difference in 3 months and 6 months creatinine between ECD and SCD groups. All recipients are alive except a DBD recipient due to CVA after >13 months.



Conclusion: ECD kidney transplants offer a comparable outcome to SCD kidney transplants. DGF was noted to be higher in ECD and DCD groups but the majority of these kidneys recover.

P047

One year outcomes and quality of life measurements in 127 ECD recipients-a single centre comparative study

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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 $>1.5\text{mg/dL}$. They can be sub-divided into a junior group (under 70yrs, jECD) and a senior group (70yrs and over, sECD). Outcome data and measurement of quality of life (QOL) from such donors is limited.

Methods: We analysed 1 year results for all deceased donor (DD) kidney transplants performed at our centre in 2012 & 2013. Patients were also asked to complete a QOL questionnaire including Life satisfaction (Satisfaction with Life Scale), Mood (Perceived Health Questionnaire-2), Distress (General Health Questionnaire) & Health-related quality of life (SF12).

Results: Of 253 DD transplants, 126 (49.8%) were from standard criteria donors (SCD) and 127 (51.2%) from ECD. 13 patients were lost to follow up. Of the ECDs, 86 were jECD and 40 were sECD. There were 5 deaths with a functioning graft, 3 SCD (at day 13, 17 & 57), and 2 ECDs (at day 104 and 132). All-cause graft loss was 13 (5%) [7 (2.8%) SCD, 8 (3.2%) ECD, 5 (5.8%) jECD & 3 (7.5%) sECD]. The Karpinsky-score was significantly different ($p < 0.001$) between 85 SCD biopsies (mean 2.67, SD 1.5) and 89 ECD biopsies (mean 4.19, SD 1.4). Primary non-function rates were 2.4% for SCD, 5.5% for ECD, 3.5% for jECD and 10% for sECD. Delayed graft function rate was 41% in the SCD, 51% in ECD, 51% in jECD and 53% in sECD. Mean MDRD eGFR was significantly higher in the SCD group than the ECD group at 3 months (47 vs 34; $p < 0.001$) and 12 months (49 vs 36; $p < 0.001$). There was no difference in GFR between jECD and sECD recipients ($p = 0.289$) and 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. Of the 127 patients who completed the QOL questionnaire, there was no statistically significant difference in any of the quality of life measures between the different categories (DBD vs. DCD; SCD vs. ECD; Single vs. double) $p < 0.005$

Conclusions: Even though there is no significant difference in patient or number of grafts surviving at 12 months ($p = 0.0690$ and $p = 0.087$) or QOL, eGFR is significantly reduced in ECDs. This should form part of consenting such recipients prior to transplantation.

P048

Two year outcomes in expanded criteria donors (ECD) recipients

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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 $>1.5\text{mg/dL}$. Diabetic donors are also considered to be marginal donors. The use of these organs has recently increased and recorded outcomes are limited.

Methods: We analysed results for all deceased donor (DD) kidney transplants performed at our centre in 2012 and followed them for two years. We compared ECD with Standard Criteria Donors (SCD). Outcomes included patient and graft survival at 24 months, Karpinski score and 24 month MDRD GFR. We also looked at diabetic and hypertensive donor outcomes in both ECD and SCDs.

Results: Of 101 DD transplants, 50 (49%) were from SCDs, 51 (51%) were from ECD, 8 (8%) were diabetic and 30 (30%) were hypertensive. There were 2 deaths with a functioning graft. 24 months patient survival was 97.7% in the ECDs and 98.1% in SCD's ($p=0.942$)- both donors were hypertensive. All-cause graft loss rates at 24 months were 9 (9%) in total. 24 month graft survival was 86.8% in ECD's and 94.4% in SCD ($p=0.127$) Four of these were hypertensive and none were diabetic. Mean MDRD GFR was significantly higher in the SCD group than the ECD group at 24 months (55 vs. 40 $p<0.001$)

There was no difference in mean GFR of recipients from diabetic donors or hypertensive donors ($p=0.56$ and $p=0.13$ respectively) in the ECD group or in the SCD group ($p=0.17$ and $p=0.52$ respectively) There was no difference in mean Karpinsky score from diabetic donors or hypertensive donors in the ECD group ($p=0.03$ and $p=0.34$) or the SCD group ($p=0.671$ and $p=0.792$)

Conclusions: Two year patient and graft survival was not significantly different in the ECD and SCD groups whereas two year GFR was significantly higher in SCD vs ECD. Diabetes mellitus and hypertension did not independently worsen GFR or Karpinsky score in both ECD and SCD groups. We acknowledge the small sample size of diabetic donors however this study should prompt further investigation into recipient outcomes using ECD kidneys.

P049

Determination of death after circulatory arrest by intensive care physicians

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Introduction: The use of organs from donation after circulatory death (DCD) donors is increasing in many countries. The determination of circulatory death is an essential part of DCD donation. However, in contrast to the criteria for brain death, which are generally well defined and accepted with clear protocols, clearly defined criteria for determination of circulatory death are so far not available. The primary objective of this study was to describe the current practices of determination of death after circulatory arrest in adults in the Netherlands by Dutch intensive care physicians. Secondary objectives included: to identify the policies and guidelines which are available to physicians, and to determine the reported occurrence of autoresuscitation (AR).

Methods: To assess determination of death practise, the Determination of Cardiac Death Practices in Intensive Care (DDePICt) Survey was used. The questionnaire consisted of eight questions about the determination of death, a format of eleven tests used to determine death, constructed using a 5-point Likert scale (from never to always) and one question about AR.

Results: The response rate was 54%, representing the opinion of 311 Dutch intensive care physicians caring for adult patients. Most respondents (44%) were not known with a guideline or written policy for the determination of death after circulatory arrest and learned from clinical practise. The most used tests were flat arterial line tracing, flat electrocardiogram (standard 3 leads ECG) and fixed and dilated pupils. Tests that were rarely used were absence of pulse by echo Doppler, absent blood pressure by non-invasive monitoring and unresponsiveness to painful stimulus. Seventy-five percent of respondents reportedly 'always' performed 2 to 5 tests. No diagnostic test or procedure for death determination was uniformly performed. Almost 80% of the intensivists reported that a standardized method of the determination of death after circulatory arrest was required. Thirty-seven percent reported witnessing AR, after withdrawal of treatment or after unsuccessful resuscitation, 53% occurred within two minutes after asystole. Six respondents witnessed AR in a patient whom life support had been withdrawn after more than 5 minutes after asystole.

Discussion: This large nationwide survey about the determination of death after cardiac arrest by intensive care physicians in the Netherlands, shows an extensive variability in the practice of determining death after circulatory arrest. There is a need for guidelines and standardization of the determination of circulatory death, especially if organ donation follows death. The phenomenon of autoresuscitation is reported, not only after unsuccessful resuscitation, but also after withdrawal of life support, which requires attention in further studies.

Category: Ethics Law and Public Policy

P050

Prisoners as living kidney donors: unlocking the potential

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Living-donor kidney transplants make up a large proportion of kidney transplantation in the UK. Kidney donation by prisoners is lawful and draft guidelines released by the British Transplantation Society recommend prisoners be permitted to donate in restricted circumstances. Minimizing the impact of imprisonment on ability to undergo living donation is important to prevent any reasonably avoidable limitation to kidney availability. In discussing the acceptability of kidney donation by prisoners, three main perspectives are of value: transplant recipients, crime victims and prisoners themselves. These perspectives must also be acknowledged when considering the possibility of expanding prisoner kidney donation. Decreasing restriction of living kidney donation by prisoners appears to be acceptable from all of these three perspectives, as long as the donation process can be safely managed. Related directed recipients would have a greater chance of receiving a transplant when required, as opposed to possibly limiting the timing of treatment. Non-directed recipients would likely value the opportunity for transplant itself more highly than reservations about accepting a kidney that could have come from a prisoner. Victims are also unlikely to be opposed to maximizing prisoner kidney donation, as prevention of donation does not appear to be relevant to victims' interests. Furthermore, inappropriate permission of kidney donation by a prisoner because of undue pressure or coercion is improbable because the compulsory independent assessment of living donors ensures each individual prospective donor is clinically and psychologically able to donate. More consideration should be made for when denial of donation may be inappropriate, such as categorical refusal of donation based on prisoners' security category. In conclusion, kidney donation by prisoners appears to be acceptable, and the circumstances in which prisoners can donate could be expanded. Understanding the perspectives of recipients and crime victims with more certainty would benefit from further research, as current suggestions are largely speculative.

P051

Organ donation after euthanasia: a Dutch guideline

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In Belgium and the Netherlands, neither many physicians nor patients know that it is legally and medically possible to donate organs after performing euthanasia. Even though this is not a frequent occurrence, often being limited by the patient's underlying pathologies, the combination of euthanasia and organ donation has nevertheless been practiced several times in both countries.

In anticipation of the situation in which a local request for a combined euthanasia and organ donation is made, and contributing to awareness of the possibility of this combination among general practitioners and medical specialists, two Dutch university medical centres, in close collaboration with all stakeholders, are currently in the process of finalizing a multidisciplinary guideline, in which the necessary steps to follow are carefully noted, and explained.

This guideline consecutively lists the various criteria to fulfil, and the strict rules and regulations that the different participants involved, e.g. the patient, the performing physician, the transplant coordinator, the municipal coroner and the intensive care physician, need to comply with to meet all due diligence requirements.

P052

When opportunity knocks twice: dual living kidney donation, autonomy and the public interest

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Introduction: Living kidney transplantation offers the best treatment in terms of life-expectancy and quality of life for those with end-stage renal disease. The long-term risks of live donor nephrectomy, although real, are very small, with evidence of good medium-term outcomes, at least in white populations. Who should be entitled to donate, and in which circumstances, is nevertheless a live question. We explore the ethical dimensions of a request by an individual for 'dual living kidney donation', that is, to donate both of their kidneys to two recipients.

Methods: Our theoretical ethical analysis is tethered to a hypothetical case study in which a father asks to donate a kidney to each of his twin boys. We explore the autonomy of the donor and consider the boundaries that might be placed around such choices by reference to the 'public interest'.

Results: The analysis is presented in five parts: i) an autonomous offer? ii) in the Public Interest? iii) protecting the recipients iv) protecting the donor and v) protecting the community (in which we consider the distribution of collective goods, as well as the potential impact of allowing 'dual donation' on doctors and the collective goods themselves). We argue that a request for 'dual donation' can be authentic and autonomous, and that, on balance, allowing it might contribute to the well-being of all of the parties. We reflect on the potential wider ramifications, by reference to collective values, including the preservation of life.

Discussion: Whilst acknowledging objections to the prospect of allowing 'dual donation', not least by reference to the harms that the donor might be expected to endure, we suggest that there is a *prima facie* case for permitting it, provided that both the donor and the recipients are willing and that due attention is paid to such considerations as the autonomy and welfare of all parties, as well as to the wider ramifications of acting on such a request. We argue for broader interpretations of the concepts of autonomy and welfare, recognising the importance of relationships and the relevance of more than merely physical well-being. With such a holistic assessment we outline a case for allowing 'dual living kidney donation'.

P053

Have we done enough to promote organ donation in BAME population in UK? An insight into contributing factors and their possible solution

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Introduction: Organ donation from minority ethnic groups in the UK is a matter of grave concern as the demand for organs far outweighs its supply. In 2011/12, only 4% of deceased organ donations came from minority ethnic groups. Ironically, as of July 2012, these very groups made up 15.25% of the active transplant waiting list. The aim of this study is to gauge the perception of individuals from minority ethnic groups in the UK, on the causes of low organ donations from their communities, and their opinions on solutions to solve this problem.

Methods: We conducted a survey using traditional and online methods of communications with use of social media networking. Over a period of one month we received 547 responses.

Results: Majority of responded were females (58%). Responded from diverse ethnic minority groups participated in survey including Pakistani 33.4%, Indian 19.5%, Afro-Caribbean 17.9%, Chinese 12%, Bangladeshi 10.2% and others 6.7%. Muslims were 47.3%, Christian 26.8%, Hindu 15.1%, Buddhist 7.1% and 3.4% were from other religions. 71.4% supported living donor transplants as compared to 34.1% supporting deceased donor transplants. 67% people were aware of UK transplant registry but only 14.4% were registered donors. Religious/moral beliefs, fear of defacement and mutilation of the dead body and family objection accounted for 61% of refusal reasons. More than 80% of people thought that by religious education, improved awareness campaigns specially targeting minority groups and support from religious leaders and family members can significantly help in improving organ donation rates among these groups.

Conclusions: To address the issue of lack of organ donation from minority ethnic groups a new approach should be adopted tailored made according to their needs and suggestions.

P054 WITHDRAWN

Category: HLA

P055

Human Neutrophil Antigen specific antibodies as a cause of multiple positive flow cytometric crossmatches

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Introduction: Most positive crossmatches are caused by HLA specific antibody (HLA Ab). Non-HLA antibodies have been implicated where no relevant HLA Ab are detected. Human neutrophil antigen-3 (HNA-3a/b) is a biallelic system expressed on neutrophils, lymphocytes, platelets, endothelial cells, kidney and spleen. 5% of Caucasians are homozygous for HNA-3b and at risk of allosensitisation to HNA-3a.

Methods: Patient 1: 55 yrs Caucasian female, ADPKD, 6 pregnancies, transfused, 7 yrs on DD list, HLA Ab with cRF of 88%. Positive T and B cell flow cytometric crossmatches (FCXM) with 3 potential DDs and 3 LDs, auto FCXM negative. CDC XM T and B cell negative. No donor specific HLA Ab detected by Luminex® single antigen bead assay (SAB). No anti-endothelial cell antibodies detected by ELISA.

Patient 2: 65 yrs Caucasian female, ADPKD, 2 pregnancies, non-transfused, 5 yrs on DD list, HLA Ab with cRF of 8%, Positive FCXM with 3 potential DDs, auto-FCXM negative. No donor specific HLA Ab detected by Luminex® SAB. Recipients were tested for HNA-3 antibodies using GIFT and LIFT assays. Both recipients and LD for patient 1 and a representative DD for patient 2 were HNA genotyped by PCR-SBT.

Results: HNA-3a specific IgG Ab was detected in the sera of both individuals. HNA genotyping by PCR-SBT showed both patients were HNA-3b3b. Patient 1's LD and Patient 2's DD were both HNA-3a3a. Patient 1 received a LD transplant (010 HLA MM). Graft function is stable at 9 months with no rejection episodes. Patient 2 remains on the list for transplantation from a HLA compatible donor, even if FCXM positive.

Discussion: Antibodies to HNA-3a can cause a positive FCXM in HNA-3b homozygous individuals. Recipients will have multiple positive FCXMs as 95% of donors express HNA-3a. The pathological significance of HNA-3a antibodies is unclear, but they are not an absolute barrier to kidney transplantation.

P056

Desensitization, rebound and accommodation

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Introduction: To date, the clinical significance of donor specific anti HLA antibodies (DSA) detected by Luminex is still unclear. The strength of an individual memory B cell pool to generate anti-donor humoral rebound responses and the accommodation capacity of recipient's immune system are probably the crucial determinants of outcome. In order to follow the kinetics of anti HLA antibodies, we studied the presence and strength of DSA levels serially in time in 3 patients during desensitization procedure in case of crossmatch positivity with living kidney donors.

Methods: DSA were measured using Luminex solid phase assay. All 3 patients needed to be desensitized in order to achieve a negative CDC test. This procedure encompasses 5- 10 courses of every other day large volume apheresis followed by low-dose intravenous immunoglobulins next to the start of standard immunosuppression.

Results: Desensitization resulted in significant decrease of DSAs consisting of both anti HLA class I and class II antibodies in all patients: in one patient no DSA could be detected after desensitization followed by a tremendous rebound against HLA- A and -DQ locus (a 5-7 fold MFI- increase compared to pre-Tx). In this patient, de novo anti HLA-B antibodies were detectable shortly after transplantation (Tx). Although a significant 2-3.4 fold decrease could be detected in the two other patients, DSA against HLA-A and -B locus remained detectable at the time of Tx with a negative CDC test result. These patients showed also a rebound after Tx but never reached the pre-transplant MFI levels. After 6 months, no DSA could be detected in all patients. Graft functions at last visit measured as serum creatinine ($\mu\text{mol/l}$) (eGFR(ml/min)) were: 108 (67), 98 (58) and 139 (33) with no significant proteinuria.

Conclusion: The kinetics of DSA in these patients signifies a common sequel of desensitization, rebound and accommodation. At the moment, a 6 months window of opportunity after Tx appears to be the critical time needed for accommodation.

P057

Historically positive complement dependent cytotoxicity cross match test is not a barrier for live-donor kidney transplantation; a pilot study

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Introduction: At present, the increasing numbers of HLA sensitized renal transplant candidates bear a need to develop new strategies to bypass the HLA barrier. One approach could be to take advantage of the kinetics in both the presence and complement binding characteristics of antibodies against HLA antigens.

Methods: Here, we report on kidney transplantation in 6 candidates (transplanted 2010-2012) with historically positive CDC cross match tests (XM). In these patients the current CDC (performed with sera 6 months till 1 year before Tx) with their donor lymphocytes were consistent negative.

Results: These patients received the standard immunosuppressive regimen consisting of CD25 mAb, prednisolone, tacrolimus and mycophenolate mofetil. The dosing and tapering scheme did not differ from routine schedule. Patient's kidney functions expressed as serum creatinine ($\mu\text{mol/l}$) (eGFR(ml/min)) at one year were : 95 (59), 94 (54), 130 (59), 66 (83), 220 (30) and 164 (38). After 2-3 years, 5/6 kidneys were still functioning with the following serum creatinine ($\mu\text{mol/l}$) (eGFR(ml/min)): 89 (63), 82 (63), 127 (60), 88 (60) and 161 (38). Protein/creatinine ratio (mg/mmol) in urine were 8, 50, 14, 140 and 100 respectively. One graft was lost due to a complicated course with opportunistic infections. 4/6 patients experienced rejection defined as acute cellular rejection, C4d negative thrombotic microangiopathy, and acute C4d positive mixed humoral and cellular rejection. In three patients donor specific antibodies were detectable. Treatment consisted of methylprednisolon, intravenous immunoglobulins and plasmapheresis when indicated.

Discussion: Live-donor kidney transplantation is feasible despite a historically positive CDC cross match test when the current CDC XM is negative with more than acceptable results on longer term. However, we need to identify patients in this particular group at risk for rejection. Desensitization treatment could be applied to prevent the occurrence of acute (humoral) rejection.

P058

Is transplant nephrectomy associated with anti-HLA antibody formation after kidney transplant failure?

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Introduction: Sensitisation to HLA antigens usually occurs around the time of kidney transplant failure and can prolong the waiting time for a second transplant, leading to inferior graft outcomes. It remains unclear whether transplant nephrectomy after graft failure can limit the formation of anti-HLA antibodies.

Methods: A retrospective analysis of 48 patients currently listed for second kidney transplant was undertaken at our centres.

Results: A transplant nephrectomy (TN) was performed in 29 patients (group A); immunosuppressive medication was gradually tapered in 19 patients without TN (group B). At the time of graft failure, there was no difference in the mean % cRF between the two groups (43 v 41, P=0.96) or in the percentage of patients with a DSA present (52 v 37, P=0.38). However at one year, the mean % cRF was significantly greater in group A (96 v 76, P=0.02) but there remained no difference in the presence of DSA (86 v 95%, P=0.64). Both groups experienced a significant increase in % cRF and % with DSA present at 1 year after graft failure compared to at the time of graft failure (all P<0.01).

Discussion: One year after graft failure, patients in our cohort had a significantly increased % cRF and DSA formation compared to at the time of graft failure. Patients undergoing a TN had a significantly increased % cRF at one year compared to those that did not undergo TN. Retrospective studies, however, are limited, as the usual indication for graft nephrectomy is rejection which is associated with an increase in anti-HLA antibody formation. Furthermore, changes in immunosuppressive drugs were not consistent in both groups and therefore this is likely to introduce bias into our study. However, we feel that this study is important as it adds to the literature and supports the need for future prospective, randomised clinical trials in this area. In addition, it highlights the importance of developing strategies to limit sensitisation at the point of graft failure. Finally, it provides useful information for power calculations to estimate the numbers of patients required for such a study.

P059

Validation of flow cytometric cross match with the BD Accuri C6

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Introduction: The Flow Cytometric Cross match (FCXM) is often used for risk establishment in organ transplantation as it has a higher sensitivity compared to CDC cross matches. Recently Becton-Dickinson (BD) has introduced a new instrument, the Flow Cytometer BD Accuri™ C6 (Accuri), as an easy alternative for the FACSCalibur™ (Calibur).

Method and results: The Accuri was validated in our laboratory and the results were compared to those obtained by the Calibur. The same test protocol for Flow Cytometric T and B cell crossmatches was used for both machines. In the procedure 3 different fluorochromes were used, CD3 PE to define the T lymphocytes, CD19 APC to define B lymphocytes and FITC anti IgG to detect antibody binding. The validation was based on several parameters: correctness (using EPT samples), detection limit, reproducibility. The comparison included more than 200 test samples and revealed a very high concordance rate (Spearman $\rho=0,91$, $p<0.0001$ for T cells and $\rho=0,85$, $p<0.0001$ for B cells). The Accuri proved to give correct and reproducible results with a comparable detection limit as obtained with the Calibur.

Conclusion: In conclusion, the BD Accuri™ C6 is a new good alternative to use for FCXM. The machine has some benefits in comparison with the Calibur. The machine is very small and half as expensive compared to the Calibur. The biggest advantage is probably the greater flexibility of this device, which makes it possible to set up templates and change compensation settings afterwards.

P060

Antibody incompatible transplantation in the UK – is access equitable?

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Introduction: Despite the success of the UK National Living Donor Kidney Sharing Schemes (NLDKSS), many patients do not achieve a match. ABO & HLA-incompatible transplantation options are well established, but confer greater risk than compatible transplantation. We aimed to establish current practice in the UK, to determine access to antibody incompatible transplantation (AIT) and inform future strategy.

Method: Electronic survey of all UK kidney transplant units, including Lead Clinicians, specialist nurses and histocompatibility & immunogenetics (H&I) staff.

Results: Responses were received from all UK renal transplant units (n=24). Of the 78 responses, 37% were by clinicians, 40% by specialist nurses & 23% from H & I staff, clinicians in 21/24 units responded (87.5%). 75% of units reported a dedicated MDM for discussion of AIT patients. 23/24 (95.8%) of units offer ABO-i transplantation (ABOi); 66.7% offer desensitisation for crossmatch positive living donor HLA-incompatible transplantation (HLAi); 56.5% of units offer combined HLA-ABOi transplantation. 25% of units without a LD HLAi program do not refer to other centres who do offer HLAi. Regarding ABOi and entry to the NLDKSS, 21% of units do not routinely test ABO titres before listing in the NLDKSS, despite 75% of those centres who do test, stating they would offer direct ABOi without entry to the NLDKSS, if baseline titre were suitable. The number of recommended runs in the NLDKSS scheme varies widely between centres, as does upper limit of baseline ABO titre. Inter-centre protocol variation was most marked for HLAi. Regarding HLAi, the commonest reasons for this not being offered related to small volume of such transplants, and consequent lack of expertise. 33% of centres reported that patients with donor specific antibody (DSA), but a negative cross match are not currently registered with NHSBT as AIT.

Discussion: ABO incompatible transplantation is offered widely, but geographical variation exists in the provision of HLAi transplantation, entry into the NLDKSS, and criteria for consideration of AIT after failing to find a match. Standardisation of testing methods and improved definition of AIT and clinical pathways are required to improve equity of access for suitable recipients across the UK.

P061

De novo donor-specific HLA antibodies after kidney transplantation are associated with donation after circulatory death and HLA-DQ mismatch

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Introduction: De novo donor-specific HLA-antibodies (dnDSA) have been associated with rejection and inferior graft survival. Purpose of this study was to investigate incidence of dnDSAs in relation to different randomized intervention studies and clinical relevance of dnDSA in relation to rejection and graft loss.

Methods: 429 kidney transplant recipients of living, brain (DBD) or circulatory death (DCD) donors with standard immunological risk (PRA <60%) were identified from 5 different randomized trials. All patients received IL2-RB induction and were stratified according to time of randomization: de novo: day 1 (N=182), early: month 6 (N=77) or late: >6 months (N=170) after transplantation between AUC-guided standard triple or interventional therapy (CNI/MMF withdrawal, conversion to mTor inhibitor). DSAs were measured before transplantation and 12 months after intervention using Luminex single antigen beads (One Lambda).

Results: Overall 12% developed dnDSA, 78% were HLA-class II, predominantly anti HLA-DQ. In the de novo group 43% developed dnDSAs, in the early group 22% and in the late group 35%. Multivariate analysis showed no significant influence of therapy or timing of therapy switch. Multivariate analysis indicated an association between DCD and dnDSA formation (OR 1.38, p=0.034). There also was a significant correlation between DQ mismatch and dnDSAs (OR 1.90, p=0.035). 64 patients with DCD donor and DQ mismatch were at highest risk: 17.2% formed HLA class II antibodies compared to 5.7% in 53 patients with DBD. In addition a significant relation between dnDSAs and treated biopsy-proven rejection (tBPAR) (OR 2.27, p=0.012) and death-censored graft loss (OR 3.32, p=0.033). Kaplan Meier analysis demonstrated inferior 15 years graft survival with dnDSAs (p=0.05).

Conclusion: In this cohort intervention in immunosuppressive regimen did not affect the appearance of dnDSA. Main risk factors for dnDSAs were DCD and DQ mismatch. The presence of dnDSAs was correlated with tBPAR and inferior graft survival. More data on MFI-thresholds and complement-binding will follow.

P062

Deceased donor HLA antibody incompatible renal transplantation without antibody removal: high incidence of acute rejection reduced by T-cell depleting induction therapy.

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Aims: Screening for HLA-specific antibodies (Ab) is routine for patients on kidney transplant waiting lists. In the UK screening is performed every 3 months, and HLA antigens to which a patient has detectable Ab are listed as 'unacceptable'. Many units use a stringent definition of unacceptable, for example any HLA antigen to which Ab can be detected with an MFI >1000 (using the Luminex® platform). Whilst this approach is effective in preventing a positive crossmatch (XM) following allocation, it also precludes the offer of organs to sensitized patients. Here we describe our experience of deceased donor (DD) renal transplantation knowingly performed in the presence of donor-specific anti-HLA Ab (DSA).

Methods: 37 patients received HLA Ab-incompatible (HLAi) DD transplants in one of two circumstances: (1) Patients in whom the threshold for 'unacceptable' for any HLA specificity was increased to a Luminex MFI >3000 (n=21), and (2) Patients with a positive flow cytometry B-cell crossmatch (FC-BXM) known to have anti-HLA-DP Ab (n=16). Since donors in the UK are not routinely DP genotyped, the presence of DP DSA was assumed, and confirmed by donor DP genotyping following transplantation. Complement-dependent cytotoxicity crossmatch (CDC-XM) using a current serum sample was negative in all patients. FC-BXM was positive in 17 (46%). The mean DSA MFI was 5240 (range 872-16356) and mean follow-up length was 32.1 months (range 2-75). All episodes of antibody-mediated rejection (AMR) and T cell-mediated rejection (TCMR) were analyzed.

Results: All patients received tacrolimus, MMF and prednisolone. Induction agents used were Basiliximab (n=15) and Alemtuzumab (n=22). No planned Ab removal was used. Death-censored 1 year graft survival was 96.3% (26/27 patients with >12 months follow-up). Acute rejection (AR) was significantly more common in those receiving basiliximab at induction compared to a T-cell depleting agent (67% (10/15: 4 with TCMR and 6 with AMR) versus 23% (5/22: 1 with TCMR and 4 with AMR) respectively, **p=0.008**, log rank test). Of the 16 patients with isolated DP DSA, 3 experienced TCMR and 3 AMR. All episodes of AMR were reversed with plasma exchange. Mean creatinine for those patients with graft function at baseline (34/37) was 133µmol/L and at 1 year was 146µmol/L (n=26). There were 4 deaths and 2 graft losses.

Conclusion: HLAi DD renal transplantation is associated with a high incidence of AR, with AMR in 27% of patients despite negative CDC-XM. Our limited experience suggests that: (1) T-cell depleting induction is beneficial and (2) donor HLA-DP genotyping should be routine practice. Given the high incidence of AR experienced by this patient cohort, and the limited potential for prospective antibody removal in the context of deceased donor transplantation, consideration should be given to the use of novel therapeutics such as Eculizumab, a monoclonal antibody directed against terminal components of the complement pathway, which has been shown to decrease the incidence of early AMR.

Nevertheless, despite high rates of AR, transplantation in these high-risk recipients is still achievable with satisfactory allograft function at up to 6 years post-transplant.

P063

New mathematical protocols for calculating binding kinetics of patient polyclonal antibody binding to HLA antigens via surface plasmon resonance experiments

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Introduction: Difficulty in determining the binding affinity for antibody antigen interactions obstructs research into the effect of how patient antibody/donor antigen affinity influences transplant outcome. Surface plasmon resonance (SPR) experiments provide detailed time series that can be used to obtain reaction kinetics, but due to complexity of antigen/antibody interactions new models are needed to interpret these data with greater accuracy. Previously we described a mathematical model that allowed for some characterization of polyclonal antibody/antigen interactions. Here we present a new model that includes the effect of antigen having multiple epitopes, allowing antibodies with different paratopes to bind simultaneously.

Methods: SPR experiments were conducted on pairings of enriched polyclonal antibodies isolated from two samples of plasma effluent with immobilised A2 and B57 HLA antigens; two patient serum samples paired with A2 and B57, and three paired with B7, B40:01 or B40.02. The time series of these experiments were used for parameter fitting and subsequent quantitative determination of binding kinetics and affinity.

Results: The novel model demonstrated a vastly improved fit, halving the residual sums of squares (RSS) for most experiments (figure 1), and eliminating systematic errors for nearly all experiments.

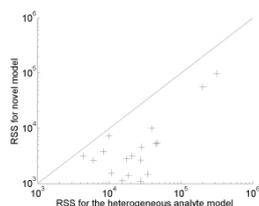


Figure 1 comparison of residual sums of squares for both models

Discussion: This measurement is quick and replicable, allowing for higher-quality systematic studies into the effects of antibody affinities for donor antigen on transplant outcomes, with potential for improved assessment of pre transplant risk stratification.

P064

Functional differences in human leucocyte antigen (HLA) antibodies directed against HLA specificities that share the Bw4 (82LR) and Bw6 (80N) epitope

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Introduction: Antibody-mediated rejection is a leading cause of renal allograft rejection and failure in which human leucocyte antigen antibodies (HLA-Abs) are most commonly implicated. Unacceptable donor antigens (UDAs) are assigned to prevent a positive crossmatch in the event of a potential deceased donor organ. For sensitised patients, UDA listing decreases the potential donor pool and can result in longer waiting times. However, it has been shown that not all HLA mismatches are equal and that functional differences exist against the same epitope when present on different HLA specificities when analysed with Monoclonal Antibodies.

Method and results: The aim was to determine whether there are functional differences between HLA-Ab specificities directed to the Bw4 and Bw6 epitopes in 11 samples (5 and 6 respectively). The functional characteristics were analysed using Luminex Single Antigen (SAg), C1q-fixing and complement-dependant cytotoxicity (CDC) assays. When tested by the SAg assay, if antibody reactivity to the Bw4 and Bw6 epitope was present, all of the specificities with the shared epitope were recognised. However a proportion of the HLA-Abs directed to the Bw4 epitope were C1q-fixing and none were CDC positive. In contrast, all of the HLA-Abs directed to the Bw6 epitope were C1q-fixing and a proportion were CDC positive.

	Number of tested specificities		
	SAg positive	C1q positive	CDC positive
Bw4	19/19	10/16	0/14
Bw6	29/29	29/29	8/15

Conclusion: The results suggest that the HLA-Ab specificities directed to the Bw4 and Bw6 epitopes may not be functionally the same. Using these findings could enable the de-listing of UDAs thus expanding the donor pool for sensitised patients.

P065

IgG4 subclass associates with early graft rejection and decreased allograft survival times in antibody incompatible transplantation

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Introduction: Donor HLA specific antibodies (DSA) represent a risk factor for early transplant rejection and influence allograft survival times. The aim of this research was to investigate the role of all DSA IgG subclasses (1-4) in the immune response in order to identify any potentially damaging antibodies and their influence on postoperative outcomes.

Methods: Samples from 80 transplants were available for the analysis, and IgG subclass DSA MFI levels were determined for all pre-treatment, peak response, and 30 day post-transplant samples. Multivariate regression analysis was performed in order to investigate the influence of DSA subclass levels and other potentially confounding variables on the risk of early rejection and graft failure.

Results: We have demonstrated that IgG4 was predictive of acute antibody mediated rejection ($p=0.003$) in the early post-transplant period and that long term graft survival times were also affected by the presence of the IgG4 in pre-treatment samples ($p=0.004$). The multiple binary regression analysis has shown that the occurrence of the early rejection was due to 3 factors: total pre-treatment IgG4 MFI levels, the highest pre-treatment MFI DSA levels and the total number of HLA mismatches. Cox proportional hazard method identified 2 significant ($p<0.05$) factors reducing graft survival times: MFI of the highest IgG and presence of IgG4 in pre-treatment samples with the hazard ratios of 161.218 and 5.945, respectively.

Discussion: These results highlight a link between the presence of IgG4 in serum before transplantation and unwanted postoperative outcomes such as acute antibody mediated rejection and long term graft failure. Therefore, IgG4 can be an additional biomarker that could be used to risk stratify kidney transplant recipients.

P066

Decision trees for small data sets: prediction of acute antibody mediated rejection in early post-transplant period in antibody incompatible transplantation

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Introduction: The limited access to the data in the area of renal transplantation and the complexity of the immunological responses to transplant require development of novel modelling approaches capable of capturing the main features of the data and allowing for prediction of post-operative outcomes.

Methods: We suggested a novel data-driven approach based on classification Decision Trees (DTs) for prediction of acute antibody mediated rejection in the early post-transplant period. The available clinical dataset featured 15 potential predictor variables including pre-treatment donor specific antibody (DSA) IgG subclass levels across 80 observations. In order to compensate for high volatility in performance due to small number of training samples, 600 separate DTs were investigated.

Results: We demonstrated that the DT approach can successfully identify the optimal hierarchy of parameters associated with early graft rejection. DT formed its predictions based on 6 out of the 15 variables including three most important: the highest MFI DSA pre-treatment level, total IgG4 MFI pre-treatment level and number of HLA mismatches. Additionally, the model provided specific levels of DSAs which associated with early graft rejection. The DT performance was evaluated in terms of classification accuracy, sensitivity and specificity separately for the training and test datasets. The best performing model achieved 86.7% accuracy during the training phase and correctly classified 85% of test cases.

Discussion: Within the limitation of the input dataset, the DT model provides an accurate prediction tool for antibody mediated rejection of renal transplants, whilst simultaneously estimating the highest risk factors and DSAs MFI levels associated with the increased risk of rejection in the early post-transplant period. The model can be used for risk factors assessment preceding transplantation.

P067

Heterogeneous immunoglobulin class levels depends on blood group of cases: high IgA response in a large population based study

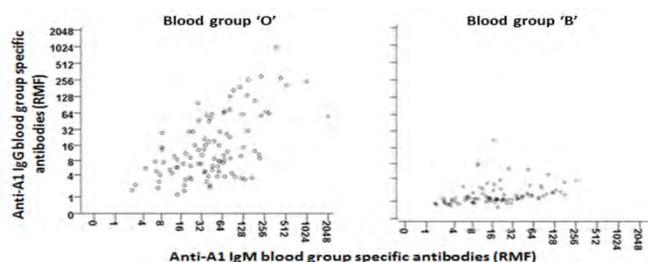
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Introduction: Higher blood-group specific antibody levels are considered a risk for rejection in blood group incompatible kidney transplantation. The risk is highest for IgG antibodies, but a rise in IgM levels during rejection has been observed clinically. IgA antibodies have not previously been studied in this context.

Method: We studied the distribution of IgG, IgM and IgA ABO antibodies in 300 healthy donors using a multi-colour flow cytometer assay. Levels of different classes were correlated between 100 cases each of blood group 'O', 'A' and 'B'. These levels were also correlated with gel-card haemagglutination assay.

Results: Correlation of levels between the assays was better for IgG compared to IgM class. Highest reactivity was observed in blood group 'O' donors for all antibody classes. There was a reduced IgG class reactivity in both blood group 'A' and 'B' cohorts compared to IgM and IgA class (see figure – shows anti-A1 antibody levels for blood group 'O' and 'B' cohorts). High levels of IgA for anti-A and anti-B were observed in this study.



Discussions: Immunoglobulin class response is heterogeneous and depends on blood groups of the cases. IgG antibody levels were lower in cases from blood group 'A' and 'B' cohorts. High IgA levels were observed in this large cohort study. The post-transplant response and role of IgA levels following ABO-incompatible transplantation still needs to be established.

P068

IgM+ antigen binding B cells in peripheral blood regulate IFN γ production in response to HLA proteins

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Introduction: Chronic antibody mediated rejection (CAMR) is a major cause of renal transplant loss. Based on previous work in our lab, we hypothesised that different phenotypes of B cells may influence different patterns of T cell reactivity to alloantigens and that an understanding of the phenotype of antigen-specific B cells is required to achieve our goal of highly tailored treatment of CAMR in each individual. Pure™ HLA proteins A*01:01 or A*02:01 were used in an indirect IFN γ ELISPOT assay and to detect HLA binding B cells in a cohort of patients with HLA A1 or A2 mismatched grafts respectively.

Results: IFN γ production in response to A1 or A2 was seen in 12/34 samples: when B cells were depleted, IFN γ spots reduced in 8/12 (=Bdep); increased in 2/12 (=Bsup) and were unaffected in 2/12 reactive and the remaining 22 non-reactive samples (=Bnon). Phenotypic analysis of whole B cells revealed no differences in gross phenotype when comparing Bdep, Bsup or Bnon. HLA binding B cells were detected in 14/34 samples from patients with A1 or A2 mismatched grafts. Detailed phenotypic analysis was performed on 8/14 samples where the frequency of HLA binding B cells was >50% above background. HLA binding B cells were predominantly non transitional and IgM+ in all of these samples. 3/8 Bdep samples had HLA binding B cells that could be phenotyped in depth; IgMhiCD45RB+ (a memory phenotype) cells represented 76 \pm 1.5% of Ag-binding cells, whereas IgM+CD45RB- cells accounted for 13 \pm 5.4%. 1/2 Bsup and 4/24 Bnon samples had HLA-binding B cells that could be phenotyped. In these, IgMhiCD45RB+ and IgM+CD45RB- cells made up 45.9 \pm 13% and 38.8 \pm 8% respectively.

Conclusion: These results complement previous data from our lab and indicate that ELISPOT reactivity correlates with the predominance of HLA binding IgM+ memory cells in patients with CAMR.

P069

Preformed anti-HLA DP donor specific antibodies are clinically significant in renal transplantation

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Introduction: Whilst preformed [PF] anti-HLA A, B, DR and DQ donor specific antibodies [DSAbs] are associated with poorer allograft outcomes secondary to antibody mediated injury, there are only a few case reports describing the clinical significance of PF anti-HLA DP DSAbs. In this study we describe the clinical importance of PF isolated anti DP DSAbs.

Results: 1273 CDC/FCXM negative renal transplant recipients [mean follow up 4.46 ± 2.50 yrs] receiving a steroid sparing, tacrolimus based maintenance regimen with monoclonal antibody induction were studied. 98 patients had ≥ 1 preformed DSAbs and 9/98 [9.2%] had an isolated PF DP DSAb. Of these 9 patients, 3/9 were sensitised via previous transplantation, 4/9 pregnancy, 2/9 transfusion and 1 unknown. DP4 was the commonest loci seen, with 4/9 having DP4 DSAb, 2/9 DP1, 2/9 DP3 and 1/9 DP17. The mean MFI at the time of transplant was 2608 ± 1039 . Allograft outcomes were compared between patients with PF DP DSAb, DSAb negative sensitised patients (S) and non-sensitised patients (NS) and the results shown in the table below. Patients with DP DSAb had increased risk of graft loss, rejection [AMR and ACR] and TG.

Survival (%)	NS	S	DP DSA	p value
Allograft	79.5	85.8	62.2	0.003
Rejection	74.2	72.9	0	0.017
AMR	91.1	59.1	41.7	0.022
ACR	80.9	78.9	72.9	0.28
TG	92.9	91.3	53.5	0.0001

Conclusion: PF DP DSAbs are rare but when present are associated with inferior allograft outcomes. Donors for patients with known PF DP HLA Abs should be typed for DP as these recipients are at higher immunological risk if the antibody is donor specific and may benefit from increased surveillance and immunosuppression.

P070

Sensitisation following the use of non-HLA matched 3rd party vessels for vascular reconstruction in renal transplantation

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Introduction: Third party donor vessels are occasionally required for vascular reconstruction, in abdominal solid organ transplantation. Whilst the current practice ensures that 3rd party vessels are blood group matched, HLA matching to the non-intended recipient is not normally performed. This practice potentially sensitizes the recipient to the non-matched HLA and may preclude future transplant from a larger pool of donors. We examined whether a series of patients receiving non-HLA matched 3rd party vessels developed donor-specific anti HLA antibodies.

Methods: Human Tissue Authority blood vessel registers and operation notes were examined to identify donor vessels and potential non-intended recipients. Donor vessel HLA status was cross-referenced with post vessel implant HLA status in recipients to identify whether donor specific antibodies to vessels had been formed.

Results: Between 2004 and 2014 five patients were identified that received 3rd party non-HLA matched vessels for vascular reconstruction during renal transplantation. Three patients (60 %) subsequently developed donor specific anti-HLA antibodies. Donor specific antibodies were not identified in the remaining two patients.

Conclusion: This data provides evidence that third party non-HLA matched vascular grafts lead to sensitization in the recipient and may preclude future transplant from a larger population of donors. Where possible a HLA matching should be performed to avoid this allogenic response

P071

New mathematical models for monoclonal antibody binding in surface plasmon resonance experiments

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Introduction: Monoclonal antibody is seeing increased clinical and pharmaceutical use. However the complexity of the interactions of multivalent antibody and non-heterogeneously scattered immobilised antigen have been a barrier to affinity estimation and the characterization of reaction kinetics. The benefits of studying monoclonal antibody are that it will help delineate the influence of affinity on the results in vitro assays, such as luminex and C1Q; and that it will allow for the systematic development of tools for studying mixtures of monoclonal antibody and patient polyclonal antibody samples that could be used in risk stratification.

Methods: ProteOn XPR was used to study 36 simultaneous interactions between HLA-protein and HLA-specific antibodies. NLC-sensor chip was used to immobilise biotinylated HLA-proteins. Two densities of HLA-proteins were immobilised (2.5 and 0.25 µg/ml) and a range of 100 to 1.6 nM concentrations of monoclonal HLA-specific antibodies were used to study the binding interactions. The experiments were performed at 37° Celsius temperature and the pH was maintained at 7.4 for running buffer. Data fitting and parameter estimation were conducted using a differential evolution algorithm, implemented using a user-contributed MATLAB Toolbox, coupled with FACSIMILE for Windows 4 (MCPA software, UK).

Results: In all but one data set the novel model performed better than the model in the literature, the bivalent analyte model. Residual sum of squares for each fit to experimental data were generally halved and antibody/antigen affinity estimates became more consistent across multiple ligand densities/ antibody concentrations.

Discussions: This development allows for new possibilities in measuring antigen/antibody reactions, particularly because modelling in detail the way binding complexes are affected by the multivalence of a single antibody is a necessary step towards understanding the development of larger complexes of antigen and polyclonal antibody, and as a result predicting patient outcomes with experiments on samples of patient antibody.

Category: Histology

P072

Fibrosis, not quantitative NGAL-staining, in day-10 protocol biopsies predicts prolonged duration of functional delayed graft function in a cohort of DCD kidney transplant recipients

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Introduction: Extended criteria deceased kidneys are associated with prolonged delayed graft function and worse patient survival. Therefore it is important to identify factors in marginal donors that affect kidney quality and function. We validated a reported donor scoring system from donation after brain death (DBD) donors in a cohort of circulatory death (DCD) transplant recipients. In addition, we related marginal donor scores, protocol biopsy characteristics and fractional NGAL excretion (FeNGAL) to duration of functionally defined delayed graft function (f-DGF) and one-year renal function (eGFR).

Methods: 92 consecutive DCD transplant recipients were included, all receiving IL2-RB induction and triple maintenance therapy (CNI, steroids, MMF). Day-10 protocol biopsies were scored according to the Banff criteria and ATN characteristics. In addition, NGAL was stained and %-surface positivity quantified using image-J. FeNGAL was calculated using day-10 urinary and serum NGAL. Statistical analysis included uni- and multi-variable binary logistic regression and ROC curves.

Results: In DCD recipients the previously reported marginal donor scoring system was also associated with impaired one-year GFR ($p < 0.0005$) and duration of f-DGF ($p = 0.002$). Multivariable analysis identified donor age, f-DGF, and mismatch degree (2DR or 1DR/2B) as independent risk factors for inferior one-year GFR. In ROC analysis this model predicted GFR ≤ 40 ml/min with an AUC of 0.87 (0.76-0.98). In histology only IF/TA scores and denudation were associated with impaired one-year GFR, increasing the AUC to 0.94 (0.88-1.00). In the analysis of patients with moderate (8-20 days) and severe (≥ 21 days) f-DGF only IF/TA score remained an independent predictor for severe f-DGF. Although NGAL staining did not discriminate, day-10 FeNGAL tended to differentiate between moderate and severe f-DGF ($p = 0.064$). Moreover FeNGAL and duration of f-DGF were strongly correlated ($R = 0.91$).

Conclusion: Also in DCD recipients a high clinical donor score was associated with inferior one-year renal function. The main predictor for prolonged f-DGF was IF/TA. In addition, sequential fractional NGAL excretion may serve as a non-invasive marker to guide management in patients with marginal donor kidneys and delayed function.

P073

Frozen versus formalin-fixed pre-implantation deceased donor kidney biopsies: which is best?

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Introduction: Some units utilise formalin-fixed pre-implantation kidney biopsies (PIKB) to assist decisions on organ usability, however, 3-4 hours are needed for sample preparation. Frozen section analysis can be performed in 15-30 mins, but doubts persist regarding its accuracy compared to gold standard formalin-fixation. We retrospectively analysed frozen PIKB to determine if the method of fixation impacted on histological scores.

Methods: Deceased donor kidneys that underwent frozen PIKB between 1.1.2006 – 1.10.2014 at our unit were analysed. Frozen biopsies were assessed using the Karpinski/Remuzzi score (0-12) and were re-scored after subsequent non-urgent formalin fixation. Biopsies with ≥ 20 glomeruli were defined as adequate. Changes in K-score, and potential impact on organ utilisation (using the Remuzzi approach: 0-3 single transplant, 4-6 double transplant, >6 discard) were assessed. Clinical decisions on organ usability were based on the frozen section analysis.

Results: Thirty-seven kidneys were biopsied from 27 deceased donors, resulting in 26 transplants (22 single, 4 double), with 7 kidneys discarded. On frozen section, 27% of biopsies were adequate, while 44% were adequate on formalin-fixation. Median frozen and formalin scores were: 0 and 1 (glomerular sclerosis); 0 and 1 (interstitial fibrosis); 1 and 1 (tubular atrophy); 2 and 2 (vascular lesions). The overall median frozen K-score was 3; on re-analysis using formalin-fixation the median score was 5. There were 6 instances when the K-score on frozen section led to a decision on usability that was different than the one suggested by subsequent formalin-fixation scoring. Two kidneys from the same donor were discarded after frozen K-scores of 7 and 7; formalin-fixation scores were 6 and 6, suggesting that double kidney transplantation should have been performed.

Discussion: Frozen-section analysis of PIKB tends to underestimate histological scores. This is likely to lead to inappropriate clinical decisions regarding usability. Formalin-fixation is preferable, except when access to histopathology services is compromised or CITs are extended beyond clinically acceptable thresholds.

P074

A comparative analysis of histological scoring in living donor renal transplants from donors above and below 60 years of age

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Background: Worldwide the population is aging. This aging population demands changes in current medical practices to fulfil requirements of new medical challenges. One such practice is living kidney transplants from donors above 60 years of age.

Material and Methods: In this present study we have compared day zero and 3 months renal transplant biopsies among living donor renal transplants from donors below and above 60 years of age. We used Remuzzi and BANFF criteria to compare their day zero and 3 months post transplant renal biopsies.

Results: Table 1: Comparison of day 0 and 3 months renal transplant biopsies using Remuzzi scoring.

Timing of biopsy	Scoring	≥ 60yrs	18-59yrs	Significant
Remuzzi day zero	0-3 (Mild)	49	169	p=NS
	4-6 (Moderate)	2	2	p=NS
	7-12 (Severe)	0	0	p=NS
Remuzzi 3 months	0-3 (Mild)	50	170	p=NS
	4-6 (Moderate)	1	1	p=NS
	7-12 (Severe)	0	0	p=NS

Table 2: Comparison of day zero and 3 months renal transplant biopsies using BANFF scoring

Timing of biopsy	Scoring	≥ 60yrs (N=51)	18-59yrs (N=171)	Significant
BANFF day zero	Acute changes			
	No	45	161	p=NS
	Mild	4	9	p=NS
	Moderate	2	1	p=NS
	Chronic			
	No	47	161	p=NS
	Mild	3	2	p<0.05
	Moderate	1	3	p=NS
BANFF 3 months	Acute changes			
	No	49	159	p=NS
	Mild	1	8	p<0.05
	Moderate	1	5	p<0.05
	Chronic			
	No	45	164	P=NS
	Mild	4	4	p<0.05
	Moderate	2	3	P=NS

Conclusion: The histological data supports clinical outcomes in LDRTx from donors above 60yrs. These organs thus form an important resource to bridge the gap between supply and demand.

The case for a National Histopathology Service for organ retrieval and transplantation: results of the first National Histopathology Audit (NHA)

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Introduction: During organ retrieval or at examination of the organ unexpected lesions may be found. Determination of the nature of these lesions and assessment of organ viability may be necessary to help the implanting surgeon decide whether to use the organs. NHSBT ODT designed a prospective audit started on 1st October 2013 for 6 months. All NORS Team and Transplant Centres (TC) participated. The Aim was to identify incidence and impact of urgent biopsies.

Definitions: Urgent biopsies (UBx) were defined as those biopsies where the report was waited in order to decide whether to proceed for retrieval or for transplantation. Type 1 biopsies were those taken for suspected malignancy, Type 2 biopsies were those taken for any other reasons (organ viability).

Outcome: Data were returned on all 654 retrievals performed in the audit period. There were **142 UBx** from 654 (21.7%) retrievals performed. Of these, there were 42 **Type 1, (29.6%) and 100 Type 2, (70.4%)**. Of the 42 Type 1 UBx a malignancy was identified in 3 out of 654 Retrievals; 0.45% (3 out of 42 type 1 Bx, 7.1%). In the Audit period there were 2322 organs retrieved of which utilized 2064 (88%). Organs Taken Accepted and Not Utilised were 258 (12%). There were 53 more livers and 182 more kidneys utilized following a UBx. 90% of UBx were sent to pathology laboratory during premium time (i.e. 'out of hours' from 7pm to 9am or weekend).

Key findings: The overall rate of UBx was higher than expected. Type 2 were significantly more than Type 1; $p < 0.0001$ (chi 2). Unexpected malignancies were rare. There were four Type 1 bx taken at TC one was malignant. Waiting for UBx result may have contributed to an increase of organs transplanted; 20% more kidneys and 16% more livers in the audit period. The majority of biopsies were taken from donors 60 years old or more; $p < 0.0001$.

Conclusion: The overall incidence of urgent biopsy in the context of organ retrieval is significant. A logistic regression analysis will confirm the real impact of urgent biopsy for organ utilization and will contribute to design a case for a national histopathology service for organ retrieval and transplantation.

P076

Histology of renal allografts with DGF provides limited prognostic information

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Introduction: DGF has been shown to be associated with adverse graft outcomes in renal transplantation. However DGF is heterogeneous histologically and the impact of various histological lesions in patients with DGF has not been previously studied. In this study patients with DGF have been classified histologically based on the 2013 Banff classification and the impact of individual Banff lesions on graft outcomes is analysed.

Method: A total of 164 patients were diagnosed with DGF based on the requirement of dialysis within the first post-transplant week between 2005 and 2013. All these patients were biopsied between day-7 to day-14 post-transplantation. The biopsies were scored by a blinded pathologist and histological scores analysed for their impact on graft outcomes.

Results: The mean tubulitis score for these patients was 0.35 with X% of patients presenting with a tubulitis score ≥ 1 . Similarly, 11% of patients had glomerulitis; 12% of patients had interstitial inflammation and 6% of patients had peritubular capillaritis. Whilst 36% of patients had tubular atrophy, only a minority presented with significant tubular scarring (3%). Similar trends were seen with interstitial fibrosis and chronic vascular changes. Significant arteriolar hyalinosis ($aah \geq 2$) was noted in 13% of the patients. Most of the patients (94%) presented with acute tubular necrosis (ATN) with a significant proportion presenting with severe ATN (34%). Despite the diverse histological changes noted in this group of patients, none of the histological parameters were associated with long-term or 1 year graft outcomes. It is noteworthy that neither tubulitis nor microcirculation inflammation was associated with worse graft outcomes in this selective group of patients with DGF.

Conclusion: To conclude, though this study reiterates the diverse histological lesions identified in patients with DGF, none of these lesions were associated with adverse graft outcomes.

Category: Immunosuppression

P077

The feasibility and safety of mTORi ab initio after liver transplantation

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Introduction: We designed a monocentric retrospective observational study to evaluate Everolimus (EVR) usage "ab initio" after liver transplantation (LT).

Material and methods: Forty-one adult patients (36M/5F, mean age was 52 ± 10.5 years) who received LT between 2009 and 2014 were included in the study. The primary endpoint was to assess the safety and feasibility of EVR after LT; the second one was to evaluate liver function, incidence of rejection and side effects, over a period of one year.

Results: LFT's were stable over the follow-up. No rejections were seen. The mean blood triglycerides level before LT was 102.76 ± 86.01 mg/dl and increased to 187.29 ± 107.59 ($p=0.0003$) after one month remaining stable over the follow-up. Four patients (9.8%) experienced surgery complication: two biliary tract stenosis recovered by stenting and two incisional hernia. Overall patient survival was 80% at one year.

Conclusions: EVR low dose regimen immediately after LT is safe and feasible when associated with low doses of CNI permitting to avoid all the side effects of standard regimens with higher doses.

P078

The reversal of iatrogenic immunosuppression-induced Kaposi's sarcoma (KS) in a renal transplant recipient treated using the mTOR inhibitor sirolimus

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Introduction: To present a case report of iatrogenic immunosuppression-induced KS in a 46 year old Nigerian cadaveric renal transplant recipient that was reversed by switching his tacrolimus to the mTOR inhibitor, sirolimus.

Method: Patient presented to a tertiary renal-transplant out-patient clinic with scattered violaceous macules, plaques and nodules consistent with a clinical diagnosis of KS 10 months post cadaveric renal transplant for hypertensive nephrosclerosis along with disabling burning pain in his feet.

Results: Serology was positive for low level BK viraemia (319 copies/ml) but HHV-8 and HIV negative. Skin biopsy showed diffuse dermal proliferation of irregular thin-walled vascular channels lined by bland endothelial cells with strongly positive immunohistochemistry for HHV-8 consistent with KS. Reduction in immunosuppression did not produce clinical improvement. Subsequent switch from tacrolimus to sirolimus (an mTOR inhibitor with established immunosuppressive and emerging anti-neoplastic properties) produced dramatic improvement in his clinical condition and clearance of BKV.



Conclusion: This case report lends further support for the use of sirolimus over tacrolimus in solid organ transplant recipients who go on to develop KS and opens up the debate as to whether targeted pre-transplant HHV-8 testing of LNA-1 (latency-associated nuclear antigen) would be helpful in identifying those patients at risk of developing immunosuppression-induced Kaposi's Sarcoma and subsequent tailoring of their immunosuppressive regime. BK virus is emerging as a possible co-factor in tumorigenesis in a number of cancers including KS and this case report lends credence to this idea.

P079

Alemtuzumab dose adjusted for weight reduces infection post-renal transplantation

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Introduction: Alemtuzumab [AL] has been increasingly used as an induction agent in renal transplantation. It causes potent lymphocyte depletion and as has been shown to reduce early rejection episodes. Given the sustained reduction in lymphocyte counts, concerns have arisen over the risk of opportunistic infection. The reported dose of AL used in transplantation is highly variable and the optimal dose is not known, although preliminary studies at our centre suggested that the optimal dose to minimise infective and rejection episodes is 0.4mg/kg.

Method: In this study, we report allograft outcomes and microbiological proven infection episodes post dose adjusted AL induction [AD] in patients receiving tacrolimus monotherapy and a steroid sparing protocol compared with a historic control group, who received a 30mg iv standard dose [SD] peri-operatively.

Results: 634 and 262 patients received the SD and AD dose respectively. There was no difference in gender, living donor, pre-emptive and ethnic distribution between the 2 groups. However, the AD group were older [52.0 ± 13.1 v 48.4 ± 13.2 yrs, $p=0.001$], more likely to be receiving a regraft [14.5% v 8.0% , $p=0.005$] and had a higher sensitisation prevalence [38.5% v 20.2% , $p=0.0001$].

Overall patient survival was 87.7% and 94.8%, $p=0.69$ and graft survival was 79.8% and 96.9%, $p=0.07$ in the SD and AD groups respectively. Rejection free survival was 74.1% and 78.4% in the SD and AD groups respectively, $p=0.63$. ACR free survival was 80.1% and 85.3%, $p=0.48$ and AMR free survival was 92.4% and 92.7%, $p=0.95$ in the SD and AD groups. DSA free survival was 71.2% and 85.1% in the SD and AD groups, $p=0.18$. However, infection free survival was inferior in the SD at 48.7% compared with 65.9% on the AD group, $p=0.03$. On multivariate analysis, factors associated with infection in the AD group were increasing age, $p=0.002$; female gender, $p=0.04$ and higher weight at transplant, $p=0.0013$.

Conclusion: This study shows that dose adjusted AL induction is associated with a reduction of overall infection rates without an increased incidence of rejection.

P080

Hydrogen sulphide as a novel therapy to reduce the nephrotoxic effects of cyclosporine

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Introduction: Calcineurin inhibitors have significant nephrotoxic side effects which can exacerbate ischaemia reperfusion injury (IRI) in renal transplantation. Novel therapeutic agents such as hydrogen sulphide (H₂S) may reduce these harmful effects. This study investigated the effects of H₂S on cyclosporine (CsA) induced nephrotoxicity.

Methods: Porcine kidneys were subjected to 15 minutes of warm ischaemia and 2 hours of static cold storage. They were reperfused for 3 hours with oxygenated normothermic autologous whole blood on an isolated organ reperfusion apparatus. Kidneys were treated with CsA during reperfusion (N=6) or CsA and 0.25 millimoles/litre of H₂S (CsA+H₂S) infused 10 minutes before and 20 minutes after reperfusion (N=6). These were compared with untreated controls (N=7).

Results: CsA caused a significant reduction in renal blood flow (RBF) during reperfusion which was reversed by H₂S [Area under the curve (AUC) RBF CsA 257 ± 93 vs. Control 477 ± 206 vs. CsA+H₂S 478 ± 271ml/min/100g.h; P=0.024]. Urine output was higher after 2 hours of reperfusion in the CsA+H₂S group (CsA+H₂S 305 ± 218 vs. CsA 78 ± 180 vs. control 210 ± 45ml; P=0.034). CsA treatment was associated with an increase in tubular injury which not reversed by H₂S (AUC Fractional excretion of sodium, control 77 ± 53 vs. CsA 100 ± 61 vs. CsA+H₂S 111 ± 57%.h; P=0.003].

Conclusion: H₂S reversed the vasoconstriction and ischaemic changes associated with cyclosporine treatment during reperfusion. H₂S has promise as a therapy to mitigate some of the nephrotoxic effects associated with calcineurin inhibitors in renal transplantation.

P081

Skin cancer and cumulative dose of immunosuppression in long-term kidney transplant recipients: a retrospective and 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. This 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 (LKTs). To assess whether SC prevalence is related to the type and/or cumulative dose (CD) of IS taken by this patient cohort.

Methods: We collected data from a retrospective cohort of all (n= 335) LKTs (> 8 years) 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. Wilcoxon signed-rank test was used to test the effect of cumulative doses of IS.

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. 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. Cumulative dose of azathioprine is significantly related to development of skin cancer.

Drug	% SC Cases	% Matched Controls	McNemar's p-value	Median CD SC Cases	Median CD Matched Controls	Wilcoxon p-value
Prednisolone	62.7	62.7	1	27,826	22,272	0.121
Azathioprine	61.2	46.2	0.05	318,800	272,350	0.041
Cyclosporine	61.2	52.2	0.21	297,500	377,950	0.723
Tacrolimus	20.8	13.4	0.30	0	0	-
Mycophenolate	26.8	31.3	0.66	0	0	-

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. Cumulative dose of azathioprine is significantly related to development of skin cancer. Further work to determine whether there are any other underlying risk factors in developing skin cancer and assess the effectiveness of available treatments is warranted.

P082

Low incidence of acute rejection using standard steroid protocol compared to early steroid withdrawal in low immunological risk live donor kidney transplant recipients

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Introduction: We previously presented (BTS 2014) our data about the use of early steroid withdrawal (ESW) in low immunological risk patients after live donor kidney transplant, which showed high acute rejection rate of 50% and the ESW protocol was stopped in our unit. We reviewed our outcome following this change, in particular, analysed the rate of rejection in low immunological risk renal transplant recipients. (Audit ID 5452 Barts Health NHS Trust)

Method: A total of 56 live donor kidney transplants were performed from 10/ 2013 to 9/2014 and 14 (25%) were excluded from the study due HLA and/or ABO incompatibility. 42 patients were included in the study, mean age was 47.9 years, 26 male and 16 female, 22 related and 20 unrelated.

The standard protocol was induction with Basilixumab, Tacrolimus, MMF, 500mg methylprednisolone (500mgs- intra-operatively) and 20mgs of prednisolone commenced on the 1st postoperative day with an intent to taper to 5mgs by 3 months. Renal allograft biopsy was performed if there was delayed graft function up to seven days or unsatisfactory drop of creatinine or unexplained rise of creatinine >20% and a protocol biopsy was performed at 3 months. .

Results: A total three patients (7%) had biopsy proven mild rejection that fulfils the Banff Criteria in comparison to our previous experience (biopsy proven rejection - 50%).

This data shows significant difference (p value< 0.05) in the acute rejection rate between standard and ESW protocol in low immunological risk renal transplant patients.

Conclusion: Standard steroid decreased the rate acute rejection in comparison to early steroid withdrawal in Basilixumab based induction protocols, in low immunological risk recipients. However, further studies might be needed to confirm our finding.

P083

Do we need a different induction therapy strategy for pre transplant donor specific antibodies positive recipients in living donor kidney transplantation? A retrospective analysis of single centre transplant unit

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Introduction: Data on Living Donor Kidney Transplant (LDKT) recipients in relation to safety and outcomes in the presence of historical or current Anti HLA antibodies (DSAs) at the time of transplant is unclear. This study has investigated the possible factors that have led to the emergence of the DSAs in the post-transplant period.

Methodology: Retrospective data was collected on LDKT recipients from Jan'09 to Oct'14. They were either historic or immediate pre-transplant DSA positives detected by Luminex test and CDC / Flow cross match negative at the time of transplant. Standard Induction therapy was used in majority of the patients (Basiliximab: 33, Alemtuzumab: 1) followed by either Dual Therapy or Triple therapy depending on immunological risk. Data was collected on Post-transplant DSAs, rejections, Immunosuppression, graft function and events such as infections and marrow suppression. Minimum follow up period was from 6 months to 2 years.

Results: Among the cohort of 500 LDKT patients in last 5 years, n=34 recipients were DSA positives either historically or currently at the time of transplant. DSAs were checked within 2 years of post-Renal Transplant. 11 (32 %) patients remained DSA +ve, mean age was 53 ± 12 yrs. 16 patients remained DSA -ve, mean age was 47 ± 13 yrs. Majority of the patients in DSA +ve group were on Triple therapy than DSA -ve group [82% Vs 44%, $p=0.04$]. Increased incidence of all cause allograft rejection was evident in DSA +ve group within 7 days of transplant [83% Vs 0% $p=0.0057$]. Events such as Infections and marrow suppression were found to be high in DSA +ve group than DSA -ve group [72% Vs 18%, $p=0.0147$].

Conclusion: General trend observed was to leave Pre-Transplant DSA positive patients on triple therapy which has led to high risk of infections and marrow suppression which subsequently leads to reducing their immunosuppression load and that may possibly lead to emergence of DSA in post-transplant period. There is a need of different Induction strategy for immunosuppression for this patient group to reduce the early risk of rejection as well as reduce the overall burden of Immunosuppression.

P084

Inpatient variability of tacrolimus blood concentrations following renal transplant – acute rejection or no connection?

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Background: A high degree of inpatient variability (IPV) of tacrolimus blood concentrations has been associated with poor long-term outcome.¹ Periods of under-exposure with increased risk of acute rejection is a possible underlying explanation.

Methods: For 250 patients in this retrospective single-centre study the coefficient of variance (CV) was calculated as a measure for IPV by using whole-blood tacrolimus concentrations drawn during the first three months after transplantation. Cases were split into high and low variability using the median CV and these groups were compared. The primary outcome was biopsy-proven acute rejection, defined as at least Banff grade 1, including subclinical rejection detected in a routine three month post-transplant protocol biopsy. This study received ethical approval from the host site.

Results: Of the 125 patients in each subgroup, biopsy-proven acute rejection was observed in 22 (20.95%) and 39 (31.20%) patients with a low and high CV for tacrolimus concentration IPV, respectively (p=0.0295). Patients of black ethnicity were more frequently observed in the high CV (n=23, 18.4%) versus low CV (n=11, 8.8%) group (p=0.0396).

Conclusion: This study demonstrates a significant association between a high IPV of tacrolimus concentrations in the first three months following renal transplant and biopsy-proven acute rejection.

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P085

Alemtuzumab in elderly renal transplant recipients is not associated with a poor outcome

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Introduction: The use and choice of induction immunosuppression in elderly kidney recipients remains unresolved. Alemtuzumab has been associated with a higher risk of death and graft loss in the elderly (>65 years). The aim of our study was to explore the use of alemtuzumab in this age group.

Methods: In this retrospective, single centre study, we report the outcomes of elderly patients (>65 years) receiving a steroid sparing, tacrolimus based regime after monoclonal antibody induction (Alemtuzumab or IL-2R mabs). Steroids were stopped 7 days post transplantation and only introduced to treat rejection.

Results: A total of 151 patients (51 females, 100 males) were included in the study. 128 of them received Alemtuzumab and 23 IL-2R mabs, and represented the two study groups, respectively. 23 (15.2%) developed post-transplantation diabetes mellitus (PTDM). 18 patients were on steroids (11.9%). During the follow-up of 52 ± 29 months, 25 patients died and 21 patients lost their grafts. Patient survival was 97.3% at 1-year and 92.4% at 3-years and graft survival (death-censored) was 96% at 1-year and 88.1 at 3-years. There was no difference between the groups regarding gender ($p=0.340$), age at transplantation ($p=0.780$), months on dialysis (0.391), kidney from deceased or live donor ($p=0.074$), pre-emptive transplantation ($p=0.210$), cardiac events ($p=0.767$), history of diabetes ($p=0.813$), cumulative incidence of PTDM ($p=0.764$), prednisolone use ($p=0.155$), deaths ($p=0.542$), cause of death ($p=0.537$) or graft failure ($p=1.0$). They were more South Asians in the Alemtuzumab group ($p=0.016$), and more patients with diagnosis of glomerulonephritis received IL-2R mabs ($p=0.012$), as expected per protocol. Survival analysis shows no difference in patient (log rank $p=0.605$) or graft survival (log rank $p=0.486$) between the groups. Multivariate analysis shows that receiving a kidney from a deceased donor ($p=0.043$) increases the risk of death.

Discussion: Alemtuzumab use was not associated with poor outcomes in our study. Although the group who received IL-2R mabs was relatively small, overall kidney and patient survival in this age group was comparable with previous studies.

P086

Pre-transplant tacrolimus exposure predicts post-transplant dose requirement

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Introduction: The aim of this study was to investigate whether pre-transplant tacrolimus (Tac) dose requirement in patients scheduled to undergo kidney transplantation correlates with post-transplantation dose requirement.

Method: The predictive value of Tac dose requirement pre-transplantation on this same parameter post-transplantation was assessed in a cohort of 57 ABO-incompatible kidney transplant recipients. These patients started with immunosuppressive therapy pre-emptively 14 days before surgery.

Results: Sixty-three percent of the Tac dose requirement on day 3 post-transplantation was explained by the Tac dose-corrected predose concentration immediately before transplantation. Serum albumin and hematocrit explained an additional 8.5% of the variance in Tac dose requirement on day 3 post-transplantation.

Discussion: Steady-state Tac exposure before transplantation largely predicts post-transplantation Tac dose requirement. Basing the Tac starting dose on pharmacokinetic information obtained after repeated, pre-transplant test doses may limit early Tac over- and under exposure.

P087

High within-patient variability in tacrolimus levels is a predictor of late rejection in young adult kidney transplant recipients

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Introduction: Non-adherence is an important risk factor for late rejection (rejection > 3 months post-transplant) and is the main reason why 17-29 year old kidney transplant recipients (KTRs) have the worst 5-year allograft survival rates compared with all other age categories. We investigated whether within-patient variability in Tacrolimus levels, a marker of non-adherence, predicts late rejection and graft loss in young adult KTRs.

Methods: Variability in Tacrolimus levels was calculated in young adult KTRs transplanted between January 2005 and May 2014 in a single centre. The 5 most recent outpatient Tacrolimus levels > 6 months post-transplant (or the 5 most recent levels prior to the late rejection episode) were utilised for the analysis. Cox regression and ROC-curve analysis was used to evaluate the ability of variability in Tacrolimus levels to predict late rejection and graft-loss.

Results: Of 75 young adult KTRs (49m,26f;aged 17-29 yrs); 5 developed late rejection and 7 graft-loss (both 10-74 months post-transplant) during a median follow-up of 63 months. Patients with late rejection / graft loss had higher median variability in Tacrolimus levels compared to patients without late rejection (50% vs 20%, $p = 0.02$) / graft loss (50% vs 20%, $p < 0.001$). Using the median of variability (21%) as a threshold, no late rejections were noted in the low variability group versus 5 in the high variability group (1 vs 6 for graft loss). In a Cox regression model adjusted for age at transplant, sex, living donor, previous transplant, pre-emptive transplant and total HLA mismatch, variability in Tacrolimus levels was the only variable significantly associated with late rejection ($p=0.012$) and graft loss ($p=0.001$) apart from age at transplant. Using a cut-off value of 21%, the AUC of the ROC-curve was 0.76 / 0.69 for predicting late rejection / graft loss.

Conclusion: Within-patient variability in Tacrolimus levels above 21% identifies young adult patients at increased risk of late rejection and graft loss. A potential strategy to improve adherence is a dedicated young adult service, previously shown to successfully reduce late rejection and graft loss.

P088

Inadequate overall immunosuppression is a risk for late acute rejection despite alemtuzumab induction in simultaneous pancreas kidney transplant recipients

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Introduction: Simultaneous pancreas-kidney transplantation (SPK) has become the treatment of choice for patients with end-stage renal disease due to Type 1 Diabetes Mellitus. SPK is associated with a relative high rate of acute rejections (AR) compared to kidney transplantation alone. Here we investigated time to and risk factors for rejection including inadequate overall immune suppression. In addition, we evaluated whether repopulation with specific alloreactive immune cells is associated with rejection.

Methods: 158 SPK recipients were included, and current induction therapy Alemtuzumab (n=73) was compared to historical controls treated with ATG (n=85). Maintenance therapy consisted of Tacrolimus, MMF and, in case of ATG, Prednisone. Data regarding trough levels, immune suppressive (IS) therapy and side effects were collected retrospectively. Peripheral blood was obtained from 30 patients (13 at time of rejection, 17 controls) for mixed lymphocyte cultures (MLC) and flow cytometric analysis of immune cells.

Results: The Alemtuzumab group showed a significant decline (20.5%) in AR rate compared to ATG (43.5%). There was no difference in the amount of infections, immunizations or Tacrolimus trough levels between both groups. Within the ATG group 94.6% of the AR occurred within 30 days. In contrast, with Alemtuzumab a biphasic distribution was seen with 20% of the AR occurring within 30 days and 80% after 90 days. In the ATG group, 3 out of 37 patients had inadequate trough levels prior to AR, however in most patients no identifiable cause was found. In the Alemtuzumab group, AR were caused in most patients (10 out of 15) by adjustments of IS due to viral infections, leukopenia and gastrointestinal symptoms. Preliminary MLC results in the latter group showed repopulation with similar alloimmune reactivity between stable and rejecting patients.

Conclusion: In SPK recipients, Alemtuzumab induction significantly reduced AR rates and showed a biphasic distribution. Rejection was attributable to adjustments of IS in the majority of the patients. Therefore a reduction in IS at the time of repopulation of immune cells must be carefully considered.

P089

Could we rationalise tacrolimus monitoring in long-term renal transplant recipients?

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Background: Tacrolimus has a narrow therapeutic window. There is no consensus on target blood concentration or how frequently tacrolimus should be measured in long-term renal transplant patients. Could we reduce cost by monitoring less frequently?

Aims: Review frequency of tacrolimus measurements in long-term (>1 year) renal transplant patients and how frequently values outside the target range led to a change in dose.

Methods: Single unit retrospective observational study. Trough tacrolimus conc. recorded >1 year post-transplant and associated data were reviewed for all patients who had received a renal transplant within a 3 year period.

Results: 100 patients were included. Average duration observed was 490 days (range 14-1078). 951 tacrolimus concs. had been taken, at mean interval of 59 days (SD 25). 384 (40%) results were outside target; 162 (42%) of these led to a change in dose or brand; 124 (32%) did not change and were not re-checked within 30 days.

Tacrolimus concentration (ng/mL)	Count	Dose changed	Brand changed	No change in dose	No change, retested within 30 days	No change, not retested within 30 days
< 5	204	70	2	132	59	73
5 – 8*	565					
> 8	182	89	1	92	41	51

*5-8ng/mL is the unit target for renal transplant recipients after 90 days

Conclusions: A significant number of abnormal results did not lead to dose changes or even re-checks. Frequency may have been greater than scheduled due to patients changing tacrolimus brand. A more efficient rationale for monitoring tacrolimus in long-term renal transplant recipients could be considered, perhaps annually.

P090

New onset diabetes after transplantation in renal patients receiving immunosuppression based on low dose tacrolimus MR regimen

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Introduction: NODAT is a serious metabolic complication following renal transplantation and is associated with reduced long-term patient survival, mainly due to cardiovascular events. Evaluation of NODAT has been complicated by a lack of an accepted definition. The Purpose of this study was to evaluate the prevalence of NODAT in a immunosuppressive regime based on low dose Tacrolimus MR (Advagraf), MMF and steroids and to determine whether any specific factors correlated with heightened risk.

Method: Retrospective analysis of non-diabetic patients who received renal transplant in Wessex Kidney Centre between January 2011 and October 2013. Patients were evaluated for NODAT based on WHO definition (Random blood glucose level >11mmol/l) or requirement for glucose lowering treatment at 1 year post transplantation. Assessment of relative importance of variety of known risk factors were analysed including BMI at the time of transplantation, weight gain within 1 year, presence of 2 trough levels of Tacrolimus >10 ng/l, age, sex, use of steroids, prevalence of CMV viraemia and acute rejection.

Results: Between January 2011 and October 2013, 144 non-diabetic patients were Transplanted at the Wessex Kidney Centre (Male 59.72%, Female 40.28%, Mean age 50.10 years SEM 1.197. Deceased donors 66.67% vs Living donors 29.17%). 14 patients (9.66%) developed NODAT using WHO criteria, but only 7 (4.86%) required treatment with Insulin or oral agents at one year. Analyses confirmed a statistically significant correlation between male gender ($p=0.03$) and Δ BMI ($p=0.001$) at one year and NODAT within the first year following transplant.

Conclusion: Overall prevalence of NODAT in our population was significantly lower than described in the literature. As previously described, male patients and those in whom there was significant weight change at one year post transplant had highest risk. It is not possible to ascertain whether the low rate of NODAT is attributable to lower trough levels of Tacrolimus currently in use or due to lower peak levels of Tacrolimus MR. This requires further study.

Category: New Immunosuppressive Drugs

P091

Analysis of samples from the RituxiCAN C4 Trial at second interim analysis

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RituxiCAN C4 is a phase 4 randomised control trial of anti-CD20 (Rituximab) in renal transplant recipients with chronic allograft nephropathy (CAN) and biopsy evidence of antibody-mediated rejection.

Since recruitment began in 2007, 61 patients with a creeping creatinine and/or proteinuria and specific biopsy features have been enrolled from 7 sites in the UK. Phase 1 comprises a 3-5 month run-in period of immunosuppression optimisation with Tacrolimus and MMF. 52/61 have reached the end of this phase and have been reassessed against clinical eligibility criteria. 16/52 patients 'failed' this reassessment and proceeded straight into 3-year observation (phase 3). These patients had either stabilised creatinine, lost proteinuria or had an eGFR that had fallen <20ml/min. 36/52 were potentially eligible for phase 2: 13/52 either refused second consent to this phase or were deemed to have additional clinical features which prevented administration of Rituximab. The other 23 consented to randomisation and 12/23 were allocated Rituximab and 11/23 allocated no-Rituximab. At the point of second interim analysis, 20 phase-2 patients have reached primary end-point. A total of 49 patients have entered into phase 3.

Peripheral blood mononuclear cells (PBMC) from 80ml of blood have been isolated and frozen from each patient at enrolment, end of phase 1, end of phase 2 and every 3 months during phase 3. IFN γ ELISPOT analyses have been performed on serial samples of PBMC from each patient to measure the contribution of B cells and regulatory T cells to the donor specific alloreactive response in each patient. In depth phenotyping of each patient's T and B cells has been performed in conjunction with the ELISPOT. The results of this analysis, along with clinical outcomes from the trial will be presented at this conference.

P092

Crossing 2 barriers: successful kidney transplantation across donor specific HLA antibodies and recurrent haemolytic uremic syndrome with the use of eculizumab

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Introduction: The presence of donor specific HLA antibodies (DSA) and recurrent haemolytic uremic syndrome (HUS) are both barriers for successful kidney transplantation. Eculizumab is a potent inhibitor of complement C5 and can effectively harness complement mediated cellular toxicity.

Methods: The patient is a 41 yr old male, who became dialysis dependent because of HUS in 1992 when he was 18 yrs old. From 1993 to 2008 he received 4 kidney transplantations that were all lost after a short period because of either recurrent HUS and/or vascular rejection. Thereafter his PRA level was 100% which later decreased to 44%. DNA complement gene analysis revealed 3 mutations in factor H gene that are associated with HUS. In June 2014 he received his 5th living unrelated donor kidney with a historically positive but current negative CDC. Before and after transplantation plasmapheresis was performed and induction with ATG was given followed by low dose tacrolimus, prednisone and MMF. Endothelial cell protection was given by rigorous control of blood pressure, and a combination of a statin, ACE-inhibition and amlodipine.

Results: Post-operatively the rapid decline in serum creatinine stopped at day 6. The renal biopsy showed a mixed pathology of both HUS and evidence for mild AHR in the presence of DSA. After unsuccessful steroid and IVIG treatment, eculizumab was started and serum creatinine stabilized at 150 umol/L with disappearance of the biochemical signs of HUS. Apart from an episode of CMV viremia and a tubulo-interstitial rejection treated at month 4 post-transplantation, no adverse events were recorded. At six months post-transplantation the renal function is stable with continuation of 1200 mg eculizumab every 2 weeks and triple immune suppression.

Conclusion: The use of eculizumab enabled kidney transplantation in a complicated patient in which both AHR and HUS were barriers that could not be overcome otherwise.

P093 WITHDRAWN

P094

Inability to re-use basiliximab induction treatment in second or subsequent kidney transplants: does it matter?

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Background: In line with NICE guidance, Basiliximab is routinely used as induction therapy to reduce risk of rejection in renal transplant recipients. It is not clear whether the risk of rejection in re-transplantation would be compounded by inability to re-use Basiliximab. We describe a single centre, retrospective analysis of re-transplant recipients with and without Basiliximab induction at time of second (or subsequent transplantation) to assess if lack of induction treatment affects graft outcomes.

Methods: Data on adult patients receiving second and subsequent kidney transplants between 2000 and 2014 were obtained. Patients were divided into (1) Basiliximab group – patients who received Basiliximab induction with no history of prior exposure (2) Basiliximab free group – patients who did not receive Basiliximab induction due to prior exposure. Outcomes were (1) Biopsy Proven Acute Rejection (BPAR) within 3 months (2) One year patient and graft survival (3) 3 and 12 month transplant function.

Results: Across 184 patients, there was no significant difference in the rate of BPAR within 3 months between Basiliximab and Basiliximab-free groups (33% vs 21.7%; $p=0.09$). The median eGFR between groups was comparable at 3 months (49 vs 50ml/min/1.73m²; $p=0.94$) and 12 months (49 vs 45ml/min/1.73m²; $p=0.75$). There was no difference in graft (3 vs 7; $p=0.33$) or patient survival (2 vs 3; $p=0.81$) between groups at one year.

Conclusions: Basiliximab free transplantation in recipients with prior exposure is associated with a trend towards higher risk of rejection but no significant difference in eGFR, graft and patient survival at one year.

P095

Sevoflurane based anesthesia in recipients reduces 2 year acute rejection in living donor kidney transplantation. Results from the VAPOR-trial

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Introduction: Volatile anaesthetic agents like sevoflurane may protect against the ischemia and reperfusion injury (IRI) that is part of organ donation and transplantation. It is also increasingly recognised that volatile anaesthetics modify immune cell functions. Our group set out to optimize the anaesthetic regimen in renal transplant recipients. We evaluated the influence of two common anaesthetic regimens, a propofol based vs. a sevoflurane based anaesthesia, on transplant outcome in living donor kidney transplantation (LDKT).

Methods: Prospective randomized controlled clinical trial. 60 couples were assigned to three groups: PROP; donor and recipient received propofol, SEVO; donor and recipient received sevoflurane and SERE; donor received propofol and recipient received sevoflurane (n=20/group). Only left kidneys were included because of the presence of the gonadal vein as a side branch through which blood samples during reperfusion could be taken. Samples were taken at different time points. Renal biopsies were taken during cold ischemia and 1 hour after reperfusion.

Results: There were no significant differences between donor and recipient demographics. Acute rejection after two years: PROP 6/17 (35,3%), SEVO 2/19 (10,5%) and SERE 1/20 (5,0%). There was a significant reduction in acute rejection in SERE vs PROP (Fisher exact, p=0.033) and when SERE and SEVO groups were combined (sevoflurane vs propofol for recipients, the difference in acute rejection was even stronger 3/39 (7,7%) in sevoflurane recipients vs 6/17 (35%) in propofol recipients, Fisher exact , p=0.017.

Conclusion: A sevoflurane based anaesthesia significantly reduces acute rejection within 2 years following living donor kidney transplantation.

P096

Monitoring of biomarkers in perfusate for quality assessment of machine-perfused ECD/DCD kidneys

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Background: DCD and ECD kidneys are associated with higher risk of failure compare to SCD kidneys. Therefore we see increasing need to identify sensitive tool to assess quality of these kidneys prior transplantation and predict their outcomes.

Hypothermic machine perfusion (HMP) is known to improve transplant outcomes compare to static storage but cannot be used as sensitive kidney quality assessment tool. However, it was suggested that monitoring of biomarkers in HMP perfusate could correlate with early post-transplant outcomes.

Some novel biomarkers (e.g. NGAL, KIM-1, AST, LDH) appears offering better accuracy compare to conventional biomarkers (i.e. creatinine) for the diagnosis of Acute Kidney Damage. We conducted study to determine correlation between concentration of NGAL, KIM-1, AST, LDH in machine perfusate of ECD/DCD kidneys and transplant outcomes.

Study: Total, we studied 10 kidney grafts preserved on a LifePort®, perfused with KPS-1 solution. Perfusate was sampled at 15 minutes, 1 hour, 2 and 3 hours. We measured level of NGAL, KIM-1, AST and LDH using automated ELISA assay and correlate with donor/recipient demographics and kidney outcomes (DGF, PNF, eGFR at 1, 3 and 6 months).

Results: Concentration of all biomarkers steadily increased during first 3 hours of HMP. Level of each biomarker at every time point well correlated with kidney function (eGFR) at 1, 3 and 6 months post-transplantation. Eight kidneys developed functional DGF but we found no correlation with the level of biomarkers in this group. No one kidney developed PNF.

Conclusion: Our data indicate that concentration of all biomarkers in perfusate correlates with post-transplant kidney function. Determination of those four biomarkers potentially can be used as sensitive kidney quality assessment tool but more data are required.

P097

Analysis of microRNA-21 (miR-21) expression in hypothermic machine perfusate as a biomarker to predict early outcomes in kidney transplantation

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Introduction: Hypothermic machine perfusion is effective in improving outcomes from kidney transplantation and molecular analyses of hypothermic machine perfusate (HMP) have the potential to identify biomarkers of organ viability prior to transplantation. The ability to predict organ-specific outcomes prior to transplantation offers enormous advantages to the transplant surgeon, and may increase the organ donor pool by allowing use of the ever-increasing 'extended criteria donors (ECD)'. MicroRNAs have considerable potential for use as biomarkers of numerous disease processes, including kidney disease. Of particular interest, significantly increased miR-21 expression in acute kidney injury has been reported. The aim of this study was to determine if miR-21 expression in HMP could determine early outcomes from kidney transplant.

Methods: Samples of HMP were taken at 15 minutes, 1 hour and 2 hours after perfusion for kidneys (ECD/DCD) placed on the LifePort® prior to transplantation. Following RNA extraction using miRNeasy Mini Kits (Qiagen), cDNA was generated using the High Capacity Reverse Transcription kit (Life Technologies) and RT-qPCR was carried out using a specific TaqMan microRNA detection assay (Life Technologies). Clinical data were collected, including demographics and eGFR at 6 months post transplantation.

Results: Eleven kidneys (ECD/DCD) were included in our analysis. MicroRNAs were readily detected and found to be stable in the HMP medium. MiR-21 expression in HMP at 1 hour after perfusion correlated significantly with eGFR at 6 months post transplantation ($r^2=0.507$, $p=0.014$).

Conclusion: MicroRNAs are emerging as important biomarkers in the context of kidney injury and transplantation. This study shows that miR-21 expression levels in HMP may be predictive of early outcomes from kidney transplantation. Further studies are needed with larger patient cohorts to confirm these findings.

P098

Gradual warming up perfusion post static cold storage reduces renal injury

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Introduction: Reperfusion injury after cold storage (CS) of organs is an inevitable consequence of a transplant procedure. We hypothesize that the sudden warm reperfusion after CS is detrimental for the graft. We therefore evaluated different warming-up procedures before reperfusion.

Methods: Rat left kidneys (n=8 per group) were retrieved and stored in University of Wisconsin solution for 24 hours at 4°C followed by immediate reperfusion at 38 °C or gradually warming up to 10°C , 25°C or 38°C, using an isolated perfused kidney (IPK). Renal function and renal injury were assessed during 90 minutes of the perfusion.

Results: The increases in the injury biomarkers such as aspartate transaminase and lactate dehydrogenase in the perfusate were lower in the gradual warming up groups vs the control group. KIM-1, HSP-70, ICAM-1, VCAM-1 expression were decreased in the 10°C and 25°C groups. Sodium re-absorption was improved in the gradual warming up groups and reached significance in the 25°C group after 90 minutes of perfusion.

Discussion: After a period of SCS, kidneys subjected to gradual warming up suffer less renal parenchymal and tubular injury and demonstrate better endothelial preservation. This study suggests that gradual warming up after CS is beneficial compared to immediate reperfusion at body temperature.

P099

The glucose – lactate paradox in hypothermic oxygenated perfusion (HOPE) of discarded human DCD livers

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Introduction: Hypothermic oxygenated perfusion (HOPE) is proposed to pre-treat livers at the end of cold ischemia to increase hepatic energy, reduce reactive oxygen species (ROS) and increase post-reperfusion bile production. To familiarize with the procedure, we pumped 8 human livers that were rejected for transplantation. Here we describe the apparent glucose – lactate paradox we observed during HOPE.

Methods: Livers were hooked up to the Airdrive™ machine and perfused for 2h with UW-MP solution at 6-10°C. Livers were rejected because of age (4), warm ischemic time (WIT; 1), steatosis (2) and 1 for unknown reason. Median donor age was 64 (56 to 71) years. Median WIT was 16 (12-28) minutes and median cold ischemic time was 8,5 hours (6-16 hrs).

Results: During 2h HOPE, all livers pumped out glucose in the closed circuit perfusate. Glucose levels rose from 9,3 mmol/l in UW-MP to 25 after 1h and 32 after 2h. Insulin up to 500 IU could not reverse glucose output. In the meanwhile, lactate increased from 1,6 mmol/l in the UW-MP to 7,6 after 1h and 9,0 after 2h, indicating ongoing anaerobic glycolysis. The mean PO₂ of the perfusate fell from 58 kPa (430 mm Hg) before installation of the liver to 30kPa after 30 min, 27kPa after 1h and 26kPa after 2h. Oxygen extraction by the liver decreased steeply from 19kPa after 30 min to 4kPa after 1h. The ATP content of the liver stabilized from end of cold storage to 2h (6,6 to 5,9 mmol/g protein; p=n.s.). MDA, as measurement of ROS lipid peroxidation, decreased significantly from 0,05 to 0,02 mmol/g protein; p=0.005.

Discussion: Interpretation of the metabolic state of these extended criteria DCD livers is difficult; consumption of oxygen leads to effective inactivation of oxygen radicals. However, this oxygen seems not to be used for oxidation of lactate to pyruvate, as part of the normal Cori cycle. At the same time, the liver is stuck in an insulin-resistant gluconeogenesis mode, instead of using the available glucose to generate ATP for hepatic recovery and sustaining metabolism. HOPE does not ameliorate carbohydrate metabolism, leading to the glucose – lactate paradox.

Category: Organ Perfusion

P100

Characterising passenger leukocyte migration from the donor lung using ex-vivo lung perfusion

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Introduction: Passenger leukocyte transfer from the donor lung to the recipient is intrinsically involved in acute allograft rejection. Direct presentation of complete alloantigen expressed on donor leukocytes is recognised by recipient T cells, inducing allospecificity which is a prerequisite for acute cellular rejection. Using ex-vivo lung perfusion (EVLP) we have characterised the natural history of the inflammatory response and passenger leukocyte migration from the donor lung.

Methods: Explanted porcine lungs (n=7) underwent 3hrs of EVLP. Perfusate samples were collected at 30-minute intervals for a total of 180 minutes, and upon completion the leukocyte filter was removed from the circuit. A range of immune cells were characterised via flow cytometry. An inflammatory profile was generated via quantification of a range of cytokines.

Results: Throughout perfusion there were continuous increases in IFN- γ (p<0.001), IL-1 α (p=0.014), IL-1 β (p<0.001), IL-1RA (p<0.001), IL-8 (p<0.001), IL-10 (p<0.001), IL-12 (p<0.001), IL-6 (p<0.001), TNF- α (p=0.003) and IL-18 (p<0.001). Significant populations of mature donor basophils, eosinophils and T cells (comprising of equal ratios of CD4+ and CD8+ cells) were identified within the first 30 minutes of perfusion. Of the monocyte repertoire, classical monocytes represented only a minor fraction, with non-classical monocytes found in much greater abundance. Minor populations of neutrophils, B cells and NK cells were also detected at all time points. On completion of perfusion we assessed cell content in the leukocyte filter, with cell populations comparable to above.

Conclusions: The donor lung possesses a significant immune compartment capable of direct presentation of self (donor) antigens, provision of costimulation via APC, T cell activation, immunologic help via B cells, innate immunity via a significant granulocyte population, and the induction of non-specific systemic inflammation via cytokine secretion. These findings also indicate that EVLP may be of benefit in removing this inflammatory content prior to transplantation.

P101

Hypothermic versus normothermic in situ regional perfusion using the extracorporeal membrane oxygenation (ECMO) technique in donation after circulatory death (DCD) in kidney and liver transplantation: a systematic review

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Introduction: DCD donors represent a large potential source of donors. We systematically reviewed the evidence for hypothermic (HRP) and normothermic (NRP) in situ regional perfusion using ECMO in DCD kidneys and livers.

Methods: We searched Medline, EMBASE, Cochrane CENTRAL and the Transplant Library for human studies on HRP or NRP in DCD kidney and liver donors reporting on discard rate, complications, patient/graft survival or an organ specific outcome. Methodological quality was evaluated with the Newcastle-Ottawa scale or a scale for case series.

Results: Out of 9,385 unique references 32 studies (3 cohorts, 29 case series/reports) met our inclusion criteria. There were 23 reports on kidney, 5 on liver and 4 that reported on both liver and kidney donors. Number of donors included in the reports ranged from 1- 641. Key methodological information was missing from many reports. Mean temperature of HRP ranged 4-22^o C versus 27-37.5^o C for NRP. The discard rate of kidneys ranged from 0-57% (18 studies) and 0-77% for livers (6 studies). After HRP in kidney donors, patient survival was 75-100% (8 studies; follow-up (f/u) ranged from hospital discharge up to 6 years) and graft survival was 72-100% (11 studies; f/u ranged from 6 months to 5 years). After NRP in kidneys patient survival was 98-100% (5 studies; f/u ranged from 3 to at least 24 months) and graft survival was 86-100% (7 studies; f/u ranged from 3 to at least 24 months). After NRP in liver donors, patient survival at 1 year ranged from 82-92% at 1 year (3 studies). The follow up time differed significantly across all studies ranging from 1 week up to 7 years.

Conclusion: The available evidence of HRP and NRP in DCD kidney and liver donors is of a low level but suggests that there are good outcomes for transplant recipients, although results were achieved at the expense of high discard rates. However there is a need for a well-designed trial to evaluate this technology further.

** The systematic review was conducted on behalf of the Consortium for Organ Preservation in Europe (COPE).

Effects of differing ischaemia on characteristics during ex-vivo normothermic perfusion (EVNP) of porcine pancreases

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Introduction: Pancreas transplantation has a 25-50% incidence of severe complications, many of which are manifestations of graft pancreatitis resultant from ischaemia reperfusion injury (IRI). Despite this, little is known about the mechanisms of pancreatic IRI as an appropriate experimental model has been lacking. We therefore aimed to use EVNP to evaluate the effects of differing ischaemic insults on pancreas perfusion, injury and function in a porcine model.

Methods: In the severe injury model (n=6), pigs were killed by electrocution and exsanguination, followed by rapid laparotomy, aortic cannulation, perfusion with cold preservation solution and pancreas retrieval. In the moderate injury model (n=5) laparotomy and aortic cannulation was performed under general anaesthesia and systemic heparinisation, followed by exsanguination and 10mins of *in situ* warm ischaemia before cold perfusion. The mild injury model (n=5) was similar but without *in situ* warm ischaemia. Pancreases underwent 2h of EVNP using a warmed autologous whole blood-based solution. Outcome measures included blood flow, weight gain, plasma amylase, and insulin secretion (basal and stimulated).

Results: Cold ischaemia times were comparable in all groups (p=0.403). The severe injury model had significantly higher pancreatic blood flow (p=0.011), with higher plasma amylase (p<0.001) and lower plasma insulin levels in response to glucose challenge (p<0.05) compared to other groups. There was no difference in the mean percentage weight gain during EVNP (58% vs. 43% vs. 50%, p=0.5825)

Conclusion: Pancreases with severe ischaemic injury had the worst function and developed more significant pancreatitis, as measured by amylase. The higher blood flow may represent a more significant endothelial injury with resultant loss of vascular tone. This study demonstrates the feasibility of EVNP to study pancreatic IRI and potentially evaluate the quality of pancreases prior to transplantation.

P103

An experimental model of *ex vivo* normothermic perfusion of porcine small bowel segments

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Introduction: Ex-vivo normothermic perfusion (EVNP) provides an opportunity to study isolated organs under controlled conditions. We aimed to establish the first model of segmental porcine small bowel EVNP and assess its suitability for the study of gut physiology, ischaemia-reperfusion injury (IRI) and therapeutic interventions in the context of transplantation.

Methods: Anaesthetised young adult (50-60kg) white pigs were used. The distal aorta was cannulated after laparotomy and systemic heparinisation, and blood was collected upon exsanguination. Following asystole and *in situ* perfusion with cold preservation solution, segments of proximal to mid-ileum (1.5-2.8m) were removed with intact vascular arcades. The small bowel was placed on an EVNP circuit after a median cold ischaemia of 5h30mins and perfused for 2h with warm re-oxygenated autologous blood. A 20% glucose solution was infused intra-luminally after 1h and plasma samples collected to investigate absorptive and secretory function.

Results: All bowel segments (n=5) appeared well perfused and demonstrated peristalsis. The mucosa appeared healthy and non-haemorrhagic. Venous glucose levels increased from 1.5 ± 0.79 to 18.6 ± 11.88 mmol/L following luminal glucose administration. Blood flow was 69 ± 40 ml/min (range 48.4-128.8 ml/min) at a perfusion pressure of 80 mmHg. Following luminal glucose stimulation, total GLP-1 levels increased from a mean basal level of 32.8 ± 8.3 pg/mL to a peak of 69.8 ± 16.2 pg/mL.

Conclusion: This is the first report of EVNP of small bowel segments in a large animal model, demonstrating that the viability, absorptive and secretory function can be maintained *ex vivo*. The model allows future study of small bowel physiology (e.g. hormone production) and investigation of mechanisms and therapeutic interventions against IRI (e.g. leucocyte depletion and drug treatment), of particular relevance in intestinal transplantation.

P104

Heparin therapy management and coagulation prevention during ex-situ normothermic machine perfusion of human donor livers using a plasma based perfusion fluid

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Introduction: *Ex-situ* normothermic machine perfusion (NMP) offers the possibility of viability testing of extended criteria donor (ECD) livers prior to transplantation. Several groups have reported the use of plasma and red blood cells for NMP. When using a plasma based fluid for NMP, calcium should be substituted and heparin is required to avoid microthrombi formation within the liver and perfusion circuit. However, little is known about the disappearance and effectiveness of heparin during NMP of the liver.

Aim of this study was to investigate the disappearance and antithrombotic effect of heparin during NMP of human livers.

Methods: Twelve ECD livers declined for transplantation underwent 6 hr of NMP following a median duration of 6.5 hr cold-storage. After adding 20,000 IU heparin, 40 ml of calcium gluconate 10% solution (137.5 mg/ml) was added to the perfusion fluid (total volume 2120 ml) during priming of the perfusion device (Liver Assist). During NMP, perfusate samples were taken every 30 minutes and plasma was obtained after centrifugation. Liver viability was assessed based on bile production and livers were grouped as "good" functioning (≥ 30 g bile during 6 hr NMP) or "poor" functioning (< 30 g bile during 6 hr NMP). Heparin plasma levels were measured using an anti-Xa activity assay. Plasma concentrations of prothrombin fragment F1+2 were determined as marker of coagulation activation using an ELISA. Biopsies of the liver parenchyma taken before and after NMP were stained with H&E and immunostaining for fibrin to detect microthrombi in the vasculature.

Results: A decline in heparin levels over 6 hours of NMP was seen in both good and poor functioning livers (median 7.7 IU/ml vs. 11.6 IU/ml). However, in both groups heparin levels at the end of NMP were still 30-fold higher than the threshold for coagulation activation. No increase in F1+2 or histological evidence of microthrombi was noted in both groups.

Discussion: A single bolus administration of 20,000 IU of heparin to a perfusion volume of about 2 l is sufficient to avoid coagulation activation and subsequent microthrombi formation during NMP of donor livers.

Category: Ischemia/Reperfusion

P105

The effect of localised ischaemic preconditioning (IPC) on histological architecture, expression of AKI markers and microRNA-21 expression in a rodent model of ischaemia-reperfusion injury (IRI)

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Introduction: Several studies have shown that microRNA (miR)-21 is important in IRI and ischaemic preconditioning (IPC), a strategy designed to protect against IRI. Here, we evaluated a continuous immediate localised IPC regime in a rat model of IRI and monitored miR-21 expression in IRI and IPC in this model.

Methods: Fifteen adult male Lewis rats undergoing surgery via an abdominal incision under general anaesthesia were divided into 3 groups: sham operation; left unilateral warm ischaemia (IRI) (45 minutes of left renal pedicle cross clamping); and IPC/IRI (15 minutes of ischaemia followed by 20 minutes of reperfusion (IPC) prior to 45 minutes of IRI). Kidney tissue was retrieved at 48 hours. Paraffin blocks were made and sectioned for H&E staining. Following RNA extraction, RT-qPCR was used to analyse expression of miR-21 as well as acute kidney injury (AKI) markers NGAL and KIM-1.

Results: Forty-five minutes of unilateral IRI in the rat caused marked histological damage at 48 hours, characterised predominantly by acute tubular necrosis, endothelial cell loss, tubulo-interstitial damage (inflammation and cast formation), and glomerular capsule thickening. There was no measurable histological difference between the IRI and IPC/IRI groups. RT-qPCR data showed a significant increase in NGAL and KIM-1 expression from sham to IRI, but no significant difference was found between IRI and IPC/IRI groups. Similarly, miR-21 expression was significantly up-regulated from sham to IRI, but IRI and IPC/IRI groups did not differ.

Conclusion: The immediate localised IPC regime used did not ameliorate IRI at the molecular or histological level. While miR-21 expression increased significantly in IRI, no changes were observed following IPC. Further studies are underway to investigate alternative IPC strategies in this model.

P106

Endogenous expression of the anti-inflammatory cytokine interleukin-37 does not protect against renal ischemia/reperfusion injury

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Introduction: Renal transplantation inevitably leads to ischemia and subsequent reperfusion (IR) of the graft. IR induces excessive local inflammation that results in tubular injury and renal dysfunction. New therapeutic opportunities to preserve graft function should therefore aim to diminish the detrimental effects of IR-induced inflammation. The recently characterized human cytokine Interleukin (IL)-37 is a fundamental innate immune inhibitor. Interestingly, IL37 was shown to confer protection against LPS-induced sepsis and myocardial infarction. Whether IL37 also can restrain renal inflammation and/or injury upon IR is unknown.

Methods: Primary tubular epithelial cells (PTECs) were isolated from wild type C57BL/6J (WT) and human IL37 transgenic (hIL37tg) kidneys. Confluent PTEC cultures were stimulated for 6 or 24 hours with 1-10-100 ng/ml LPS after which supernatant was isolated for ELISA, whereas cells were used for RNA processing and subsequent quantitative RT-PCR. WT and hIL37tg mice were subjected to renal IR by bilateral clamping of renal pedicles or sham-operation and sacrificed after 1 or 2 days of reperfusion. Blood and kidney tissue were harvested.

Results: WT PTECs stimulated with LPS for either 6 or 24 hours displayed a clear dose-dependent inflammatory response, indicated by elevated CXCL1, TNF α and CCL2 mRNA expression compared to non-stimulated cells. However, no differences were observed between WT and hIL37tg PTECs at either 6 or 24 hours. In line, LPS stimulation for 6 hours induced a comparable CXCL1 secretion by both WT and hIL37tg PTECs. Compared to sham-operation, in WT mice renal IR caused a significant degree of renal dysfunction, as reflected by increased plasma concentrations of urea and creatinine. No differences were observed however in plasma urea and creatinine levels between WT and hIL37tg mice after 1 or 2 days of reperfusion.

Discussion: Our preliminary data suggest that endogenous IL37 expression does not have a major effect on the inflammatory response of renal epithelium *in vitro*, and does not confer protection against renal I/R injury *in vivo*.

P107

A double blinded randomised controlled trial of remote ischaemic conditioning in live donor renal transplantation

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Introduction: Remote ischaemic Conditioning (RiC) may reduce the effects of ischaemia reperfusion injury (IRI) and improve initial graft function in renal transplantation. The aim of this study was to assess the effects of RiC in live donor kidney transplantation.

Methods: Recipients of a live donor kidney transplant were randomised into either a control group (n = 40) or Remote ischaemic Conditioning (RiC) (n = 40). RiC was performed by applying 4 cycles of 5 minutes ischaemia using a lower limb tourniquet prior to reperfusion. Serum creatinine and eGFR was measured up to 3 months post-transplant.

Results: Two patients were excluded in the control group due to complications during surgery. Donor and recipient age and gender were similar in both groups (P >0.50). There were no complications associated with the RiC procedure. Four patients had DGF in the control group (10.5%) compared to 0 in the RiC (P=0.052). The creatinine reduction ratio (CRR2) was <30% in 8 patients in the control group compared to 13 in the RiC (P = 0.212). There was no significant difference in serum creatinine or eGFR levels at 7 days post-transplant or at 1 and 3 months between the groups (Cr Day 7; control 151 ± 120 vs RiC 136 ± 40 $\mu\text{mol/L}$; P=0.250, eGFR control 54 ± 21 vs RiC 51 ± 16 ml/min; P=0.636; Cr 1 month; control 128 ± 39 vs RiC 132 ± 35 $\mu\text{mol/L}$; P=0.705; eGFR control 53 ± 14 vs RiC 54 ± 17 ml/min; P = 0.832; Cr 3 month control 137 ± 47 vs RiC 147 ± 52 $\mu\text{mol/L}$; P = 0.565; eGFR control 51 ± 14 vs RiC 49 ± 18 ml/min; P = 0.340).

Conclusion: RiC did not improve early graft function in recipients of a live donor kidney transplant. Further studies are needed to assess the effects of different conditioning strategies in renal transplantation.

P108

Complement expression in donation after circulatory death and deceased donor kidneys

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Introduction: Kidney graft function and survival is influenced by many pre-determined and unavoidable factors. The up-regulation of complement C3 in the donor kidney in response to brain stem death reduces graft function and graft survival. The expression of complement in kidneys from donation after circulatory death (DCD) donors prior to transplantation has not been previously described.

Methods: Sixty human kidneys declined for transplantation were recruited into the research study (DBD n=24, DCD n=36). Donor characteristics were recorded and a biopsy was taken after static cold for evaluation. The level of injury and expression of C3 and C4d were measured using histopathology, western blot and immunohistochemistry techniques.

Results: Donor age was similar between the groups (DBD 61 ± 15 vs DCD 61 ± 12 y; $P = 0.495$). More DBD donors (16/24) had a history of hypertension compared to DCDs (8/36) $P=0.001$ and death was caused by an intracranial haemorrhage in 88% of the DBD donors compared to 33% in the DCDs ($P<0.0001$). The mean warm ischaemic time was 12.8 ± 3.9 minutes in the DCD kidneys. C4d reactivity was similar in both groups ($P>0.05$). Seventy one percent of the DBD kidneys were positive for C3 activation compared to 44% of the DCD, however this did not reach statistical significance ($P = 0.062$). The level injury determined by the Remuzzi score varied between kidneys but there was no difference between the donor types.

Conclusion: This study has shown a high level of complement expression in DCD kidneys that is likely to contribute to early graft dysfunction and reduce graft survival. This necessitates further investigation in DCD kidney transplantation.

P109

MicroRNAs in kidney graft preservation fluid as novel biomarkers for delayed graft function

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Introduction: Delayed graft function is a common complication after deceased donor kidney transplantation (KT), which affects both short and long-term outcome. Currently available biomarkers in perfusate lack sensitivity in predicting graft outcome. The aim of this study is to reveal microRNA profiles in preservation fluid of kidney grafts that correlate with graft outcome.

Methods: In this study, perfusate samples were collected during kidney transplantations from both living and deceased donors. The graft outcome was defined as immediate graft function (IF) and delayed graft function (DGF). As a discovery cohort 9 IF samples and 9 DGF samples were analysed for six known kidney miRNAs selected from the literature. As validation cohort, we analysed 10 living donor samples with IF, 10 deceased donor samples with IF and 10 deceased donor samples with DGF and tested two miRNAs that gave most promising results during the discovery stage.

Results: All baseline characteristics of the groups were comparable except for cold ischemia time, 152 minutes in the IF group vs. 798 minutes in DGF group, $P < 0.001$. Levels of miR-199, -194, -192 and -182 were mostly undetectable. However, levels of miR-21 and miR-155 were significantly different between the IF and DGF groups. Mean level of miR-21 was 52 in IF group versus 8 in DGF group, $P = 0.005$. Mean level miR-155 in the IF group was 16 and 1 in the DGF group, $P = 0.026$. In the validation cohort, the mean level of miR-21 for living donor samples with IF was 59, and 12 in the deceased donor group with IF and in the deceased donor group with DGF the miR-21 level was 0.2, $P < 0.001$. Mean level of miR-155 was not significantly different in the three groups.

Discussion: MiRNAs in graft preservation fluids are promising novel biomarkers for predicting outcome prior to kidney transplantation. In the era of extended criteria donor organs, this may have great clinical impact for graft reconditioning strategies to improve transplant outcome.

P110

Capsulotomy improves microvascular perfusion of ischemically damaged porcine kidneys

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Introduction: Kidneys from donors after circulatory death suffer from ischemic injury. Ischemia leads to endothelial damage and causes edema. Because the renal capsule withholds the renal tissue from expanding, renal compartment syndrome with reduced tissue perfusion may develop. We studied the effect of capsulotomy on the perfusion of ischemically damaged machine perfused porcine kidneys.

Methods: Kidney pairs were retrieved from eight slaughterhouse pigs and assigned into two groups: 20 minutes and 45 minutes of warm ischemia. Kidneys were perfused for 21 hours on a hypothermic perfusion machine, after which a capsulotomy was performed. During perfusion, flow, renal resistance, renovascular circulating volume, intraparenchymal pressure and weight were recorded. Parenchymal injury was examined with a methylene blue infusion.

Results: There was a direct effect of capsulotomy in all kidneys. Mean flow and renovascular circulating volume increased after capsulotomy (percentage increase [95% confidence interval], Δ flow = 32% [17-47], $p=.001$ and Δ renovascular circulating volume = 19% [3-35], $p=.023$). Renal resistance decreased (Δ renal resistance = -23% [-31- -15], $p<.001$). None of the kidneys showed methylene blue leakage after capsulotomy. We found no different effect of capsulotomy between groups.

Discussion: Renal compartment syndrome of ischemically damaged donor kidneys may cause allograft dysfunction and worsen transplant outcome. Opening the renal capsule may be beneficial for tissue perfusion and viability of the organ, but is rarely done. In this study, we show that microvascular perfusion can be improved with capsulotomy, without damaging the renal parenchyma. It remains uncertain which kidneys benefit most.

P111

Compliance and safety of a preoperative caloric and protein-restricted diet - a randomized controlled trial in live kidney donation and bariatric surgery

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Introduction: Surgery-induced oxidative stress leads to higher risks of perioperative complications and a delay in postoperative recovery. Patients with co-morbidities such as obesity may have an increased risk due to a pre-existing chronic subclinical inflammation status. Previous research in our laboratory showed that preoperative dietary restriction protects against oxidative stress induced by ischemia-reperfusion injury, and that the absence of protein is responsible for this protection. A previous clinical pilot study showed the feasibility of a caloric restricted diet in healthy live kidney donors, but the beneficial effects of this diet were marginal. In this pilot multicentre randomized controlled trial, we investigated the compliance, feasibility and safety of a preoperative caloric and protein-restriction diet in two different patient populations.

Methods: Thirty live kidney donors and forty morbid obese patients awaiting bariatric surgery were randomized in three groups, namely: 5 days of a 30% caloric and 70% protein restricted diet, 5 days of an isocaloric diet, or no diet. Daily energy requirements and subsequent restriction percentages were calculated via the validated Harris-Benedict formula. Both diets were given as synthetic meal replacements in the period prior to surgery. Feasibility and safety were scored via both questionnaires and reported side effects of the diets. Compliance was examined via measurement of glucose, insulin, lipid profile parameters, prealbumin and retinol binding protein levels in blood before and after the dietary interventions.

Results: A total of 71% of the patients adhered to the restricted diet as reported via questionnaires. The isocaloric control diet was completed by 65%. No major side effects of both diets occurred. Minor discomfort during the diet was experienced by 70-75% of the patients which included stool change, nausea and headache. The restricted diet did not result in differences in serum levels of glucose, insulin and lipid profiles parameters. Both prealbumin and retinol binding protein resulted in a significant decrease after the restricted diet compared to the isocaloric controls and patients without diet.

Conclusions: A preoperative caloric and protein-restricted diet is feasible and safe in both live kidney donors as well as morbid obese patients awaiting bariatric surgery. Compliance to the diet could objectively be measured via the metabolic parameters prealbumin and retinol binding protein. These results suggest that the restricted diet given in this pilot clinical trial is a good candidate to study the effects of preoperative dietary restriction on surgery-induced oxidative stress in a clinical setting.

P112

Changes in plasma nitrite levels are associated with reperfusion injury and may be influenced by induction immunosuppression

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Introduction: Serum nitrite (NO₂) sensitively reflects endothelial nitric oxide (NO) formation corresponding to acute changes in regional eNOS activity. Pro-inflammatory cytokines stimulate endothelial cells causing secretion of NO. Varying induction immunosuppression regimens have a differential impact on the pattern of cytokine release. We have previously shown that the change of plasma NO₂ post perfusion differs between donation after brain death (DBD) and donation after cardiac death (DCD) kidneys. The aim of the current study was to see if among DCD kidneys the change of NO₂ depends on factors associated with reperfusion injury and if differential induction influences this change.

Methods: In 35 DCD transplants we measured the plasma levels of NO₂ and nitrate (NO₃) by ozone chemiluminescence prior to anaesthesia and at 7 other time points pre and post perfusion and analysed their change. We also measured the level of various cytokines using a Luminex multi-cytokine kit and correlated them with the induction regime used.

Results: At regression analysis the change of NO₂ at 8 h post perfusion was related to the primary WIT (p=0.001), the age of the recipient (p=0.004) and to induction with Campath (p=0.04). ATG increases the release of TNF- α , IFN- γ , IL-6, IL-10 and IL-17. IL-2, TNF- α and IL-10 are increased more by ATG compared to Campath (p=0.003, 0.07, and 0.03 respectively) at 2h post perfusion. In addition the respective areas under the curve of cytokine values over time are larger in the ATG patients for all of the above three cytokines. In order to see if the change in NO₂ was attributable solely to the pro-inflammatory cytokine release caused by ATG or Campath, we checked separately the changes of NO₂ in patients who received Simulect. In patients in the Simulect group the change of NO₂ at 8h post perfusion was still dependent on the primary warm ischemia (p=0.008) and the recipient age (p=0.01). Moreover in patients who received ATG the change of NO₂ at 2h post perfusion correlated with the age of the donor (p=0.03), the primary WIT (p=0.04), and to the secondary WIT.

Conclusion: The levels of NO₂ post perfusion in DCD transplants are affected by warm ischemia in the donor and the age of the donor and the recipient. In spite of the up-regulation of various cytokines by ATG and/or Campath this change of NO₂ seems not to be dependent entirely on induction since it also occurs on patients receiving Simulect. This study suggests that NO₂ levels post perfusion are linked to factors affecting reperfusion injury and differential induction regimes might be modifying those factors.

P113

Cold ischaemia time is an independent risk factor for infectious complications following cadaveric liver transplantation

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Introduction: Infectious complications are common following liver transplantation and are associated with increased morbidity and mortality. Preservation injury to the graft increases ischaemia reperfusion injury and may predispose to post-operative infectious complications. A prolonged cold ischaemia time (CIT) is an important factor to preservation injury. The present study examined CIT as a risk factor for post-liver transplant infections.

Methods: A prospectively maintained database including 1299 consecutive cases of cadaveric liver transplantation was retrospectively accessed for relevant data collection. Donor, recipient and follow up data were reviewed. Bivariate and multivariate analysis was conducted examining the correlation between CIT and various infections (chest, abdominal, wound) of different pathogen groups (bacterial, viral, fungal).

Results: Prolonged CIT was an independent risk factor for chest infection ($p=0.035$), wound infection ($p=0.014$), intra-abdominal infection ($p=0.005$) and particularly of bacterial pathogens ($p=0.005$).

Conclusion: CIT predisposes to infectious complications following liver transplant. An understanding of mechanism is required, with ischaemia/reperfusion injury of sinusoidal endothelial cells and imbalance of pro- and anti-inflammatory cytokines being the main postulated causes.

Category: Brain Death

P114

Quality of donor lung grafts: A comparative study between explosive and gradual brain death induction models in rats

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Introduction: Brain dead donors are the major source of lungs for transplantation. Despite the fact that brain death induces pro-inflammatory changes, correlating with the reduction of graft quality and outcome after transplantation. This study is designed to test whether acute or gradual increase in intra cranial pressure, to induce brain death, have a differential effect on the graft quality, and to identify deleterious mechanisms.

Method: Fischer (F344) rats were randomly assigned into three donor groups: 1) no intervention and immediate sacrifice, 2) acute (explosive) - and 3) gradual brain death induction model, the latter were subdivided in sacrifice time points 30 minutes, 1 hour, 2hrs. and 4 hrs. after brain death induction. During the brain death period the animals were hemodynamically stabilized (MAP > 80 mmHg) and lung protective ventilated (VT = 6.5 ml/kg of body weight and a PEEP of 3 cmH₂O). Hemodynamic changes and pulmonary inspiratory pressure were monitored, the lungs (n = 8/ group; excluding lost animals) were analyzed with a histological scoring system and for pro-inflammatory changes in gene expression with polymerase chain reaction.

Results: Immediately after acute traumatic brain death induction 6 rats were lost, developing severe lung edema and subsequent failure of ventilation compared to none in the gradual model. Remarkable was the considerably higher need of inotropic support in the first hour of explosive brain death. In both groups patho-histological changes were found, but in the explosive model parenchyma injury was already pronounced immediately after confirmation of brain death. The over time increasing pro-inflammatory changes in gene expression differ not substantially between the models.

Conclusion: Patho-histological changes evolve predominantly after the onset of acute traumatic brain death compared to gradual brain death onset. In further studies it needs to be determined if this injury results from enhanced hemodynamic instability or subsequent hemodynamic support.

P115

Anti-apoptotic but not mitotic effects of 3, 3',5-triiodo-L-thyronine in the liver of brain dead rats

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Introduction: Thyroid hormone treatment in brain dead organ donors has been extensively studied and applied in the clinical setting. However, its effectiveness remains controversial due to a varying degree of success and a lack of knowledge about the therapeutic effects of 3,3',5-triiodo-L-thyronine (T₃). T₃ pre-conditioning leads to anti-apoptotic and pro-mitotic effects in liver tissue following ischemia/reperfusion injury. Therefore, we aimed to study the effects of T₃ pre-conditioning in the liver of brain dead rats.

Method: Brain death (BD) was induced in mechanically ventilated rats by inflation of a Fogarty catheter in the epidural space. T₃ (0.1 mg/Kg) or vehicle was administered intraperitoneally 2 hrs prior to BD induction. After 4 hrs of BD, serum and liver tissue were collected. RT-qPCR, routine biochemistry, and immunohistochemistry were performed.

Results: Brain dead animals treated with T₃ had lower plasma levels of ASAT and ALAT, reduced BAX gene expression, and less hepatic Caspase-3 activation and HO-1 expression compared to brain-dead animals treated with vehicle. Interestingly, no differences in the expression of inflammatory genes (IL-6, MCP-1, IL-1b and TNF-a) or the presence of pro-mitotic markers (Cyclin-D and Ki-67) were found in brain dead animals treated with T₃ compared to vehicle-treated animals.

Conclusion: T₃ pre-conditioning leads to beneficial effects in the liver of brain dead rats, as seen by lower cellular injury, reduced apoptosis and less oxidative stress, and suggests an important role for T₃ hormone therapy in the management of brain dead donors.

P116

Down-regulation of autophagy correlates with increased apoptosis in the kidney, but not in the liver, of brain dead rats

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Introduction: Organs from brain dead donors have inferior quality and show higher rejection rates after transplantation compared to living donors. Brain death (BD) in the donor results in increased tissue injury and apoptosis. Apoptosis is closely linked to autophagy, a stress-adaptation mechanism to avoid cell death. Dysregulation of autophagy has been linked to a number of diseases that show molecular resemblances to the BD setting, such as ischemia/reperfusion-injury and sepsis. This study aimed to investigate autophagy in the BD setting, by looking at the dynamics between autophagy, apoptosis, and tissue injury in the kidney and liver of brain dead rats.

Method: BD was induced in mechanically ventilated rats by inflation of a Fogarty catheter in the epidural space. After 4 hrs of BD, serum, kidney, and liver tissue were collected. Routine biochemistry was performed, as well as RT-qPCR for apoptotic genes BAX and Bcl-2, and autophagy genes LC3, Beclin 1, and p62, immunohistochemistry for apoptosis-effector cleaved Caspase 3 (cC3), and Western-blot (WB) analyses for autophagy proteins (LC3-I, LC3-II, p62, pS6) and apoptosis protein cC3.

Results: Brain dead animals had increased ASAT, ALAT, creatinine, and urea plasma levels. In the kidney, BD reduced levels of autophagic marker LC3-II, and increased activation of autophagy-inhibitor mTOR, which significantly correlated with increased levels of apoptosis protein cC3. In the liver, BD increased gene expression of BAX and BAX/Bcl-2 ratio, as well as cC3 expression. However, signs of increased apoptosis or affected autophagy were not observed on a protein level in the liver.

Conclusion: BD causes tissue injury in the liver and kidney of brain dead rats. However, BD had differential effects on autophagy in the liver and the kidney. While a decrease in autophagy correlated with increased apoptosis in the kidney, autophagy was not significantly altered in the liver. These results suggest a possible role for autophagy in protection against BD-induced kidney damage.

P117

The use of systems biology to identify mitochondrial dysfunction and metabolic dysregulation as targets for intervening in the brain dead organ donor

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Introduction: Understanding how kidneys are injured during brain death (BD) will allow the development of new strategies to protect kidneys in the donor. We previously reported, using proteomics and metabolomics that mitochondrial dysfunction and metabolic dysregulation occurs following BD [WTC 2014]. To gain further insight into this have we now characterised the effects of BD on mitochondrial morphology, enzyme function and oxidative stress.

Methods: Kidney samples were compared from BD rats against sham and living donor controls as previously described. Following BD, ventilation was continued for 4 hrs. Transmission electron microscopy (TEM) was performed using 80nm sections cut and stained in uranyl acetate and lead citrate prior to EM examination. Complex II/III activity was performed on isolated mitochondrial as previously described. RT-PCR was used to investigate mRNA levels of HO-1 as a surrogate marker of oxidative stress.

Results: Morphology of mitochondria in the proximal tubular compartments of the cortex demonstrated heterogeneous appearances. Increased detachment of cristae were noted in the BD group compared to sham and living donor controls (Fig 2). A progressive increase in complex II/III activity was found in the BD group (1.49 +/- 1.17 nmol cytc/mg/sec/nmol DTNB) compared to living donor (0.37 +/-0.27) and sham controls (0.85 +/- 0.77). Relative quantitation of HO-1 mRNA level demonstrated a similar pattern.

Conclusion: This study confirms the omics profile previously described and shows morphological evidence of mitochondrial injury in comparison to controls. In addition we detected a trend towards increased complex II/III activity in the BD group that together with the omics data and HO-1 levels suggests metabolic disturbance and oxidative stress.

Future strategies to improve outcomes of kidney transplantation from BD donors need to address the increased metabolic demands and mitochondrial injury occurring during BD possibly by using the HIF pathway.

P118

Characterisation of the effects of brain death on hypoxia inducible factors in the kidney

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Introduction: We have previously reported that modulation of the hypoxia inducible factors (HIF) offers therapeutic potential in transplantation [1]. Our recent work suggests that brain death (BD) leads to metabolic disturbances and therefore metabolic reprogramming by modulation of HIF could be particularly advantageous in the organ donor. To begin to address this we characterised the effects of BD on the HIF pathway.

Methods: Kidney samples were procured from BD rats at 1, 2 and 4 hour time points after BD induction and compared against sham and living donor controls as previously described. Western blotting (WB) was performed on kidney samples against HIF1 α (Cayman) and prolyl hydroxylase (PHD) 1 and 2 (Novus). Results were normalised and band intensity semi-quantitatively expressed. Immunohistochemistry (IHC) against HIF1 α (Cayman) was performed (Dako). Downstream target genes of HIF1 α were characterised comparing the control groups against the 4 hour BD using RT-PCR for heme-oxygenase 1, glucose transporter 1 and PHD1.

Results: WB and IHC showed a non-significant increase in HIF1 α comparing the 4 hour BD animals against shorter time periods of BD and the controls ($P=0.44$). The majority of HIF1 α expression was observed in the medulla. PHD1 and 2 were not significantly different between the BD groups and the controls and HIF target genes were not significantly up-regulated within the 4 hour post BD time period.

Conclusion: Our results indicate that BD results in some activation of HIF1 α in the kidney, however this was not significantly different compared to controls. None of the target genes of HIF1 α appeared to be significantly affected by BD. A longer follow-up period may reveal changes in gene expression. These results indicate scope to up-regulate HIF and its target genes during BD. Further evaluation will require establishing the effects of HIF modulation on preservation and reperfusion injury.

1) Akhtar MZ, *et al.* Am J Transplant. 2014 Jul;14(7):1481-7.

P119

Speed of onset of donor brain death leads to differences in renal function and expression of inflammatory and oxidative stress markers in rat kidneys

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Introduction: Donor brain death (BD) is an independent risk factor for primary and delayed renal graft function. Furthermore, the speed of onset of brain death, traumatic (sudden) or hemorrhagic (gradual), influences graft function after transplantation. No explanation has been reported so far to explain the differential effect of cause of donor BD on renal graft function. This study was conducted to elucidate potential underlying processes initiated by either sudden or gradual brain injury leading to BD.

Materials and methods: Gradual- and sudden onset BD was induced in 64 mechanically ventilated male Fisher rats by inflating a 4.0F Fogarty catheter in the epidural space. Rats were observed for 0.5 h, 1 h, 2 h, or 4 h following BD induction. Tissue and serum from 8 non brain dead rats were used to obtain baseline values. Gradual onset BD was achieved by inflating the catheter at a speed of 0.015 ml/min until confirmation of BD by the increase in blood pressure (BP) due to the characteristic catecholamine storm. Sudden onset of brain death was achieved by inflating the catheter at 0.45 ml/min for 1 minute. BP was kept above 80 mmHg through the administration of plasma expanders or nor-epinephrine. Temperature, end tidal CO₂ and oxygen saturation were regulated and kept at normal values.

Results: Gradual-onset BD led to a consistent drop in BP below 60 mm Hg during induction whereas sudden-onset BD led to a rise in BP above 200 mmHg. Sudden-onset BD rats required more inotropic support during the first hour of BD. Plasma creatinine values were significantly higher in gradual-onset BD rats at all time points. Gradual-onset of BD led to significant higher renal levels of, MDA, glutathione reductase activity, oxidized glutathione and mRNA expression of IL-6, HO-1, iNOS, and MnSOD after 4 h of BD.

Conclusion: Gradual-onset of BD leads to increased renal inflammation and oxidative stress compared to sudden-onset of BD. The hypotensive period during gradual-onset BD induction could be a possible explanation for these results.

P120

Kidney temperature course during living organ procurement and transplantation

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Objective: The second warm ischemia time (WIT2) during living donor kidney transplantation (LDKT) is considered an important outcome measure for future organ function and survival. Experimental studies show that after cold storage metabolism will already resume at 15 °C. Our aim is to determine the temperature course and variations during WIT2 in kidney transplantation.

Methods: Data were prospectively collected on 90 consecutive adult LDKTs. During the preoperative, intraoperative and postoperative periods kidney temperature and function related markers were measured periodically using standardized data forms. Patient demographics were extracted from digital patient records. Kidney temperature was measured using an infrared thermometer (Votcraft, 10 09 17, IR 800-20D). All statistical analyses were done using SPSS (IBM© SPSS Statistics©, Version 20).

Results: The mean temperature of the donor and recipient at the start of the operation were respectively 36.2°C and 35.8 °C. After cold storage the mean kidney temperature was 1.7 °C. The mean WIT2 was 44 minutes with a temperature of 5.4°C at the start which gradually raised towards 13.7 °C and 17.4 °C after 10 and 20 minutes respectively. After 30 minutes the mean temperature measured was 20.2 °C. The percentage of kidneys with a temperature of 15 °C or higher was 29.7 %, after 10 minutes 81,2 % after 20 minutes and 97.5 % after 30 minutes. Creatinine levels at day 1,3,7 en 30 did not significantly differ between groups reaching the 15 °C threshold after 10, 20 or 30 minutes during WIT2.

Conclusions: This study shows that there is a rapid increase in temperature of the donor kidney during WIT2, wherein the 15°C threshold of active tissue metabolism is already reached after 20 minutes in more than 80% of the patients. More research is necessary to determine the effect of this increase in temperature during transplantation in association with metabolic influences during this period for further optimization the conditions during kidney transplantation in favor of overall graft survival.

Category: Infections

P121

Investigation of a cluster of infections due to *Pneumocystis jiroveci*

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Introduction: *Pneumocystis jiroveci* pneumonia (PJP) is a life-threatening complication of immunosuppression. In response to a local increase in cases, we undertook a five year retrospective analysis to identify individual patient and epidemiological risk factors, and determine whether there was a potential contribution by any changes in post-transplant management over this period.

Methods: Potential infections were identified by pharmacy records of high dose co-trimoxazole prescriptions over the study period, and confirmed cases identified by microbiology records. For all cases, the following data was extracted: age, gender, residential address, primary renal disease, dialysis vintage, number and date of all transplants, date of PJP diagnosis, last three clinic dates prior to diagnosis, immunosuppression and lymphocyte count at time of PJP, timing and treatment of any previous episodes of rejection, CMV status pre-transplantation and episodes of CMV viraemia. The PJP cohort was compared with a matched control group of 20 PJP negative renal transplant patients.

Results: Of the 47 potential cases identified by co-trimoxazole administration, confirmatory testing was positive for 12 (26%), negative for 17 (36%) and not done for 18 (38%). There were 0 – 2 confirmed cases per year in the four years prior to August 2013, but 8 cases occurred between then and June 2014. We found no evidence to support nosocomial transmission. The median time from transplant and from rejection episode to PJP was 682 (range 122-3729) days and 188 (range 89-728) days respectively, with 25% occurring within six months of rejection treatment. No patients were taking co-trimoxazole prophylaxis at diagnosis. The only significant difference between those with infection and controls was the lymphocyte count at diagnosis (cohort: 0.79×10^3 vs. control: $1.65 \times 10^3/\mu\text{L}$, $P = 0.04$) with trends for previous rejection episode ($P = 0.06$), CMV IgG positivity at time of transplant ($P = 0.06$) and post-transplant CMV viraemia ($P = 0.07$).

Conclusions: Post-transplantation PJP remains a serious and unpredictable infection, and clinicians should be vigilant for its occurrence, even many years after transplantation.

P122

The outcome of carbapenemase-producing enterobacteriaceae (CPE) infection in adult solid organ transplant population at a university teaching hospital

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Background: Over the last decade CPE infection has been reported globally and is now endemic in healthcare facilities in many countries. There has been no report of the effect of CPE infection in Transplant population as yet. Therefore, we aimed to study the epidemiology and outcomes of CPE infection in our pancreatic-renal transplant unit.

Method: All Transplant patients tested positive for CPE over last 10 years from Hospital CPE database were identified. Rapid CPE test was used to screen patients and CPE infection was defined as positive CPE culture from a subsequent clinical isolate. Hospital notes of CPE infection patients were retrospectively reviewed to identify risk factors of infection and transplant outcomes. Stats-direct version 3 was used for statistical calculation.

Results: 272 patients were screened positive for CPE infection. 46/272 (17%) patients had subsequent positive clinical isolate requiring treatment. 12/46 (26%) patients developed positive blood culture requiring IV antibiotics according to sensitivity. 09/46 (19%) of CPE isolated patients required ITU support. 02/46 (4%) patients with other multiple co-morbidities died. The incidence of CPE increased over last 3 years with the first patient identified in 2010; log increase was 266% in 2011, 162% in 2012, 138% in 2013 to expected 111% in 2014. The Interquartile age distribution of CPE infected patients was 32-81 years, 95% CI 49.2-57.9, $p=0.20$, with equal gender distribution. CPE infection was associated with prolonged hospital stay (> 15 days) 95% CI 15.5-32.9 days, $p<0.001$ on multivariable linear regression model. CPE infection was not statistically associated with poor graft function ($p=0.33$). The death censored graft loss rate was 2%. ($p=0.12$)

Conclusion: Prolonged hospital stay is associated to CPE infection. Urgent preventive steps like hand washing, early hospital discharge may minimize the infection risk. More experience is required to augment our strategies to control CPE infection rate.

P123

Small bowel transplantation and infections: defining the role of antifungal therapy in a single centre over 5 years

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Background: Small bowel transplantation is the treatment of choice for a select group of patients that fulfil the criteria set out by the American Gastroenterology Association. Although immunosuppressive therapies have evolved over the years, the transplant recipients overall immunosuppressed status predisposes them to infectious complications. Depending on the organ transplanted, the incidence of invasive mycoses ranges from 5 to 42%. *Candida* and *Aspergillus* spp. produce most of these mycoses.

Aims: In this study, we assessed the incidence of invasive aspergillosis after SBT and the role, safety and peculiar side effects of AmBisome as drug of choice for antifungal prophylaxis in small bowel transplant patients over a period of 5-years.

Methods: We retrospectively investigated from October 2008 to date, 28 SBT's have been done at our centre. There were 9 sustained episodes of neutropenia in the last 5 years. The first 2 patients with neutropenia did not get any AmBisome cover during the episode of neutropenia. These two patients died from an invasive *Aspergillus* abscess in the brain. The unit policy was changed at this point to include AmBisome therapy in patients having sustained neutropenia and thus the second phase was defined. Since the Institution of the 'second phase' of anti-fungal delivery, there has been no more incidence of invasive *Aspergillus* infection.

Conclusion: Institution of AmBisome during neutropenic periods was adopted for all patients post SBT with sustained neutropenia. This we believe may be one of the reasons that we have not seen any more invasive *Aspergillus* infections. AmBisome is generally a safe drug for antifungal prophylaxis in small bowel transplant patients.

P124

Coxiella burnetii seroprevalence in tissue donors after the great Q fever outbreak in the Netherlands

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Introduction: In the Netherlands a great Q fever outbreak has taken place from 2007 until 2010. Before this outbreak a seroprevalence of antibodies against *Coxiella burnetii* of 2.4% had been reported. During the outbreak the seroprevalence among blood donors raised to 12.2% in high risk areas. The council of health advised to test donors who donated high risk tissues for a past infection with *Coxiella burnetii*. In this study antibodies against *Coxiella burnetii* in the past 4 years have been analyzed.

Methods: Tissue donors from October 2010 to October 2014 have been tested on antibodies against *Coxiella burnetii* (anti-phase II IgG EIA). In case of a positive result the test was confirmed by an immune fluorescence assay (IFA).

Results: Post mortem donors of cornea, skin, heart valves, bone/tendon (N=4183), living donors of femoral heads of the two biggest bone banks in the Netherlands, Nijmegen (N=2267) and Leiden (N=3619) and cord blood donors (N=992) were tested. Totally 254 donors tested with a positive result (2.3%, of which 154 positive and 100 borderline positive) and in 73 of the donors the test was probably false positive where the positive EIA result could not be confirmed by the IFA (0.7%). In post mortem donors the sero positivity was 3.2%, in femoral heads 2.2% in Nijmegen and 1.4% in Leiden and 1.7% in cord blood donors. In the past 4 years the seroprevalence has dropped from around 4% in 2011 to 1.4% in 2014 and it seems to stabilizing there.

Conclusion: The seroprevalence of antibodies against *Coxiella burnetii* has dropped in the past years after the outbreak and seems to stabilize around 1.5%. This is comparable with the situation before the outbreak. Now it is important to discuss when testing for antibodies against *Coxiella burnetii* in tissue donors can be stopped.

P125

The value of perfusion fluid culture analysis in deceased donor renal transplants: 5 years single centre experience

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Introduction: Microbiological analysis of kidney perfusion/transport solution is not routinely performed in all UK transplant centres. The aim of this study is to assess the impact of routine analysis on patient management and outcome.

Methods: Data were collected retrospectively on all deceased donor transplants performed between 2009-2013. Organisms detected were classified as either pathological, uncertain pathogenicity, or contaminants. Treatment was guided by the microbiology team. Outcomes including type and duration of treatment, morbidity and mortality, length of hospital stay (LOS) and biopsy-proven acute rejection (BPAR) were compared between recipients receiving grafts with culture-positive (PF+) and culture-negative (PF-) perfusate.

Results: In total 328 deceased donor transplants were included, of which 273/328 (83.2%) had perfusate samples analyzed. Organisms were cultured in 50/273 (18.3%) of these samples. Twenty-three different organisms were identified in the PF+ specimens, of which 15/23 (67%) were pathological the most common of which were *Escherichia coli*, *Enterobacter cloacae* and 3/50 (6%) cases involved candida. LOS in patients with PF+ was 11 days compared with 7 in PF- patients. There was no difference in morbidity, BPAR rates or mortality between the 2 groups. Directly attributable complications of pathogenic PF+ included wound infection (n=2) and urosepsis (n=3). A statistically significant proportion of PF+ samples came from donors after circulatory death (DCD) perfusate 33/50 (66%) compared with brain-dead (DBD) perfusate 17/50 (34%) ($p = 0.0004$, Chi-squared test).

Discussion: Identification of organisms in perfusate is common (18.3%) and in 2/3 of cases the organisms are potentially pathological. The similarity in outcomes between PF+ and PF- graft recipients may be secondary to the pro-active identification and treatment of pathological organisms. PF+ graft recipients may subsequently experience longer LOS. PF+ was more frequent in DCD grafts compared to DBD grafts possibly as a result of bacterial translocation during warm ischaemia. Further studies are needed to assess the impact of pro-active treatment PF+ on patient outcomes.

P126

Urinary tract infection and the use of transplant ureteric stents in renal transplant recipients – a single centre experience

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Introduction: There is no clear evidence that the use of a transplant ureteric stent is beneficial or detrimental to the kidney transplant recipient, hence the lack of uniformity in practise in the transplant surgical community. We have previously shown that stenting patients resulted in an increase in the number of positive mid-stream urine (MSU) specimens. We were unable to correlate this with clinical symptoms and diagnose a urinary tract infection (UTI) and therefore the relevance of presenting with a positive MSU.

Methods: Data was collected prospectively for 6 months using a proforma. We collected data on blood and urine results, urinalysis and urinary symptoms. Symptoms and investigation findings were correlated with MSU samples and the use of a ureteric stent.

Results: 53 kidney transplant recipients (34 men) with a mean age of 51.8yrs attended clinic 605 times. 32 patients had a ureteric stent for a median duration of 34 days. 49 +ive MSUs in 20 patients were identified. 8 of these were within one week of a previous +ive MSU, and so counted as the same MSU result. 8 of these patients had stents. E.Coli and Enterococcus were the most common organisms grown. Only one urological complication (urine leak) occurred during the study period. This patient had a stent in situ. Urinalysis results were available for 598 clinic visits. The presence of blood, protein and leukocytes, high WCC or high CRP showed specificity of 87%, 83%, 98%, 93% and 94% respectively for MSU positivity, but sensitivity was poor. 17 patients presented to clinic with symptoms a total of 31 times. 35% of patients who presented with symptoms had a +ive MSU and were labelled as having a UTI. This figure was 6.8% in the absence of symptoms. No patients with +ive MSU and a ureteric stent had symptoms.

Conclusions: There is a 1 in 3 chance of a patient having a UTI (+ive MSU and symptoms) if they present post-transplant with urinary symptoms. In this prospective audit, the presence of a ureteric stent does not infer an increased risk of UTI and therefore the practise of individual surgeons should not change.

P127

Epidemiology of bacteremia in kidney transplant recipients and its therapeutic implications

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Background: Infection is a significant cause of morbidity and mortality in solid organ transplantation. The aim of this study is to understand the epidemiology of bacteremias within our renal transplant population, and thus optimise prevention and treatment strategies.

Methods: A retrospective review of all adult patients who received a kidney transplant at our center, from July 2009 to May 2014, was conducted. All positive blood cultures were identified and data gathered on cultured organisms, antibiotic susceptibilities, and patient demographics.

Results: There were 104 positive blood cultures from 78 patients (age range: 23 – 78 years (median 56 years)), 55.13 % males and 44.87% females. Enterobacteriaceae represented 66.35 % of the culprit organisms, with E coli the most common (42.31%). Pseudomonas and Enterococci were encountered in 7.69 % and 5.77 % of cultures respectively. The urinary tract was the source of infection in 49.04 % of cases followed by the GIT (9.62 %). Among the Enterobacteriaceae, all the strains retained susceptibility to Carbapenems and Amikacin. Colistin and Fosfomycin were effective in over 90 % of cases, Tazocin and gentamicin in 82.5% and 69.23 % respectively, and Ciprofloxacin and Ceftriaxone in about half the cultures. There were high rates of resistance to Amoxicillin (82.93%), Trimethoprim (63.41%), Septrin (56.67 %), and Augmentin (56.1 %).

Conclusions: UTI remains the commonest source of systemic infections post-transplant, thus prevention and early detection remain important. It is paramount to get the right choice of antibiotic in a septic immunosuppressed patient, but this must be balanced against the overuse of broad spectrum antibiotics in the era of rapidly increasing antibiotic resistance. Tazocin would be a possible choice but does not cover 100% of the organisms. Amikacin is an option but clinicians remain concerned about the risk of nephrotoxicity. Each unit needs to understand the epidemiology of the organisms causing sepsis in their transplant patients.

Category: Miscellaneous

P128

“How was it for you?” Post kidney transplant patients’ and carers’ experience and education feedback

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Aim and introduction: Patients’ report that meeting with their carers outside a clinic setting can enhance their experience of having a kidney transplant. These meetings may also help healthcare professionals improve healthcare delivery in response to feedback, particularly after a major change in service delivery.

Methods: As part of a planned decentralisation strategy a cohort of renal transplant patients were moved to a transplant clinic at a community hospital. We were interested in hearing from these patients one year on. Those involved in planning the event included patients, doctors, nurses, pharmacists, and the trust’s patient experience team. We advertised using posters, leaflets and personal contact, and, in order to encourage attendance, the event for patients and carers was run straight after the clinic with lunch and short talks by patients and members of the multidisciplinary team. All present were invited to contribute to subsequent discussion; service users completed a brief questionnaire.

Results: There were 13 attendees, 3 carers, 10 patients (from a cohort of 70): each completed an evaluation form. Demographics showed diversity in terms of gender, age and ethnicity. 40% of patients had undergone kidney transplantation more than once. Time range from transplant ranged 10 months-23 years. 100% of patients reported that the meeting was helpful; 90% understood reasons for having the event; 80% thought enough time available to speak, be listened to and understood. All patients reported that they were happy with care received at the satellite transplant clinic. All felt the event was enjoyable and valuable and should be repeated regularly.

Discussion: Patient involvement and feedback is high on the NHS agenda. We show here that kidney transplant patients and carers value the opportunity to discuss their experiences and give feedback about the service. The success of the renal transplant meeting has led to it being used as a model in the trust’s strategy for patient involvement which attracts local CQUINS. Future events are planned at targeted groups, first anniversary and the wider renal transplant population.

P129

Increasing organ donation awareness amongst black and minority ethnic communities

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Introduction: To describe the methods we have employed to engage with people in BAME communities to raise awareness of kidney disease risk and organ donation and to overcome the barriers to donation.

Methods: Peer Educators (PEs) are people from the targeted community who are recruited and trained to engage with members of their community. They have an empathy with the target groups in terms of culture, religion and language and engage with groups at both special meetings and pre-arranged major events. We have developed a structure which enables us to deploy the model in a sustainable way, but which can also be adapted to meet the specific requirements for both gender and age which are key to achieving behavioural change.

Results: Across all programmes, we have trained 120 PEs, reached over 25,000 'at risk' people, and, in the organ donation awareness projects, more than 2,500 have signed the ODR, 136 at one event alone. The model was also used to disseminate the findings of a previous research study on attitudinal barriers to organ donation; this work led to an award from the Association of Medical Research Charities (AMRC).

Discussion: The model has been found to be a culturally sensitive, flexible and highly adaptable approach to addressing health and organ donation issues. It can address early disease detection, prevention, end-of-life issues and organ donation. It has been well evaluated in the area of organ donation and the intent is to continue to build on our 10+ years of experience to address key challenges in organ donation and consent. Recognising the need for sustainability and greater impact, the programme also reaches out to key opinion leaders and health care professionals, who are members of these communities. The work is ongoing and the session will explore current projects in two locations in the UK.

P130

Hearing voices: patients' and carers' feedback at the national kidney patients' and carers' forum

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Aim and introduction: Kidney transplant outcomes are generally good but we recognise that living with a transplant may not be straightforward. We wanted to engage patients and their families to hear their experiences and ideas and provide some education. This was the third of such meetings held away from a clinical environment to promote discussion in an informal, 'clinician light' environment with an agenda set by the participants.

Method: Participants' experience of a conference-style meeting in which talks in a main auditorium, followed break-out workshops conducted by a nephrology specialist registrar, a clinical health psychologist and a transplant nurse, was evaluated using a 30-item questionnaire designed specifically for the event. Additionally, information was collected on patients' pre- and post-transplantation experience and their access to different services.

Results: Of the 44 participants, 19 completed the evaluation questionnaire. Forty-seven percent were male, the median age was 58 years and respondents were ethnically well represented. All but one respondent had received dialysis treatment and most (78%) had received just one kidney at one of five different transplant centres. Most were very satisfied and rated their transplant experience, quality of life, and overall health as a 9 or 10 out of 10 (58%, 63% and 74% respectively). Improvement pertained to more education/improved communication and the need for additional formal psychosocial support.

Conclusion: This initiative started in 2007, pre-Francis but fulfils the Francis and Berwick reports' requirement for finding ways of hearing the voices of patients and their families to deliver better, more responsive services. Transplant patients and their relatives valued the peer support and networking opportunity.

P131

Dutch educational programs have effect on organ donation

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Introduction: Between February 2010 and September 2012 the NTS launched a line of educational programs on organ donation for youngsters between 10-20 years old. The goal is preparing youth for deciding about organ donation. Our study examined if DonorWise (secondary school) and Xtralife (occupational training) fulfil this goal.

Methods: The programs present neutral information; provoke opinion forming; urge discussion with contemporaries and families and stimulate registration of donor preferences: 'yes' or 'no'. Quantitative fieldwork: 317 students answered questions about their knowledge, opinion and behaviour towards organ donation before and after the lessons with the educational programs. In addition 898 teachers were questioned.

Results: The research shows positive effects. After lessons with DonorWise and Xtralife: students know more and say they know enough to make their own decision (increase of 20%). 17% of the students with no opinion before the lesson formed a stronger opinion afterwards. The programs show stronger impact on students at occupational training than at secondary school. After following lessons: more higher educated students are willing to donate (increase of 20%); they more often discussed donation with their friends and families; and 25% of them even intent or already have registered after the lessons. This is probably due to their higher average age (21 compared to 15 years old) and education level.

Conclusion: The educational programs DonorWise and Xtralife have a strong impact on the decision making process on organ donation. After lessons with DonorWise or Xtralife students are able to make a deliberate decision about organ donation and register their preferences more often than before the lessons.

P132

Are transplant related websites useful to patients and clinicians?

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Introduction: The use of the internet as a source for medical information has become increasingly popular in recent years. The only study to assess the quality of renal transplant websites, conducted in 2007, found their quality to be generally poor. This research explores the current quality of renal transplant information on the World Wide Web.

Methods: Four search engines were used to generate a list of websites for analysis using the search term 'kidney transplantation'. Websites were scored independently on the quality of information, presence of kite-marks, degree of referencing, and readability. A modified weighted Information Score (IS) was used to analyse the clinical content of each site. Readability was assessed using a Flesh-Kincaid score. References were a scored using a 4 point scale.

Results: A total of 160 potential websites were selected, of which the repeated (n=77), non-accessible (n=11) and non-relevant websites (n=37) were excluded. Thirty-five websites were assessed, the median IS score for which was 36/100 (IQR 24-43). 'Normal kidney function' was covered most frequently scoring 60% of all possible IS points. There was no significant difference between the IS scores of kite-marked compared with non kite-marked websites (p=0.310). There was also no observable difference in quality scores from the UK (average IS = 32) compared with the USA (average IS = 34) (p=0.890). There was also no correlation between website quality and readability (p=0.200) or referencing type (p=0.230). There was no difference between the two observers (p=0.690).

Conclusion: The quality of renal transplant websites remains poor regardless of country of origin. The presence of a kitemark or academic references may be deceptive and are not good indicators of the quality of clinical content of the website. Renal transplant websites require significant improvement to ensure comprehensive and high quality information is available to renal transplant patients in the future.

P133

An evaluation of the effectiveness of information given to potential renal transplant recipients going through the listing process

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Background: Information provision for potential renal transplant recipients is usually a combination of written patient information and a subsequent 'face-to-face' consultation with a member of the transplant team. The aim of this study was to discern to what extent patient understanding of renal transplantation was improved by face-to-face interaction in comparison to patient information leaflets alone.

Methods: A previously validated 19-item, single best answer multiple choice questionnaire was distributed to a sample of 30 patients recently eligible for renal transplantation. It aimed to evaluate patients' knowledge about the basic elements of the renal transplant process in addition to long-term follow-up and complications. Participants completed the same questionnaire preceding, and immediately following, their consultation. Outcomes were compared and underwent statistical analysis using SPSS software.

Results: Twenty seven participants enrolled in the study. The questionnaire score before consultation was median (Range), 15 (8 – 19) and following consultation was 18 (13 – 19) ($p < 0.001$). Significant improvement was found in 6 of the questions. Questions pertaining to the success of renal transplantation were answered most poorly with $\leq 70\%$ of participants answering correctly after the consultation.

Discussion: Patients in the process of being listed for renal transplant appear to be a well informed group. However patient understanding of the renal transplantation process can be improved by 'face-to-face' consultation. Furthermore, particular attention should be paid to graft outcome when informing and consenting this patient group.

P134

A unique event: exchanging experiences between donor families and intensivists during expert meeting in the Netherlands

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Introduction: Organ donation is not a daily practice in ICU's, therefore it is difficult for intensivists to obtain expertise in this field. The Dutch Masterplan Organ Donation introduced 'donation intensivists' (DI) as the key person, in comparison to the 'Clinical Lead Organ Donation' (CLOD) in the UK. DI's are supported in their new role by the Dutch Transplant Foundation, which organizes 'Expert meetings'. These meetings aim at providing better knowledge and answers to complex situations in the practice of organ donation. The fourth meeting contained a unique event intending exchange of experiences between donor families and intensivists, in order to improve the process of organ donation in the future.

Methods: Under guidance of psychologists, thirty donor families and fifteen DI's, divided into five subgroups, shared their experiences. Donor families and intensivists were screened to prevent that they were familiar. The relative who donated organ(s) passed away over a year ago.

Results: Essential information for intensivists was the explanation to the family of the term 'brain death' by showing the EEG or the apnea test and the provision of clear information about duration and timing of the different parts of the procedure. A prolonged duration of the procedure is positively experienced, and allows families extra time with their loved one. Being clear about the death of their relative is not experienced as harsh, but is necessary for the family to accept the message. Intensivists should avoid talking about the organs, and talk about the deceased patient as a person. Surprisingly, errors in communication or organization were forgiven as long as it was honestly told. Further, a farewell at the intensive care after retrieval of the organ(s) is experienced as very helpful in handling grief. For donor families the meeting was a success, knowing that sharing their experiences contributed to increased knowledge.

Conclusion: Exchanging experiences was extremely useful for both the intensivists and the families. The information provided gives rise to a change in the approach and guidance of potential donor families.

P135

Kidney transplant patients' attitudes towards self-management support: a q-methodological study

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Introduction: The objective of this study was to identify profiles of kidney transplant recipients with varying preferences and needs for self-management support (SMS). Insight in these profiles can help to design tailored SMS interventions.

Methods: Patients <6 months after transplantation were invited to participate to ensure a sample with varying self-management experiences. Inclusion criteria were age (over 18 years), Dutch-speaking and a functioning graft. Patient profiles were generated using Q-methodology. Participants rank-ordered opinion statements according to agreement on various aspects of SMS. Factor analysis was used to analyse the rankings. The resulting factors represent patients with comparable attitudes towards SMS.

Results: Thirty-four patients (mean age 56; 79% male) participated. The majority were married (68%), unemployed (68%) and Dutch (91%). We identified three patient profiles: Profile A (adherent and transplant-focused), Profile B (collaborative and holistic) and Profile C (autonomous and life-focused). Patients in Profile A are more likely than the others to agree that their lives revolve around their transplant, that medication alone is not enough for recovery, and that they are adherent to health care providers' recommendations. Patients in Profile B are more likely to agree that their health is a shared responsibility with health care providers, that an interdisciplinary approach is needed and that they find it difficult to adhere to self-management recommendations. Patients in Profile C are more likely to agree that they want to be autonomous in decision-making, that they strive to minimize the impact of the transplantation on their daily lives as much as possible, and that they only expect SMS from professionals in the medical domain.

Discussion: Three profiles of attitudes toward SMS after transplantation were identified, indicating the need to provide personalized self-management support.

P136

Is the outcome for the kidney transplant recipients dependant on who takes the kidney offer?

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Introduction: The process of accepting or declining kidney offers is complex and based on multiple factors related to both the donor and recipient. The decisions are often made in the middle of the night when cerebral function may not be ideal. The UNOS KDRI is a tool that can be used to help stratify the quality of the deceased donor kidneys using various donor criteria and linking this to graft outcomes.

Methods: We have looked retrospectively at 6 years of deceased donor kidney offers between 2008 and 2013 made to our unit. This coincides with continuity in the consultant workforce in our unit. Kidney offers, where possible, have been risk scored using the KDRI calculator and this has been stratified against the surgeon taking the offer and the graft function post operatively. The surgeon accepting the kidney is not necessarily the same as the implanting surgeon.

Results: During this time frame we accepted and transplanted 279 deceased donor kidneys. We also accepted 113 kidney offers that then did not proceed for a variety of reasons. These cases were analysed together. The KDRI score across this time period for accepted and declined kidneys was 1.34+/-0.44 and 1.53+/-0.48 respectively (mean+/-SD). The median creatinine has decreased from 136 to 124 and MDRD GFR has increased from 46 to 50 over this time period.

Surgeon	KDRI (mean+/-SD)	Offers declined	Offers accepted	Creatinine at 1yr (median)	MDRD GFR at 1yr (median)
1	1.38+/-0.45	32	36	143	51
2	1.31+/-0.42	54	100	130	48
3	1.35+/-0.46	46	118	131	52
4	1.33+/-0.43	64	110	134	47

Data for kidneys offered to Portsmouth

Conclusion: This data demonstrates that despite the complex nature of the decision to accept or decline a kidney offer, it does not matter who is on call surgically as the type of kidneys we are accepting are comparable with equivalent graft function at one year.

Category: Clinical - Heart and Lung

P137

Too frail to transplant?

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Background: The impact of frailty on outcomes after lung transplantation is not known. We hypothesized that the frailty phenotype might help identify patients at high risk for 1- year mortality after lung transplantation. We studied: 1) the prevalence of frailty in patients awaiting lung transplantation. 2) The relationship between frailty and severity of pulmonary diseases and which risk factors affect 1-year survival rate.

Methods: Patients on the waiting list for lung transplantation in our institution underwent frailty assessment. Frailty was assessed using Fried Index objectified with 5 criteria: weight loss, exhaustion, weakness, slow walking, low physical activity. Patients scored frail at ≥ 3 criteria. The severity of pulmonary diseases was determined via the Lung Allocation Score (LAS). We used cross tables to determine the relationship between frailty index, diseases and the LAS. Retrospective we used univariate cox regression to analyze the influences of disease, hospitalization, respiration, pulmonary hypertension and age of death in the first year after transplantation.

Results: 40 patients were included (72,7% of all listed). 17 (42,5%) patients were categorized as frail. COPD patients were more frail than patients with CF, pulmonary fibrosis and PH. Frailty index and LAS were not related. The 1-year mortality of 11.4% (n at risk = 79) in our institution lies under the reported national proportion of 15-20%. Patients with CF have a decreased risk of death (HR 0.67; 95% CI 0.08-5.42) than COPD (HR 1.15; 95% CI 0.31-4.29), pulmonary fibrosis (HR 0.78; 95% CI 0.16-3.78) and PH (HR 0.67; 95% CI 0.08-5.42). Higher age (HR 1.62; 95% CI 0.86-3.05) and artificial respiration (HR 28.42; 95% CI 0.25-31829.09) confer an increased chance of death.

Conclusion: 1- year mortality is especially high in patients with COPD. COPD patients are most often frail of all patients. These findings merit a prospective study investigating whether the frailty index may yield additional information (next to the LAS) in identifying patients suitable for transplant.

P138

Tolerance to exercise in high-altitude in organ transplant recipients

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Introduction: An expedition to Mount Kilimanjaro was undertaken to raise donor awareness, show the capabilities after transplantation (Tx) and study the tolerance to exercise on high-altitude in organ transplant recipients.

Methods: Eligible participants were preselected by their physician. Final selection was based on maximal exercise capacity, muscle strength and structured interview. Twelve Tx-recipients were selected (2 heart-Tx, 2 lung-Tx, 2 kidney-Tx, 4 liver-Tx, 1 stemcel-Tx and 1 small bowel-Tx) and received an individual training program. A convenience control group was used (medical team and joining family of participants, $n=14$). During the climb blood pressure (BP), heart rate (HR), oxygen saturation (saO₂) and symptoms of acute mountain sickness (AMS) were measured twice daily. At three points during the climb capillary blood was analysed and an additional measurement was done at sea level.

Results: In October 2014 the ascend to the summit was made in seven days. Eleven of the Tx-participants and all controls started the final ascent from 4680 meters. Three Tx-participants returned early due to shortness of breath (one) or hypothermia/ altitude sickness (two), one control returned to provide care. Eight Tx-participants (73%) and 13 controls (93%) reached the summit at 5895 meters. Preliminary results show no significant difference in BP, HR, saO₂ and AMS scores.

Discussion: After finalizing the analysis data will be presented at the congress.

P139

Efficacy of valganciclovir prophylaxis after lung transplantation: one size fits all? A single-center, retrospective, long-term follow-up analysis

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Background: Cytomegalovirus (CMV) infection is the most prevalent and potentially life threatening opportunistic infection in lung transplant recipients. Currently, CMV prophylaxis during the first 3 months after lung transplantation (LTx) is applied in case of seropositivity of either recipient or donor or both. Extension of prophylaxis by an additional 9 months has been suggested to significantly reduce CMV infection, disease, and disease severity. The objective of the current study is to asses first the clinical and viral spectrum of active CMV infection in relation to sero (mis)match between donor and recipient after LTx, and, additionally, to propose extension of prophylaxis in defined cohorts.

Methods: This analysis included a cohort of 188 patients who received an uni- or bilateral lung transplant in a 6,5 year period, and who survived at least 3 months after LTx. CMV prophylaxis with valganciclovir (900 mg OD) was given during the first 3 postoperative months in case of seropositivity of donor and/or recipient. All patients underwent consistent serial monitoring of whole blood for CMV DNA. Active CMV infection was defined as CMV-DNAemia > 500 copies/ml. CMV syndrome was defined as active CMV infection in combination with fever, malaise, pneumonitis or gastro-enteritis. For statistical analysis Fisher exact test was used.

Results: After completion of the prophylactic regime, CMV syndrome was seen in 1 and 5 patients of the D-R+ (N=48) and D+R+ (N=63) group, respectively (2% and 8% resp., i.e. comparable risk (p=0.23)). In contrast, CMV syndrome occurred in 20 patients in the D+R- group (51%, i.e. significantly different to the R+ group (N=72), p<0.0001).

Conclusion: Since over 50% of the D+R- patients receiving 3 months of valganciclovir prophylaxis still develop CMV syndrome after completion, extending this prophylaxis in these seromismatched recipients is strongly suggested, e.g. by an additional 9 months. In contrast, extending prophylaxis in the CMV-seropositive recipients is not indicated.

P140

Mediterranean and low-fat dietary education programmes reduce post-transplant obesity – preliminary data from a randomised controlled food trial

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Introduction: Obesity following heart and lung transplantation remains a significant obstacle to recipient health. Strategies that optimise body mass index (BMI) are therefore essential for long-term health. In this randomized study, patients were recruited to either a low-fat or Mediterranean-eating pattern for 6 months. Serial anthropometric, clinical and biochemical data was recorded.

Methods: 11 Heart and 12 lung recipients were randomly assigned to either a Mediterranean or low-fat dietary education programme. Data was collected at weeks 0 and 25. Comparative data was attained from 20 heart and 23 lung recipients that met our inclusion criteria and were contacted for the study, but declined dietary education.

Results: No differences in weight change was observed between Mediterranean and low-fat groups in either heart ($p=0.773$) or lung ($p=0.261$) recipients. Fluctuations in BMI followed a similar trend between groups ($p=0.804$ and $p=0.292$ respectively). When both dietary interventions were compared against non-intervening subjects, our results demonstrate significant weight loss ($p=0.024$) and improved BMI ($p=0.021$).

Conclusions: Strategies to maintain optimal post-transplant body weight and BMI are essential. This preliminary data indicates that conversion to Mediterranean or low fat diets positively influences weight changes in heart and lung recipients. Therefore, the strategy laid out in this study may provide a therapeutic option with the potential to improve patient health.

P141

Size does matter in lung transplantation for restrictive disease

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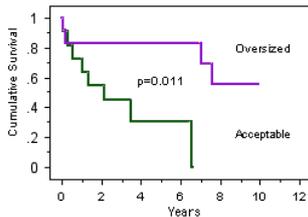
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Introduction: Lung transplant recipients with fibrotic or restrictive disease have less good long-term outcomes. The smaller chest cavity makes choice of donor size difficult, particularly for bilateral (BLT) transplants. Oversized lungs are technically difficult to implant and early compression may hinder recovery. The same consideration applies to single (SLT) lung implants, but there is thought to be more scope for variation. Larger volume lungs might give better long term survival

Methods: We studied the records of 43 SLT and 23 BLT recipients over the period 2003 to 2013 in a single institution. Donor and recipient predicted total lung capacity defined acceptable and oversized pairings for BLT by published criteria. Single lung recipients were divided into two, equal, larger and smaller cohorts.

Results: Size did not affect outcome in SLT. For BLT, oversized lungs, had a trend to shorter median ITU stay (5 days vs 7 days p =0.24), the same 30-day survival, (91%), higher 1-year survival (83% vs 64%) and higher 5-year survival (83% vs 32%) with survival difference being statistically significant p=0.01. FEV1, an indication of function, at 1 year for both BLT groups were similar.

Figure 1: Survival in BLT for Idiopathic Pulmonary Fibrosis



Discussion: It is clearly better to receive a larger volume of lung tissue if both lungs are implanted. The lack of effect is more difficult to explain after SLT, but these patients are older and frailer and some may die of non-pulmonary causes. An examination of national data is planned, aiming to determine optimal size recommendations.

P142

Medical issues in organ transplant recipients to summit Mount Kilimanjaro

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Introduction: In 2012 a lung transplant (LTx) recipient 16 years after LTx suggested to climb Mount Kilimanjaro to increase donor awareness.

Methods: After careful risk assessment, candidates were selected from transplant programs part of the Groningen Transplant Center (GTC). Exclusion criteria were: creatinine clearance <40ml/min and diabetes. A selection procedure (maximal exercise testing, muscle strength and motivation) was started and 12 transplant recipients were selected (2 Heart-Tx, 2 lung-Tx, 2 kidney-Tx, 4 liver-Tx, 1 allogeneic stemcell Tx and 1 smallbowel-Tx). All received an individual training scheme. Control group was formed by the medical team and relatives.

Results: In October 2014, 12 candidates and control group climbed Mount Kilimanjaro. 11 out of 12 Tx-recipients started the final ascent from 4700 meters and all reached over 5000 meters. 3 returned early due to shortness of breath (1) or hypothermia/altitude sickness(2). 8 reached the summit at 5895 meters. Medical issues currently evaluated are: vaccination effectiveness, and difficulties in differentiating between altitude sickness, side effects of Malaria prophylaxis and gastro-intestinal infections. Although all patients returned safe and apparently healthy from Mount Kilimanjaro, they are still monitored for (travel related) illnesses and allograft dysfunction.

Conclusion: Preliminary conclusion is that, with adequate precautions, transplant recipients can safely climb Mount Kilimanjaro.

P143

Mortality of primary sclerosing cholangitis patients on the liver transplantation waiting list: a competing risk analysis

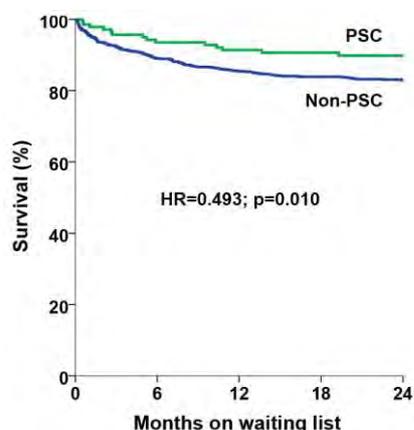
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Introduction: It has been questioned whether current MELD driven allocation system adequately prioritizes PSC patients. Therefore, we aimed to study the mortality of PSC patients on the liver transplantation waiting list compared with patients with other indications.

Methods: The primary outcome was mortality defined as the survival to the combined endpoint of death or removal from the liver transplantation waiting list due to clinical deterioration from the time of listing. Survival analysis was computed with the competing risk analysis. Patients listed for liver transplantation between 16 December, 2006 and 31 December, 2013 were included. Patients listed for retransplantation, acute liver failure or combined liver and kidney transplantation were excluded.

Results: A total of 805 patients (median age 54 years; M/F 539/266) was listed, of whom 552 (69%) underwent liver transplantation, 135 (17%) died or deteriorated while waiting, 46 (6%) were withdrawn for other reasons and 72 (9%) were still waiting as of November, 2014. In 139 patients PSC was the main indication for liver transplantation. PSC patients have a significant lower mortality on the waiting list compared with non-PSC patients (HR=0.493; p=0.010). There was a nonsignificant trend toward PSC patients having a lower chance of undergoing liver transplantation (HR=0.815; p=0.07).



Conclusion. PSC patients have a lower mortality compared with patients with other indications on the Dutch liver transplantation waiting list and an equal chance of receiving a transplant.

P144

Acute kidney injury after liver transplantation: mind the gap

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Introduction: Acute Kidney Injury (AKI) after liver transplantation (LT) is associated with impaired early postoperative and long-term survival. AKI after LT is more frequently observed with Donation-after-Circulatory-Death (DCD) grafts, compared to Donation-after-Brain-Death (DBD) grafts. It has been suggested that hepatic Ischemia/Reperfusion Injury (IRI) could also play an important role in this process. The postreperfusion syndrome (PRS), characterized by hemodynamic instability directly after reperfusion, may be an early manifestation of hepatic IRI. However, the relationship between PRS and AKI after LT remains unknown. Our objective was to explore the relationship between PRS and AKI after LT.

Methods: Patients who underwent LT from July 2008 until October 2014 in our hospital, were retrospectively assessed. PRS was defined as a >30% decrease of Mean Arterial Pressure (MAP) ≥ 1 minute within the first five minutes after portal reperfusion. AKI in the first week after LT, according to AKIN criteria, was evaluated using univariate analysis.

Results: Out of 330 reviewed patient records, 221 patients were included. Ninety-six patients (43%) developed AKI, of whom 69%, 19%, and 11% developed AKIN stage 1, 2, and 3, respectively. Patients developing AKI had a higher creatinine ($P = 0.031$), higher labMELD-score ($P = 0.015$), and more frequently pre-existent hypertension ($P = 0.04$) at baseline. Patients receiving a DCD graft were more prone to develop AKI (OR 3.1; 95% CI 1.7-5.6). PRS was present in 40% of the patients and more frequently seen in the AKI group (53 vs 30%; $P = 0.001$). The incidence of PRS was higher in the DCD group (53 vs 34%; $P = 0.009$). Patients in the DBD group who experienced PRS were more likely to develop AKI (OR 2.9; 95% CI 1.4-5.8).

Conclusion: PRS is associated with a higher incidence of AKI in the first week after LT. AKI is more frequently observed in DCD grafts and in this group not related to PRS. However, DBD recipients who experience PRS have an increased likelihood of developing AKI, putting them almost at par with recipients of DCD grafts.

P145

The evidence base for guidelines for a healthy life after liver transplantation

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Introduction: Leading a healthy life after liver transplantation (LT) is important for graft survival. Transplant recipients receive guidelines to integrate into their daily lives. However, these guidelines can interfere with the recipients daily activities and can be experienced as a burden. The aim of this study was to examine the scientific evidence and the clinical experiences of health care professionals (HCP) that underlie these guidelines and how patients experience these guidelines.

Method: A systematic review of the literature on LT guidelines was performed. To examine the experiences with the guidelines of HCP's and transplant recipients semi-structured interviews were conducted.

Results: Seven relevant articles were identified, which provided scientific evidence for the guidelines: skin cancer checks, immunosuppressant, prevention of obesity, using painkillers, vaccination, visiting dentist and self-measurement of vital body functions. Five HCPs and five transplant recipients were interviewed. Clinical evidence was found for the seven guidelines mentioned before and also for hygiene, depilate and nutrition.

Conclusion: Our study provided scientific evidence for seven guidelines and clinical evidence for three guidelines more. This research project gives insight into the evidence base for the guidelines received after LT, and it shows how recipients experience the current guidelines. Although additional clinical evidence was found, the evidence for several guidelines remains contradictory. Regarding, for example hygiene, visiting the dentist and nutrition recipients experience this guidelines as part of their lives and do not see them as a burden. More research is needed on the evidence base for guidelines and patients' experiences.

P146

Higher MELD score correlates more strongly than higher UKELD score with increased one year mortality following orthotopic liver transplantation in a cohort of UK patients.

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Introduction: Model for End Stage Liver Disease (MELD) is an algorithm used to grade the severity of chronic liver disease and to prioritise patients for liver transplantation. United Kingdom Model for End Stage Liver Disease (UKELD) is a similar system but one which includes serum sodium concentration and excluded recent dialysis. UKELD has been optimised for use in the UK. Whether MELD or UKELD is adequate to predict outcomes following orthotopic liver transplantation remains controversial. Recent studies have suggested that MELD may not predict mortality after liver transplantation. Our aim was to compare UKELD and MELD score in predicting 1 year mortality following liver transplantation in a large single centre UK transplant database.

Methods: Data was reviewed for patients undergoing liver transplantation between 2006 and 2012. Clinical data collected was recipient age, gender, pre-operative haemoglobin, donor age, cold ischaemic time, secondary warm ischaemic time, type of graft (DCD, DBD, split, domino), graft appearance and one year mortality rates. MELD and UKELD scores were calculated and correlated with 1 year patient survival. Analysis was performed by binary logistic regression using SPSS.

Results: 304 patients were identified. 15 (4.93%) patients died within 1 year.

The mean MELD score was 18.43 (21.38 in patients that died vs 17.74 in patients that survived) the mean UKELD score was 54.95 (55.6 in patients that died vs 54.93 in patients that survived).

When corrected for all prognostic variables MELD scores predict increased risk of dying within one year of liver transplantation (p=0.017). UKELD had no predictive role in 1 year mortality (p=0.146).

Conclusions: Higher pre-operative MELD rather than UKELD scores are associated with increased 1 year mortality following liver transplantation in a UK population.

P147

Raised bilirubin and alanine aminotransferase levels on the 30th day post orthotopic liver transplantation predict late graft loss between 3 months and 5 years

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Introduction: Liver transplantation is associated with a high risk of mortality, predominantly within the first 30 days. 30 day mortality is therefore often used as an end point of transplant outcomes. There is however ongoing graft loss due to chronic rejection and no validated markers to predict chronic graft loss. Our aim was to correlate liver function tests with long term graft survival in a large single centre prospective database.

Methods: Data was reviewed for patients undergoing liver transplantation between 1988 and 2012. All patients were followed up for 5 years or till the graft was lost. Clinical outcome was reviewed and liver function tests on the 1st, 3rd, 7th, 15th and 30th post-operative day were documented along with donor and recipient age, recipient gender, cold ischaemic time and pre-operative MELD score. Liver specific graft failure was accepted as patients that died or required re-transplantation secondary to chronic rejection, ductopaenic or biliary complications. Vascular complications and grafts that failed within the first 3 months post transplantation were excluded. A binary logistic regression analysis was used to compare LFTs between functioning and failing grafts.

Results: 726 patients (374M/352F) were included in the analysis. Mean age at time of transplantation was 47 years. 60 grafts were lost secondary to a liver specific cause between 3 months and 5 years. A logarithmic regression analysis demonstrated that higher bilirubin ($p=0.034$) and ALT ($p=0.025$) levels on day 30 predicted late graft failure. Mean bilirubin levels on day 30 in grafts that failed (135.47) were significantly higher than in those still functioning (48.3) ($p<0.001$) as were mean ALT levels (203.9 vs 87.9) ($p<0.001$).

Conclusions: Bilirubin and ALT levels on the 30th post-operative day correlate with late graft loss between 3 months and 5 years following liver transplantation.

P148

Histological injury detected in biopsies of the extrahepatic bile duct of donor livers is representative for the degree of injury in the rest of the biliary tree, including the intrahepatic bile ducts

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Introduction: Histological examinations of biopsies from the distal end of the extrahepatic bile duct (EHBD) of donor livers at the time of transplantation have revealed signs of severe injury, characterized by a loss of biliary epithelium, mural stroma necrosis and injury of the peribiliary glands (PBG) and vasculature. It is unknown whether the amount of injury in the distal EHBD is representative for the amount of injury in the rest of the biliary tree, including the intrahepatic bile ducts (IHBD).

Aim of this study was to examine whether the degree of histological injury in the distal EHBD of donor livers is representative for the rest of the biliary tree, including the IHBD.

Methods: Ten donor livers that were declined for transplantation for various reasons were included in this study after informed consent was obtained from the relatives. All livers were procured in a regular fashion and preserved by cold flush out with and storage in UW preservation solution. After a median of 6 hrs of cold ischemia time, biopsies were taken from the distal EHBD and at least two different levels of the IHBD: sectoral and segmental ducts.

Results: Biliary epithelial loss of >50% of the bile duct lumen was observed at all levels of the biliary tree. The degree of mural stroma necrosis was not different between the EHBD and different levels of IHBD. Minimal intramural bleeding (<50% of the bile duct wall) was found in 5% of all biopsies. Minor injury of the peribiliary vascular plexus (<50% vascular changes) was observed in 91.9% of all biopsies, with no significant differences between EHBD and IHBD. There were no signs of microthrombi in the peribiliary vasculature at any level. Injury of the periluminal and deep PBG in the bile duct wall was observed at all levels of the biliary tree. Injury was more severe in the periluminal compared to the deep PBG (>50% loss of PBG observed in 43% and 6.25%, resp.; p=0.002).

Discussion: Histological injury detected in EHBD biopsies of donor livers after cold preservation is representative for the degree of injury in the rest of the biliary tree, including the IHBD. This indicates that EHBD biopsies are a valuable tool to assess preservation injury of donor bile ducts.

P149

Low muscle mass is an independent predictor of long-term mortality after liver transplantation

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Introduction: Low muscle mass is a predictor of peri-operative morbidity and mortality after orthotopic liver transplantation (OLTx). It is not known whether muscle mass is associated with long-term outcomes. We therefore analyzed the association of muscle mass, as reflected by 24h urinary creatinine excretion (UCE), with all-cause mortality after OLTx.

Methods: The study population consisted of all adult recipients of a first OLTx transplanted between April 1979 and December 2000. At the 1-year post-OLTx visit standard clinical and laboratory parameters were determined, and UCE was measured. Follow-up was prospectively recorded until November 2014 or until 15 years of follow-up. Cox regression analyses were applied to investigate the association of log₂-transformed UCE with all-cause mortality.

Results: In this cohort of 313 patients (mean age 43 ± 12 years, F/M 54%/46%) the mean UCE at 1 year after OLTx was 12 ± 6 mmol/24h. After 15 years of follow-up, 92 (30%) of the patients had died. UCE was inversely and independently associated with mortality in an age-, sex-, and length-adjusted analysis (hazard ratio [HR] per doubling of UCE, 0.58 [95% Confidence Interval 0.38-0.90]; P=0.014). This association remained significant after adjustment for systolic blood pressure, diabetes mellitus, smoking, corticosteroid use, statin use, and total cholesterol (HR, 0.62 [0.39-0.98]; P=0.042).

Discussion: Low muscle mass, as reflected by UCE, is a strong, independent risk factor for mortality after OLTx. Prospective studies should determine whether recovery of muscle mass by exercise training will improve long-term survival.

P150

The significance of current nutritional assessment in patients undergoing liver transplantation

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Introduction: Nutritional status influences outcome in major surgery. There have been conflicting results regarding the implications of recipient Body Mass Index (BMI) and the outcome of orthotopic liver transplantation (OLT).

Methods: We retrospectively reviewed our prospective database of patients undergoing liver transplant at the Royal Free Hospital and correlated the nutritional assessment of the recipients including their BMI along with other variables which could influence the risk of post-operative infective complications. Results: A total of 1299 patients were transplanted during 1998-2012. Grading of standard nutritional assessment was not associated with any of the postoperative complications. A low BMI (<16) was associated with an increased risk of wound infection (p=0.037) whilst a high recipient's BMI (≥30) was a risk factor for non-wound related infection (p=0.016).

Discussion: Body mass index is an independent prognostic factor for the development of wound and chest infection in the postoperative course after liver transplantation. Current nutritional classification fails to identify individuals at risk of infective complications following liver transplantation and requires being refined for a transplant population.

P151

Royal free scoring system for risk assessment of early graft failure and postoperative mortality after cadaveric liver transplantation

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Introduction: Identification of prognostic markers in liver transplantation allows resources to be focused on high-risk individuals. Surrogate markers of outcome can also be used to evaluate new therapies. A scoring system to classify patients' risk of graft failure and postoperative mortality is required in liver transplantation.

Methods: We retrospectively reviewed our prospective database of transplanted patients. Early graft failure and postoperative mortality were correlated with liver function tests in postoperative days 1, 3 and 7 as well as with the reduction rate of the transaminases levels in the first 3 and 7 days. A cut-off value of the independent variables was estimated and included in a scoring system to classify patients' risk of graft failure and postoperative mortality.

Results: A total of 1,299 patients that received an adult cadaveric liver transplantation at Royal Free Hospital between 1988 and 2012 were analysed. Aspartate-aminotransferase on postoperative day one, aspartate-aminotransferase reduction rate and the trend of the alanine-aminotransferase in the first 48 hours post-transplantation showed significant correlation with early graft failure and early postoperative mortality on bivariate and multivariate correlation. Cut-off values were determined to divide patients in favourable and non-favourable group for each predictor, scoring 0 and 1 respectively. The sum of scoring points was used as a classification system, assigning patients to low, intermediate and high risk groups. The proposed scoring system predicts a 15.9% risk of 30-day mortality and a 20.6% risk of early graft failure for patients allocated in the high-risk group.

Discussion: A scoring system has been established based on routine liver function tests which can be used to predict early post-transplant outcomes. The results require validation in an independent patient cohort.

P152

Anxiety, depression and health-related quality of life in patients with biliary strictures after orthotopic liver transplantation

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Introduction: The presence of biliary strictures after Orthotopic Liver Transplantation (OLT) may impair Quality of Life (QOL), as they often lead to clinical symptoms and invasive treatment procedures. We evaluated differences in QOL between patients and controls, and between patients with or without (a history of) biliary strictures after OLT.

Methods: A cross-sectional study with validated questionnaires, i.e., Short-Form 36 (SF-36), Multidimensional Fatigue Index 20 (MFI-20), Euroqol 5D (EQ-5D) and adjusted Liver Disease Symptom Index (LDSI), was performed among patients > 3 months after OLT. Patients were requested to provide a control person of similar age and gender. Biliary strictures were diagnosed based on cholangiography. Using linear regression analysis, continuous scale scores of the SF-36 and MFI-20 were adjusted for age, gender, marital status, unemployment, ethnicity and self-reported comorbidity. P-value <0.05 was considered a significant difference.

Results: In total 142 patients and 71 patient-provided controls were included. Patients reported significantly impaired QOL scores ($p < 0.01$) on all subscales of the SF-36, MFI-20 and EQ-5D compared to their controls. Patients with ($n=55$) and without ($n=87$) biliary strictures showed similar QOL scores on the SF-36 and MFI-20. Only in patients with a follow-up of ≤ 4 years after OLT, patients with biliary strictures ($n=21$) showed a trend towards a worse QOL on the SF-36 and MFI-20. Overall, patients with biliary strictures reported more symptoms of depression and anxiety on the EQ-5D ($p < 0.04$) and LSDI (Odds ratio 2.07 [1.01 – 4.26], $p < 0.05$). This may partly be explained by differences between patients with and without depression in reported frequencies of fear of complications (64% vs. 16%, $p < 0.01$), fear of complication-related treatment (32% vs. 8%, $p < 0.04$) and worries about the impact of the OLT on the family situation (56% vs. 8%, $p < 0.01$).

Conclusion: General QOL-scores were not significantly different between patients with or without biliary strictures. However, patients with biliary strictures reported more anxiety and depression. This may be associated with disease-related worries in this subgroup.

Category: Nurses and Specialist Nurse in Organ Donation

P153 WITHDRAWN

P154

A medication instruction protocol for kidney transplant patients to increase self management and compliance

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Introduction: After transplantation kidney transplant patients are confronted with a whole new and complicated medication scheme. Compliance to this scheme is very important to prevent rejection of the donor kidney. Early after transplantation we teach patients to take their new medication in the correct way. This is an important part of their admission. We developed a standardized protocol to teach and instruct patients to apply to their medication regimen. In this protocol we train them to become self-reliant and to anticipate to medication changes. In addition this protocol helps to detect in an early phase patients that need additional help at home in taking their medication.

Methods: Prior to transplantation we hand out a folder with information on medication. At day three post surgery the instruction starts. An estimate on the feasibility of self management will be made. If we think self management is feasible the patient receives a copy of their current medication list. The objective is that the patient is able to prepare and take the medication faultlessly by himself. To accomplish this we check and record every action the patient makes with their medication. This makes sure that the handling of medication is also done by hospital guidelines and international safety standards. Every day we evaluate the progress the patient makes in taking their medication in the correct way.

Results: This training enables us to determine in an early stage if the patient is able to follow up their strict medication regime and to name the (by-) effects of their medication. Most patients complete their training in 7 days. Within 2 weeks after admission patients get a follow up by our nurse practitioner. We hope this method increases compliance and in the end allograft survival.

Discussion: Hospital regulation regarding medication distribution and storage becomes stricter. We must implement these new requirements in our training in order to be able to train the patients in a safe and responsible manner.

Patients do not always strictly adhere to the protocol, so sometimes medication has already been taken even though the nurse has not checked it.

P155

Establishing a regional senior transplant nurse group – experiences after 18 months

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Introduction: The Peninsula and Portsmouth Regional Senior Transplant Nurse Group was established in March 2013 in order to bring together senior transplant nurses with the aims of [1] providing peer support, [2] sharing learning, experience and best practice, and [3] delivering change to improve service provision within the local units. An unconditional educational grant was obtained from a pharmaceutical company. Full day meetings have run on a quarterly basis and have featured: updates on important topics within transplantation; presentations of audits from individual units; reports of existing practice and innovative projects from individual units; and, workshops addressing the implementation of national guidelines. The group has 12 members representing 3 transplant centres and 3 District General Hospitals (DGHs) providing care to kidney and/or pancreas transplant recipients. The value of the group to the members and their local units was evaluated at 18 months to inform its further evolution and the use of resources.

Methods: The experiences of the 12 members were evaluated from the completion of a non-anonymised questionnaire with the responses returned to a single individual.

Results: 10 of the 12 (83%) of the members completed the questionnaire. Feedback was uniformly positive with all 10 respondents (100%) reporting that they found the group to be 'extremely useful'. Reported improvements in local practices arising as a result of attendance at the group meetings included: the instigation of telephone clinics; improvements in the Transplant Assessment process; re-design of the patient pathway for Living Kidney Transplantation; and, improved monitoring of pancreas patients. Feedback highlighted the opportunity for net-working and the consequent improvements in communication between units (particular transplant centres and DGH units). Despite travel times, XX of the respondents (xx%) wished to continue to meet at least twice per year.

Discussion: This Senior Transplant Nurse Group has rapidly and successfully brought together senior nurses across the region and is meeting its stated aims. Similar groups might benefit other regions.

P156

How using evidence based design improved the patient experience

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Introduction: May 2012 saw the restructuring of renal outpatients with patients losing their dedicated renal clinic. A routine patient satisfaction survey showed that although patients were generally satisfied with their care there were a number of other factors which impacted on patient experience within the Trust.

Methods: Evidence Based Design (EBD) is a tool developed by the NHS Institute for Innovation and Improvement. Using a renal patient group a process matching approach was used to define the issues and propose solutions addressing patient's experiences with outpatient care.

Results: The issues raised were as follows: Lack of patient peer group to support and help other patients, the cost and difficulty of car parking. The outpatient environment breached dignity and privacy. Administration changes have led to missed and overdue appointments and some patients felt they didn't need to come into the hospital for their appointments.

Solutions: A patient peer group has been developed and a patient Facebook page. The Trust is looking into subsidised car parking for regular attendees and information leaflet has been developed with other travel options. The outpatient layout has been restructured to accommodate the privacy of patients and issues relating to poor signage seating and communication have been addressed. Renal patients now have their own personalised outcome forms and a preliminary bid has gone to the commissioners to advertise for a band 3 post to facilitate bloods and telephone triage linking in with primary care to reduce hospital follow up in a selected group of patients.

Conclusion: The success of EBD was based on co-design involving both patients and professionals. It enabled the patient experience to be shared and solutions to be tested for feasibility and ideas to be discussed from alternative perspectives. Improvements have already been made which will be measured by a further patient satisfaction survey. This model offers hidden benefits of greater transparency, accountability, trust and democratic participation. It is a helpful tool for anyone interested in improving the experiences of patients, the efficiency of the service and in formulating a strategic direction for a department. However, caution must be given that this is not a panacea for all issues facing healthcare providers but it can be used as a complementary tool.

P157

The impact of the taskforce recommendations on the provision of end of life care and organ donation practice in a level 2 critical care unit

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Background: In a response to the shortfall of donors, a government commissioned Taskforce report in 2008 identified 14 recommendations (Department of Health, 2008) which, if implemented, was anticipated could achieve a 50% increase in organ donation rates. This was an ambitious target that would require all practitioners to think about organ donation and their role within the donation process. The success of a level 2 critical care unit in an acute Trust in Northern Ireland – achieving an outstanding ‘350%’ increase - highlights that simple changes in the process can save and transform the lives of patients. The aim of this paper is to reflect on the key elements that influenced this change in the critical care unit and within the multidisciplinary team practice in end of life care and organ donation.

Methods: A reflective model (Johns, 1995) was used to analyse key aspects of the changes that took place namely the introduction of the roles of the Specialist Nurse and Clinical Lead for Organ Donation, collaboration within the critical care team (Rose 2011), communication with key stake-holders, introduction of referral systems, and the development and implementation of protocols and a Trust policy for Organ and Tissue Donation.

Findings: Following reflection and review of the literature, it is evident that the 350% increase in organ donation rates in the critical care unit was influenced by multiple factors. These factors have led to an increase in both organ and tissue donation in this critical care unit which has ultimately led to many lives being saved and transformed through the gift of donation.

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P158

Dedicated guidance: multi-dimensional cooperation leads to more pre-emptive kidney transplantation

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Introduction: In time start of the process of education and pre-transplant medical investigations may increase the possibility of pre-emptive (living) renal transplantation. We enrolled a work-up programme by close cooperation between a specialised nurse and the team of social workers in a large non-academic teaching hospital.

Method: The electronic hospital patient form is used to inform all involved disciplines at once. The programme then starts with a home visit by a social worker. At this visit, general information about renal replacement therapy and the possibility of renal transplantation is explained to the patient and accompanying family and friends. The specialised nurse will explain the transplantation options and the medical work-up of the recipient and the potential donor. She further ensures that the required investigations are planned and completed in the shortest possible time frame. Close daily cooperation between the specialised nurse and the team of social workers will optimize the transplantation work-up and can result in a quick change in the process, for instance a change of the potential donor by medical reasons.

Results: In 2013, 79 patients entered the programme. That year, 22 donor-recipient pairs were transferred for transplantation, of which 12 were transplanted by the end of the year. The median work-up time was 169 days (range: 23- 639). Several patient and medical factors delayed the programme. They will be discussed at the meeting.

Discussion: By the current transplant work-up programme, patients and family/friends are well informed about renal replacement therapy and the possibility of (living) transplantation. Close cooperation between a specialised nurse and the team of social workers results in a significant improvement of the possibility of pre-emptive renal transplantation or, otherwise, patients are earlier registered on the waiting list.

P159

Renal transplant group education session – benefits for patients and staff

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Introduction: Guidance for practice states that transplant information should be given to patients in both written and oral form. Providing oral information in a timely fashion to allow treatment option decisions to be made by patients had increased workload for the renal team. Renal recipient coordinators identified that a change in practice was necessary and implemented group education sessions.

Method: Referrals to group education sessions were accepted for all patients with a GFR<25. An adapted presentation was developed to be delivered in a group session. The presentation aim was to provide the required information about risk versus benefit for transplantation. Sessions were set up on a monthly basis as a clinic appointment.

Results: Over the 47months a total of 405 patients have received education in a group session. Sessions were set at 2 hours with the total number of hours of education provided being 150hrs. Individual sessions, previously scheduled as hour long sessions, would have required 405hrs of recipient coordinators working time. A time saving of 255hrs has been made by the unit. Patients have fed back for 47% this was a first meeting with recipient coordinator and 100% of the evaluations state they found the sessions useful and provided the information they expected to hear.

Conclusion: Group education continues to be the main delivery method used in providing transplantation information to patients. It allows the education to be provided by those who have specialist knowledge. As sessions can be provided in satellite units it reduces the amount of visits required by individuals to the main transplant centre. It is understood that group sessions are not suitable for all patients and one to one sessions are carried for those who require or request them.

P160

A novel approach to renal transplant for patients with learning difficulties

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Introduction: Due to the increase in referrals for renal transplant work up for patients with learning difficulties (LD) as a team we identified a deficit in supporting this group of challenging patients.

Method: I inherited the role of LD link nurse for renal by default, in August 2012 following all these referrals. The team supported my enrolment on to some short courses run by the local council covering safeguarding legislation. Patients would be identified and discussed at our multidisciplinary(MD) team meeting and would be invited to a one stop clinic in order for members of the MD team to carry out vital assessment of the patient's needs. I would organize and chair Best Interest Meetings; a comprehensive admission and discharge plan would be formulated and customized to the patient's needs. The Trust has a carer charter and we were able to incorporate this in to the individualized plan in order for the patient to be supported.

Results: Within the last 2 years we have received 18 referrals for patients with some degree of learning difficulty ranging from mild to very severe. Four are in Work up for listing, 6 have been transplanted at this centre and 7 are active on the transplant waiting list. We have not declined to assess any patient with learning difficulties in the last 2 years; however 1 of these patients is currently unsuitable for listing due to other issues.

Conclusion: The move to a purpose built modern hospital has not made the challenges we face any easier, however it has enabled us to improve the patient and carer experience. We are not sure if other centres are facing these challenges. It would be interesting to engage with other centres to establish how complex cases such as these are approached in order to address these challenges at a national level.

P161

Case management by nurse practitioner in complicated live donor kidney transplantation

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Introduction: Our center is a large kidney transplant center. Donors and recipients follow a clinical care pathway from screening until follow up. In this pathway, they visit different departments and professionals. Besides very close collaboration on medical specialist's level in multi-disciplinary teams, nurse practitioners play a key role in these teams as case managers for the patients. They act as a "spider in the web" in the complex structure and are the main contact and advocate for patients and their social environment in the clinical care pathway. The case below is illustrative for the role of nurse practitioner as depicted above.

Case report: A 63 year old patient received a pre-emptive kidney transplantation with his 38 year old son as donor. The donor had a complicated course due to severe gastritis, leading to distress for the donor and his family. He recovered spontaneously and was dismissed after one week. In the first week post-transplantation, the recipient developed a retroperitoneal infection for which a reoperation was necessary. He needed to be treated for acute cellular rejection with solumedrol, after which he quickly recovered and was sent home. A month post-transplantation, he had a rise in creatinine. Analysis revealed a mycotic aneurysm of the renal artery of the graft. To protect him from life-threatening bleeding, a wall stent was placed in the external iliac artery. However, due to the stent, the kidney was deprived from blood flow, and had to be removed within 3 days. Consequently, he had to start hemodialysis. The clinical course of the donor and recipient severely impacted on the entire family. By staying in close contact with the patients and the family and offering support and reassurance the nurse practitioner could help processing emotions. Although there was a complicated postoperative course related to donation as well as transplantation confidence in the program eventually remained by the pivotal role of the patients advocate.

P162

Utilizing a “traffic light protocol” for triage of donor kidney offers in a single centre

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Introduction: The “Traffic Light Protocol” was developed in response to a steep increase in kidney offers – this impacted on co-ordinator and nephrologist workload. Before its introduction in August 2011 all offers to the co-ordinators were discussed with the medical staff. This audit reviews the offers received, criteria for acceptance and application of the protocol by the recipient team.

Methods: Data was collected for offers 1 year prior to implementation of the “Traffic Light Protocol” and for the last year of activity whilst the protocol has been in place. Offers are categorised as Red-Amber- Green. Green in straightforward offers and results in mostly unconditional acceptance; Red is unconditional refusal (this can be done by the Co-ordinator on-call without discussion with the medical staff). Amber is all remaining offers necessitates MDT discussion during the decision making process.

Results:

Criterion	July 2010- June 2011	November 2013 – October 2014
Total offers/o	180	265
Accepted/Declined offers	74/106	83/182
“All refusals/ “Red” refusals+	N/A/106	70/112
Offer time	49 minutes	23 minutes

Discussion/conclusion: A proportion of offers can now be declined utilizing the “Traffic Light Protocol”. This optimizes offering time for SNOD’s and NHSBT. The protocol also allows the Recipient Co-ordinators the opportunity to practice autonomously whilst operating under the umbrella of safety the protocol provides. The protocol has been reviewed, re-audited, reconfigured and tweaked twice. This has been completed retrospectively and the next step will be to audit prospectively all declined kidneys (especially those transplanted elsewhere to ensure practice/protocol is applied consistently).

P163

Towards an uncontrolled donation

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Introduction: In Europe, organ donation from donors in whom resuscitation has been unsuccessful after cardiac arrest has been practised for years. Maastricht DCD Category II donors (DCD II) represent a potential source of organs for transplantation which have not been utilised in the UK in the recent past. Principles of organ retrieval from a DCD II donor being fundamentally the same as that for a DCD Category III donor, the practicalities present a different challenge. These include a limitation of the normal pre donation time available to the specialist nurse (SN OD) and an almost immediate attendance of the retrieval team in the Emergency Department(ED) to facilitate the introduction of Normothermic Regional Perfusion (NRP).

Method: The principle of a legal requirement to fulfil the wishes of those who had expressed a wish to donate after death was fundamental. Development of policy involved widespread consultation across the NHS and also included legal and ethical opinion. Early work indicated that public were not averse to organ donation being discussed shortly after ED death, with the pilot site based within an area where 49.8% of the local population are on the Organ Donor Register (ODR). This is on a background of local survival to discharge rate of witnessed shockable arrests within the pilot ED rising from 0.7% in 2007 to 32% in 2013.

Results: Data demonstrates true potential within the ED which has not as yet been converted into donation. It also demonstrated a further group of patients that could be considered i.e. those not on the ODR.

Discussion: Although no conversion to donation as yet, the pilot has raised the profile of donation, brought departments together, strengthened links between ITU and ED and further identified a group of patients that may be included that would ensure that donation is considered for all as part of end of life care.

P164 WITHDRAWN

Category: Clinical - Paediatric

P165

Transplantation of adult living donor kidneys in small children

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Introduction: We evaluate our programme for adult kidney transplantation (RTx) in children under the age of 4 yrs. Eight children are included since October 2012.

Methods: Donor and recipient characteristics, data on surgical technique and ischaemia times were analyzed, as well as outcome measurements, such as serum creatinine, GFR, graft and patient survival.

Results: The mean age of the 8 recipients (6 boys and 2 girls) was 2.6 yr (1.5-4.1), length 87.1 cm (72.5-97) and weight 13.5 kg (10.0-17.9). All had congenital origin for ESRF, including posterior urethral valves, polycystic kidney disease, reflux nephropathy, nephronophtisis and renal dysplasia. Three children were on haemodialysis and 5 were transplanted pre-emptively. All donors were parents (3 males and 5 females), age 36.8 yr (24-45). The length of the graft was 11.2 cm (10-12.1). Following laparoscopic donornephrectomies all recipients underwent a transverse laparotomy with a right intestinal media rotation and with vascular anastomoses on the abdominal aorta and inferior caval vein. The warm (combined 1st and 2nd) and cold ischemic times were 37.8 min (16.9-51) and 3.5 hr (2.5-3.9), respectively. All children received immunosuppression according to the TWIST protocol (Basiliximab, Tacrolimus and Mycophenolate), with allometric dosing. There were no cases of delayed graft function. Patient and graft survival are both 100%, with a mean follow-up of 12.5 mo. Early complications were drug induced delirium in two cases, septicaemia in one and early postoperative haemorrhage in another, necessitating reoperation. In the case of nephronophtisis with pre-existent liver fibrosis excessive postoperative ascites and lymph leakage was encountered. The mean stay on ICU was 9.7 days (5-17) (n=7). The mean serum creatinine at 3 mo was 45.6 umol/L. Mean GFR was 6.7 before RTx (n=8), 106 at 1 mo (n=7) and 84 ml/min/1.73m² at 3 mo after RTx (n=5).

Conclusion: RTx of adult living donor kidneys in small children is challenging, but feasible, with excellent graft function, making pre-emptive living donor RTx also an option for the very young recipient.

P166

Outcomes of ABO incompatible kidney transplantation in children

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Purpose: ABO blood group incompatible transplantation (ABOi) has become increasingly common, in part due to shortage of suitable deceased donor allografts. Whilst encouraging data is emerging on short and medium term graft outcomes in adults, ABOi in children is rare. Encouraged by good results in a large number of adult ABOi transplants, we extended our programme to paediatric recipients, and here report the largest European cohort.

Methods: A retrospective analysis of all ABOi paediatric renal transplant recipients in 2 largest centres in the UK sharing the same tailored desensitisation protocol. Patients with pre-transplant titres 1 in 8 or above received rituximab one month prior to transplant; tacrolimus and mycophenolate mofetil were started one week pre-op. Antibody removal was performed to reduce titres to 1 in 8 or less at surgery. No routine post-op removal was performed.

Results: Ten children underwent an ABOi kidney transplant. Graft and patient survival was 100%. Baseline titres ranged from neat to 1 in 128. Two patients had rituximab only; 5 had rituximab and DFPP; 2 had rituximab and immunoadsorption; one had no additional pre-transplant therapy. One patient developed grade IIa rejection after two weeks successfully treated with anti-thymocyte globulin; no histological evidence of rejection in other patients. Another patient had rise in titre of 2 dilutions at week one treated with 2 immunoadsorption sessions. Nine patients had good graft function (eGFR 30-130 ml/min/1.73m²) at last follow up (range 1-36 months); 1 had eGFR 22ml/min/1.73m². One patient developed CMV and BK, another EBV and BK; no other infectious complications.

Conclusion: ABOi transplantation in children appears to have an optimal outcome with good graft survival and a low risk of rejection and infectious complications.

P167

UK experience in paediatric HLA incompatible renal transplantation

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Introduction: Renal transplantation is an optimal treatment that improves quality of life and facilitates development of children requiring renal replacement therapy. Sensitization as a result of previous transplant or transfusion is an increasing problem. There are concerns of applying desensitization strategies in children due to anxiety over increased risk, meaning that highly sensitized children may expect a long or indefinite wait for a deceased donor kidney.

Methods: We undertook an HLA incompatible living donor renal transplant in two highly sensitized children with cRF of 100% adopting our well-established adult desensitization protocol. The first patient was a 14-year-old girl with positive B cell flow cross-match (RMF of 4.41) and total donor specific antibody MFI of 11602 prior to desensitisation. This was the first UK living donor HLA incompatible renal transplant in a paediatric unit. The second patient was a 13-year-old boy with positive B cell flow cross-match (RMF of 3.24) and total donor specific antibody MFI of 22548. Both patients underwent a test plasma exchange to assess the feasibility of desensitisation. They required one session of plasma exchange on the day before surgery to achieve a negative cross-match against their donors.

Results: The first patient has a functioning renal allograft six months after her transplant and no infectious complications to date. Biopsies at 2 and 7 weeks, as well 6 months post-transplant showed no features of acute rejection. Renal function remains stable with the most recent eGFR 64ml/min/1.73m² despite fluctuating levels of donor specific antibodies. The second patient recovered well from surgery with creatinine of 54 umol/L two weeks after his transplant.

Discussion: According to the UK Renal Registry the median waiting time of a highly sensitized child is 1241 days, which is not advantageous over the adult median waiting time of 1160 days despite prioritisation of paediatric patients on the deceased donor waiting list. An HLA incompatible renal transplant from a living donor is a feasible alternative that should be offered to selected patients by centres experienced in antibody incompatible transplantation.

P168

Luminex DSA screening in pediatric renal transplant recipients

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Introduction: Donor specific HLA antibodies (DSA) are associated with poor renal allograft outcome. Renal biopsy is not routinely performed in children after kidney transplantation (tx). This study assessed the correlation between clinical outcome (GFR and graft rejection) and the presence of Luminex DSA.

Methods: Between 2004 and 2014, 76 renal tx were performed in 68 children. Children were divided in two groups: with renal biopsy (B+) and without clinical indication for biopsy (B-). B+ consisted of 37 children (44 tx) and B- of 31 children (32 tx). The complement-dependent-cytotoxicity (CDC) test and Luminex screen/Luminex Single Antigen test assays were performed to detect HLA class I and/or HLA class II DSA. Last GFR (Schwartz formula) measurement was at last visit, age 18 yrs, or graft failure. Results are given in median (ranges).

Results: The GFR at last measurement was lower in B+ (43, 6-74 ml/min/1.73 m²) compared to B- (67, 8-115) (p< 0.05). In B+ 23 had biopsy-proven cellular and/or humoral rejection. In both, B+ and B- group, there was no CDC DSA detectable prior to tx. In B+ Luminex class I and/or class II antibodies were positive in 60%, in comparison to 33% in B- group. There was no difference in the prevalence of Luminex detectable DSA between humoral and cellular rejection episodes. In B+ with positive Luminex screening 14 (56%) had DSA (single antigen Luminex test), in B- only 2 (20%). In CDC test 11 (B+) and 0 (B-) positive DSA results were found. In B+, GFR was lower (38,6-71 ml/min/1.73 m²) in the Luminex class I and/or class II positive patients in comparison to the Luminex negative patients (52, 16-74 ml/min/1.73 m²) (p<0.05). In B-, GFR was not different between Luminex positive or negative screening results (67, 8-114 versus 67, 32-115 ml/min/1.73 m² resp, ns).

Discussion: Luminex screening test only does not differentiate in GFR outcome. The necessity of routinely Luminex screening in all children after Tx is subject to debate. When clinical indication of biopsy is made, additional testing for Luminex detectable DSA gives more insight in GFR outcome and might be useful in the decision what rejection treatment should be given.

Recommendations on paediatric deceased donation: a report of the transplantation society Geneva meeting

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Purpose: To provide ethically informed practical recommendations for health professionals and policy makers seeking to establish or improve existing paediatric organ donation programs globally, and identify neglected opportunities for research in this field.

Methods: An international meeting was convened in Geneva, Switzerland, on March 21 and 22, 2014 by the Ethics Committee of The Transplantation Society. The intent was to explore practical and ethical issues pertaining to paediatric organ donation. 34 experts from Africa, Asia, the Middle East, Oceania, Europe and North and South America, representing paediatric intensive care, internal medicine, surgery, nursing, ethics, organ donation and procurement, psychology, law, and sociology participated in this meeting.

Results: Recommendations based on available literature, expert opinion, and consensus highlight the need for multidisciplinary research, dedicated training, and education in the field of paediatric deceased donation among public and healthcare professionals, to preserve and provide opportunities for donation where possible for children and their families. Priority interventions should aim to promote public and professional awareness of paediatric deceased donation; improve public and professional understanding and support for donation through education; expand paediatric donation research; improve organ allocation and implementation of policies and protocols to increase authorization rates for donation and organs recovered and utilised for transplantation.

Conclusion: The report of the Geneva meeting is an international call to action for development of evidence based and best practice resources to globally increase awareness, enhance opportunities, and promote research for deceased donation in neonates and children.

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Poor prognosis with plasma cell infiltrates in paediatric renal transplant biopsies leading to renal allograft failure

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Introduction: The aetiopathogenesis and immunological reason for plasma cell infiltrates in paediatric renal transplant biopsies remains unknown. We investigated the prognosis of paediatric renal transplant recipients (pRTR) in a case-control study.

Materials and methods: Prospective study of plasma cell infiltrates on histopathology from biopsies of pRTR from April 1996 to March 2014. Cases were defined as plasma cells present at time of biopsy and were matched to control cohort for grade of rejection according to BANFF classification, type of Tx (LRD vs DD), age at Tx and Tx age at biopsy.

Results: 14 (6 male (43%)) pRTR aged 3.2 - 17.5 (median 13.4) years at time of transplantation of whom 13 (93%) received deceased donor renal transplants had plasma cell infiltrates in renal transplant biopsies. Compared to 14 pRTR without plasma cells biopsies there were no significant differences in sex, age and type of transplant. CMV/EBV status of recipient at Tx was comparable in both groups. There was no significant difference in patients and Tx age at biopsy. There was no significant difference in number and grade of rejection according to BANFF classification between cases and controls. Plasma cells were present in case biopsies with a density of 14 - 116 (median 32.5) cells/hpf/x40. Plasma cells were associated with decreased eGFR at biopsy (22.3 vs 48.8 mls/min/1.73m²; p < 0.001), but not with eGFR at baseline or four weeks prior to biopsy. Mean eGFR post biopsy was significantly lower in patients with plasma cells (25.8 vs 55.7 mls/min/1.73m²; p < 0.001). Plasma cells were associated with renal allograft loss (71% vs 7%; p < 0.001) at 0 - 27 (median 2) months after biopsy.

Conclusion: The presence of plasma cell infiltrates in paediatric renal transplant biopsies is associated with reduced renal allograft survival. National and international collaborative studies are required to investigate the incidence and significance of plasma cell infiltrates in paediatric renal transplant biopsies. In the future, bortezomib a proteasome inhibitor which induces apoptosis in mature plasma cells may play a role in patient management.

P171

Is there a difference in patient and graft survival in children weighing <20 kg versus those weighing >20 kg at the time of renal transplantation?

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Introduction: Renal transplantation (RTx) is the gold standard treatment modality for end-stage kidney disease. There are increased challenges in paediatric renal transplant recipients (pRTR) under 20kg with immunological, metabolic and surgical difficulties.

Methods: Data was retrieved from a prospectively collected database (apart from the weight at time of transplant and the last eGFR, which was collected retrospectively) from two large Paediatric Transplant Units in UK. Cases with incomplete data were excluded.

Results: A total of 350 children underwent kidney transplantation between 2005 and 2014. Group 1 included 90 cases (57M, 33F) of pRTR with a weight <20kg (Median age 3, IQR 2.25) and Group 2 had 260 pRTR (146M, 114F) with a weight ≥20kg (Median age 13, IQR 5, p<0.001). 83 cases from Group 1 have a functioning graft at last follow up (5 failed, 2 died) and 230 in Group 2 (29 failed, 1 died). In Group 2 there were 5 en-bloc kidneys, one of which thrombosed intra-operatively. The median donor age (years) was 38 (IQR13) and 41 (IQR12) for Group 1 (66M, 24F) and 2 (142M, 117F) respectively (p<0.001). In Group1 there were 63 live donors, 25 DBD and 2 DCD donors. In Group 2 there were 150 live donors, 104 DBD and 6 DCD donors. 1/90 in Group 1 and 25/260 in Group 2 underwent their 2nd or 3rd transplant. The last median eGFR was 59 (IQR26) and 49 (IQR23) in Group 1 and 2 respectively (p<0.001). Both groups had equal median follow up of 3 years (IQR 4).

Conclusion: Despite the obvious differences between the two groups, we conclude that the overall patient and graft survival is comparable between children <20kgs and >20kgs at the time of transplantation in this large paediatric cohort.

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Paediatric renal transplantation in the United Kingdom: changing practice and improved outcomes over 20 years

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Introduction: Since the first recorded paediatric renal transplant in the United Kingdom in 1962, transplant activity has increased and is now between 111 and 151 transplants per annum, which are performed in ten (out of a total of thirteen) paediatric nephrology units. There have been changes over the last two decades with the kidney allocation schemes of 1989, 1998 and 2006.

Methods: UK Transplant Registry data on 2,584 paediatric renal transplants from deceased after brain and cardiac death (DBD/DCD) and living donors performed between 1 January 1992 and 31 December 2011 were analysed. An additional 476 transplants performed between 1 January 1987 and 31 December 1991 were included in the survival analysis to enable 20 year outcomes to be reported. Excluded are 52 multi-organ transplants: 46 liver and kidney transplants, 5 kidney and pancreas transplants and 1 heart and kidney transplant.

Results: The median age of deceased donors has increased steadily from 10 years in 1992 to 17 years in 1998, 34 years in 2006 and 39 years in 2011 with only 20 DCD donors. Significant improvements in HLA matching have been achieved: 81% of recipients received 0/0 or favourable (0 DR and 0/1 B) mismatches in 2011 compared with 27% in 1991. However, the median waiting time has doubled from 126 days in 1999 to 265 days in 2011. Ciclosporin was replaced by tacrolimus in most immunosuppressive regimens after 2002. Renal transplant outcome has improved significantly, mainly due to a reduction in early renal allograft loss. One year DBD graft survival for those transplanted from 2007 - 2011 was 95%, compared with 72% for those transplanted from 1987 - 1991. Renal allograft survival in recipients for first kidney only transplants between 1987 and 2011 inclusive at one, five, ten and twenty years is 88%, 77%, 63% and 39%, respectively. Twenty year DBD kidney graft survival is significantly lower than following living donor transplant: 38% compared with 45% ($p < 0.0001$).

Conclusions: Changes in immunosuppression regimens and improvements in HLA matching in part explain the improvements in the renal allograft survival.

Category: Clinical – Pancreas

P173

Does cardiac risk quantification have a role in assessment for pancreas transplantation?

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Introduction: Pancreas transplantation (PT) is the gold-standard treatment for complicated insulin dependent diabetes mellitus. Perceptions of high cardiac risk persist, which currently mandate exhaustive cardiac investigations prior to listing. However, the validity of this approach is not verified and requires further examination.

Methods: Retrospective analysis was made of patients undergoing PT in a single centre, examining cardiac assessment and transplant outcomes. Patients were categorised by myocardial perfusion scan (MPS) into normal perfusion (NP), reversible ischaemia (RI) and permanent ischaemia (PI) groups. Primary endpoints were cardiac death, patient and graft survival. Secondary endpoints were hospital length of stay (HLoS), reoperations and complications.

Results: 314 PTs were performed (01/01-03/14), with 152 MPS results available. (60.1% male; mean age 43.8, 82.9% SPK, 12% PAK, PTA 5.1%). 109 (71.7%) MPS showed NP, 24 (15.8%) RI and 12 (7.9%) PI. There was no difference in graft and patient survival between groups (p=0.31, 0.33 (log rank test)). No significant difference was seen for HLoS (NP: 32.7; RI: 53.3 PI: 35.0), mean reoperation number (NP: 0.8, RI: 0.8, PI: 1.0) or complications (NP: 2.4, RI: 1.0, PI: 1.4) (p=0.45, 0.12, 0.89 (ANOVA)). Angiography was performed in 11.1%, 100% and 83.3% of patients in NP, RI and PI groups respectively since 2011 with no subsequent revascularisations as a result of investigations. Of patients with available MPS results, cardiac causes accounted for 6.5% (n=2; NP: 1, RI: 1) of 31 deaths with median follow-up time from transplant of 1224 days (IQR=2230).

Conclusion: MPS poorly stratifies outcome prediction for cardiovascular mortality and angiography appears unnecessary, ultimately resulting in a delay to listing. Post-operative cardiac mortality is minimal compared to waiting list, suggesting a requirement for expedited workup.

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Can the US Pancreas Donor Risk Index (PDRI) predict outcomes in UK pancreas transplant patients?

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Introduction: The US Pancreas Donor Risk Index (PDRI) was developed and adapted into an iPhone application designed to provide a quick and easy calculation of risk and estimated 1-year graft survival. The aim of this study was to use this application to determine whether its predicted risk and survival correlated with actual outcomes from our patients.

Methods: The 'PDRI' iPhone application was used to generate the PDRI for 116 consecutive pancreas transplant recipients. Data was retrieved retrospectively from a prospectively maintained database. The patients were transplanted between January 2004 and December 2013 in a single centre. The patients were stratified according to type of transplant and their PDRI. Correlation was made between PDRI and graft survival in PTA, PAK, and SPK transplants.

Results: Over a 10-year period, 119 pancreas transplants were performed in a single transplant centre, of which data was available for 116 to calculate the PDRI. Mean graft survival was 49.1 ± 3.2 months, with 5-year graft survival being 83%. The mean (\pm SEM) PDRI score was 1.66 (± 0.229), 1.70 (± 0.099) and 2.19 (± 0.089) for PTA, PAK and SPK respectively. The PDRI score was significantly higher in SPK transplants compared with PTA ($p=0.0397$) and PAK ($p=0.0029$) patients. Actual 1-year graft survival was 55%, 82%, and 84% for PTA, PAK and SPK patients respectively. The PDRI score did not correlate with actual graft survival ($p=0.438$). Estimated 1-year graft survival derived from the PDRI did not correlate with actual 1-year survival.

Conclusion: This study shows that the US PDRI does not predict the actual graft outcomes from data available at the time of organ offer in this cohort of UK pancreas transplants. This may be reflective of the smaller volume of transplants reported in this study and a different population of pancreas donors. Donors in this cohort have a higher PDRI than those reported in the US study. PDRI may not be a useful measure of graft quality in informing UK organ acceptance practice highlighting the need for a UK-specific criteria.

Comparing quality of life following simultaneous pancreas and kidney transplantation and kidney only transplantation: a qualitative interview sub-study of the ATTOM programme

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Background: Simultaneous pancreas and kidney (SPK) transplantation is increasingly used as a treatment for chronic kidney disease in people with Type 1 diabetes, but there are few studies about its effect on Quality of Life (QoL). As part of the NIHR-funded Access to Transplantation and Transplant Outcome Measures (ATTOM) study we interviewed patients from 7 treatment subgroups including SPK recipients with diabetes or deceased-donor Kidney Alone (KA) recipients without diabetes, investigating and comparing the impact on their quality of life (QoL).

Method: In-depth interviews with a purposive sample of 10 KA and 10 SPK transplant recipients were conducted 13-18 months post-transplant. Semi-structured phone interviews examined the impact of diabetes and the renal condition and associated treatment on QoL. Interviews were transcribed and coded thematically, using an interpretative phenomenological analysis approach.

Results: Two main themes emerged. Theme 1 focused on the need for both groups to hold realistic expectations of transplantation. Being advised of potential risks and problems was advantageous, whilst patients who held overly optimistic expectations reported poorer QoL post-transplant. Theme 2 focused on anxieties about transplant failure. Although having an SPK transplant reduced the negative impact of their diabetes/renal conditions on QoL, patients were far more anxious than KA recipients about transplant failure. Two thirds of SPK recipients reported checking their blood glucose levels regularly or avoiding sugar intake post-transplant, believing this will protect the transplanted pancreas. An awareness that the pancreas may fail in the future was commonly reported. In contrast, only those KA recipients who had received a previous kidney transplant raised the possibility that their transplant may fail.

Implications: Appropriate information needs to be provided to manage expectations of transplant for all patients. It is important to recognise that SPK patients have more adjustment challenges following transplant and some seek a more active role. Discussion with patients is needed about how their newly transplanted pancreas and QoL can best be protected.

P176

Transport perfusion fluid analysis from deceased donor kidney transplants (DD KT) and pancreas transplants (SPK; PAK; PTA)

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Introduction: Candida cultured in transplant perfusion fluid (TPF) may have adverse consequences (Mai 2006). TPF culture rates, frequency of positive culture results and associated clinical outcomes were audited.

Method: Retrospective analysis of prospective data from Jan 2013–June 2014. Culture results of paired organs transplanted elsewhere were obtained via NHSBT

Results: 198/259 (76%) deceased donor transplants had TPF sent for culture.

	Total	Total Tested	%	Positive	%	Bacterial	%	Candida	%
DD KT	207	152	73	26	17	23	15	3	2
SPK	48	42	87.5	10	24	6	14	4	10
PAK/PTA	4	4	100	0	0	0	0	0	0

36/198 (18%) samples were culture positive at 48 hours. Positive bacteria culture rates were similar in DD KT and SPK. Candida culture was 5 times more frequent in SPK compared to DD KT. All Candida culture positive patients received additional anti-fungal therapy and had no direct adverse outcomes. Regarding 29 bacteria positive TPF; 17/29 (59%) patients received extra antibiotics: 2 patients for concurrent chest infection that covered TPF results; 3 patients at re-exploration early post-transplant for unrelated reasons; and 12 patients based only on TPF result and sensitivity. Of these, 11/12 were successfully treated but one DD KT with *E. coli* in TPF required nephrectomy on day 12 for infection after multiple cultures of the same organism. 4 DD KT and 1 SPK did not receive extra antibiotic after consultant review. Documentation was less clear in 7 patients but all had good outcome. Regarding paired organs with positive TPF: at our unit 9 single organ pairs had 5 concordant positive TPF results; 4 were discordant. The 16 other "pair" kidneys went to 11 UK units (2 for research): 7 units (receiving 10 kidneys) do not routinely culture TPF; 3 units (receiving 4 kidneys) culture TPF, of which, 3 were culture positive.

Conclusion: TPF positive cultures were common, with Candida more frequent in SPK than DD KT. Treatment of positive TPF cultures led to good clinical outcomes. We recommend routine TPF culture until a RCT advises otherwise. Communication of positive TPF culture results between UK units may be advised.

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Cardiopulmonary exercise testing as independent predictor of pancreas transplant survival

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Introduction: Patients who undergo pancreas transplantation are inherently high-risk candidates due to the comorbidities associated with diabetes and renal failure. Cardiopulmonary exercise testing (CPeT) has been shown to accurately predict the outcome of other major abdominal operations, including liver transplantation. We aimed to establish its validity in predicting the outcome for pancreas transplant patients.

A retrospective review of prospectively captured data was carried out for all consecutive pancreas transplants in a single centre over a 7 year period. CPeT was carried out on all patients prior to placing them on the waiting list. The test was conducted in a consistent environment and reviewed by a trained physician to determine standard objective measures of cardiorespiratory reserve (anaerobic threshold AT, peak oxygen consumption VO_2).

Results: 68 patients had either pancreas-alone or simultaneous pancreas/ kidney transplants. 17 patients were excluded as they were assessed prior to implementation of the CPeT service. 1 patient didn't reach their AT, so was excluded from the analysis. 50 patients underwent a successful CPeT and were transplanted. The mean AT for patients with a functioning graft at last follow up was 13.2 (SD 2.8) compared with 11.1 (SD 1.6) for those either deceased or who no longer have a functioning graft ($p=0.006$, t -test). There was also a significant difference when comparing the peak VO_2 (functioning 16.7 ± 3.9 , non-functioning 14.1 ± 2.6 , $p=0.015$).

Discussion: Preoperative markers of cardiorespiratory reserve determined by CPeT testing can predict graft and patient survival after pancreas transplantation.

P178

Graft survival after solitary pancreas transplantation. Is there a difference between enteric vs bladder drainage? Results from a UK database over 10 years

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Background: Solitary pancreas transplant is a procedure that is currently recommended for patients with Type 1 Diabetes with severe, life threatening hypoglycemic unawareness and preserved renal function. The current options for the exocrine secretion management are either enteric or bladder drainage of the transplanted pancreas. Furthermore SPT poses a unique scenario where there is an absence of a reliable biochemical marker to detect rejection apart from urinary amylase.

Methods: This is a retrospective study where we evaluate a total of 336 cadaveric SPT performed from January 2004 until October 2013. Graft and patient survival were available for 245 cases and pancreatic exocrine drainage was documented for 228 cases (183 Enteric drainage vs. 45 Bladder drainage).

Results: One-year, 3-year and 5-year pancreatic graft and patient survival were 66%, 53% and 44% and 96%, 90% and 85% for the enteric drainage group and 81%, 55% and 45% and 97%, 97% and 97% for the bladder drainage group respectively.

Conclusion: Our data shows that there is clearly a trend to better graft survival of bladder drainage pancreas in the first year. However this benefit is lost at 3 and 5 years. This data demonstrates that it may be crucial to have another marker to monitor the graft after it has been converted to enteric drainage and It would be imperative for the transplant community to find a more accurate marker, biochemical, radiological or remote (sentinel) with low complications to monitor rejection in Solitary pancreas transplant.

P179

The use of early post-operative continuous glucose monitoring in pancreas transplant recipients

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Background: Continuous glucose monitoring (CGM) is used in people with type 1 diabetes to help with insulin treatment regimens. Its value in whole organ pancreas transplantation is largely unknown. This study aimed to use CGM to assess the metabolic profile of pancreas transplant recipients in the early post-transplant period.

Methods: We studied CGM data in 30 pancreas transplant recipients and related findings to an early oral glucose tolerance test (OGTT). Complete data was available for 26 recipients.

Results: Within the first 7 days of a pancreas transplant, normoglycaemia was present 77.9% of the time. Hypoglycaemic events (glucose <3.9 mmol/l) occurred in 10/26 (38.5%) of the cohort, but were infrequent (present 1.4% of the time). Hyperglycaemia (glucose >7.8mmol/l) was present for 20.7% of the study period and correlated with a diagnosis of abnormal glucose tolerance. Those with normal glucose tolerance (NGT) spent a significantly higher percentage of time within the normal range compared to those with impaired (IGT) and diabetic glucose tolerance (DGT) (94.2% NGT vs 59.8% IGT vs 52.0% DGT, p=0.008). The characteristics of the continuous glucose monitoring profile for the SPK and PTA group were comparable.

Conclusion: CGM can provide detailed 24 hour blood glucose profiles in patients undergoing pancreas transplantation. Whilst normoglycaemia is successfully achieved for the majority of the time, hypoglycaemia can occur. Hyperglycaemia is more common and correlates well with the early post-operative OGTT. CGM is easy to perform, and provides data that could inform clinical decision making in patients in the post-operative period.

P180

From offer to recipient – how can we increase organ utilisation in pancreas transplantation?

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Background: Pancreas transplantation is an established treatment option for some patients with advanced complications of diabetes. There is however a shortage in the supply of suitable organs for transplantation and there has been considerable research to try to optimise the donor pool for better organ utilisation. Nevertheless, pancreas transplantation suffers the lowest conversion rate from initial organ offer to transplantation. The aim of this study was to assess the reasons for attrition between initial organ offer and subsequent transplantation.

Methods: A retrospective analysis was performed of a prospectively maintained database of all organ offers to the Oxford Transplant Centre between October 2013 and October 2014. Data relating to reasons for refusal and outcomes were collected by transplant type and compared using Fisher's Exact test.

Results: There were 488 pancreas offers during the study period (407 SPK, 81 PTA). 114 (23%) were accepted (99 SPK, 15 PTA) with 55 subsequently being transplanted (49 SPK, 6 PTA). The conversion rate from pancreas offer to transplantation in this study was only 11%. The most common reasons for offer decline were donor characteristics (45%), ITU capacity (14%), subjective assessment of the graft (6%), and anatomy (2%). Reasons were comparable between SPK and PTA groups, although the PTA group were more often DCD where retrieval did not progress (6% vs. 2%, p=0.05).

Conclusions: The reasons for declining an organ are multifactorial. The development of a more sophisticated method of donor risk analysis could avoid discarding potentially viable organs whilst stratification of recipients may identify those patients most likely to benefit from ITU care. Furthermore, the physical assessment of organs can be particularly subjective and therefore a mechanism for standardising this process could potentially increase the number of organs available.

Category: Basic Science - Pancreas

P181 Withdrawn

P182

Postoperative CRP and serum amylase levels predict early pancreas graft survival in simultaneous pancreas-kidney transplantation

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Introduction: The impact of ischemia-reperfusion (IR) injury on pancreatic graft survival after simultaneous pancreas-kidney (SPK) transplantation remains unknown. We investigated the role of early postoperative CRP and serum amylase (AMS) levels in predicting 1-year pancreas survival in our cohort of SPK recipients.

Methods: CRP and serum AMS levels on postoperative days (POD) 1 to 3 were correlated to 1-year pancreatic graft survival. We defined the optimal cut-off levels by ROC curve analysis and explored the differences in survival between low/high CRP and AMS groups. Univariate and multivariate analysis were performed for the detection of significant predictors of pancreatic graft survival.

Results: 277 SPKs performed between 1996 - 2013, were analyzed. Higher CRP ($p=0.04$) and AMS ($p=0.002$) levels on POD3 were associated with poorer graft survival at 1-year. A similar pattern was noted for CRP and AMS levels on POD2. Using optimal cut-off levels for both parameters, a significantly increased graft survival was shown for recipients with low CRP and low AMS compared to the groups with high levels, on both POD2 ($p=0.03$ and $p=0.005$, respectively) and POD3 ($p=0.005$ and $p<0.001$, respectively). Additionally, a rate of serum AMS decline greater than 51.8% from POD1 to POD3 was associated with better graft survival ($p=0.015$). In multivariate analysis, serum AMS on POD3 emerged as a significant predictor of graft survival at 1-year (OR 5.67, 95% CI 1.04-30.92), with a cut-off value of 129.5 IU/L.

Discussion: Our results suggest that high early postoperative CRP and serum AMS levels are associated with poorer pancreatic graft survival at 1-year after SPK transplant. These findings may prove useful in monitoring the effect of protective strategies against IR injury of the pancreatic graft.

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Effect of islet cell transplantation (ICT) on long-term diabetes complications two years post transplantation

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Introduction: ICT is a promising therapy to improve glycaemic control and refractory hypoglycaemia in type 1 diabetes. The aim of this study was to determine the impact of ICT on progression of diabetes long-term complications.

Methods: A total of 18 subjects with type 1 diabetes and recurrent severe hypoglycaemia, 9 subsequently received ICT, were studied. Data including HbA1c, Hyposcore, mean & standard deviation (SD) glucose and % time of hypo- & hyperglycaemic were collected. Complication screenings were performed at baseline and 2 years following intensive insulin therapy or ICT. Peripheral neuropathy was assessed using thresholds for hot, cold & vibration; retinopathy was graded by retinal photography/ external ophthalmologist; nephropathy by microalbumin excretion; autonomic dysfunction by pupillary response time.

Results: Clinical characteristics of control group and ICT group were similar at baseline. Two years post transplant, there were significant between group differences in HbA1c, total daily insulin, Hyposcore, mean & SD glucose and % time hyperglycaemic. At 2 years, the ICT group showed less progression in peripheral neuropathy (0% vs. 33%, $\chi^2=0.13$) and retinopathy (22% vs. 44%, $\chi^2=0.15$). Using GEE, differences in peripheral neuropathy were predicted by Hyposcore ($p=0.006$), mean glucose ($p=0.007$), total daily insulin ($p=0.01$), % time hyperglycaemic ($p=0.02$) and HbA1c ($p=0.04$). There was no predictor of change in retinopathy at 2 years. Differences in autonomic dysfunction were predicted by mean glucose ($p=0.005$) and % time hyperglycaemic ($p=0.04$).

Discussion: Significant improvement in glucose control and reduced hypoglycaemia is achieved after ICT. Data suggests reduced progression of neuropathy and retinopathy at 2 years. Further analysis using complications data out to 4 years post transplant with analysis of change over time is planned.

P184

Outcomes of simultaneous pancreas and kidney transplantation with a high level of preformed antibodies

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Background: There is paucity of data of outcomes of simultaneous pancreas and kidney transplantation in recipients with preformed antibodies. Newer induction agents have been used with variable success rates.

Methods: We analyzed the significance of high sensitization, defined based on the presence of high levels of preformed antibodies (cPRA >60%), on the outcomes of simultaneous pancreas and kidney (SPK) transplantation. We reviewed 273 SPK transplants performed at our center over last 10 years and identified 13 patients who met high sensitization criteria. All recipients had campath induction. Stats-direct 3 was used for statistical analysis.

Results: The 5-year graft survival was 69% (95% CI, 0.51-0.86), the 5-year patient survival was 93% (95% CI, 0.74-0.96), (There were four pancreatic allograft failures within first three months of transplantation). There were no immunological causes of these allograft failures. The adjusted hazard ratio associated with the risk of allograft failure was 0.4. There were no statistically significant correlation between grafts function and age of recipient - $p=0.91$; peak antibody levels and biopsy proven acute rejection episodes $p=0.68$; peak antibody levels and delayed graft function $p=0.93$ on multiple regression model.

Conclusion: Sensitization does not appear to have a significant negative impact on the survival and long-term outcomes of SPK transplant patients.

P185

Vascular remodelling following whole pancreas transplantation

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Background: Vascular remodelling is a physiological process that is recognised after a number of insults and differs from pathological stenotic disease which can be associated with rejection and donor specific antibodies in transplanted grafts. This study examined the incidence of vascular remodelling following combined kidney and pancreas transplantation

Methods: In 2012 CT angiography became routine for pancreas transplants in the early (<5 days) and late (< 6 months) post-transplant period. This study examined changes in axial/coronal diameters of associated transplant vasculature.

Results: 8 transplants were performed with the necessary follow-up scans (6 SPK, 2 PAK). All patients received standard immunosuppression of tacrolimus, MMF +/- prednisolone. Significant uniform luminal narrowing was observed in all vessels except the renal arteries (see table, mean diameters - mm). One episode of pancreatic graft rejection was encountered which resolved with steroids. Two patients developed arterial branch thrombosis (1 early, 1 late) requiring anti-coagulation. Other morbidity included collection (n=2) and graft pancreatitis (n=1). All grafts were functioning at a median follow up of 15 months (range 10-21) and all patients were insulin independent.

	Renal artery	SMA	Splenic	EIA	IIA	Conduit
Early	5.4	7	6.1	7.5	5.9	10.1
Late	5.4	3.3	1.8	3	2.2	6.9
% change	0	-50	-60	-70.8	-57.8	-30.7
P value	n/a	<0.01	0.012	<0.01	<0.01	<0.01

Conclusions: Our data suggests luminal narrowing of all arteries associated with the pancreatic allograft without corresponding changes in the renal arteries. This does not appear to impact on short term graft function. It is difficult to determine if this remodelling process directly contributes to the development of vascular pathology. Further studies are required to discover whether this phenomenon is detrimental in the long-term, and determine if therapeutic intervention is required.

Different genetic factors within pancreas transplant donors and recipients correlate with decreased long-term graft function

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Introduction: Genetic variation within *caveolin-1*, involved in signal transduction and tissue fibrosis, in pancreas transplant donors has been previously shown to correlate with decreased long-term graft function in type 1 diabetics (T1D). As variation within *caveolin-1* in pancreas transplant recipients did not correlate with long-term graft function, this suggests the presence of unique pathways in both donors and recipients which lead to loss of graft function. Genetic contributors to T1D, including *CTLA-4*, *PTPN22*, *IL-2RA* and *INS-VNTR*, have been well established, however it is currently unknown whether these susceptibility genes impact upon long-term pancreas graft function in T1D pancreas transplant recipients. The aim of this study was to determine if T1D gene variants can predict long-term pancreas graft function.

Methods: We genotyped 435 pancreas donors and 431 transplant recipients who had undergone pancreas transplantation at the Oxford Transplant Centre, UK, for *CTLA-4* rs3087243, *PTPN22* rs2476601, *IL-2RA* rs12251307 and *INS-VNTR* rs689 single nucleotide polymorphisms. Death-censored cumulative events were analysed using Kaplan-Meier and Cox regression.

Results: Presence of *CTLA-4* rs3087243 GG genotype in our recipients was predictive of reduced long-term pancreas function compared to recipients with AG or AA genotypes (log rank P=0.007). Multivariate Cox regression, adjusting for donor and recipient transplant factors, confirmed association of the rs3087243 GG genotype (P=0.027, HR=2.28 [95%CI=1.10-4.74]) with long-term graft function. Variation within donor rs3087243 genotype did not predict long-term graft function (log rank P=0.507). No other variant screened predicted long-term graft function.

Discussion: This study provides evidence for recipient *CTLA-4* genotype in predicting long-term pancreas graft function. Screening *CTLA-4* in other datasets is required to confirm these pilot results and determine how *CTLA-4* variation within the recipient's immune response leads to loss of graft function.

Does genetic variation in pancreas transplant Recipient's *HMOX1* cytoprotective mechanisms correlate with long-term graft function?

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Introduction: Variation within the heme oxygenase 1 (*HMOX1*) gene, essential for heme catabolism and a known inflammatory and immune regulator, has been purported to be involved in protecting against loss of renal transplant function. Identifying genetic variants that protect against or alter protection against graft loss will undoubtedly provide opportunities to develop therapeutics to preserve graft function. The objective of this study was to determine if common variants in *HMOX1* in pancreas donors and transplant recipients correlated with long-term pancreas graft function in type 1 diabetics.

Methods: We genotyped 435 pancreas transplant donors and 431 transplant recipients, all of whom had undergone pancreas transplantation at the Oxford Transplant Centre UK, for all common variation in *HMOX1* using 6 tag single nucleotide polymorphisms (SNPs). Death-censored cumulative events were analysed using Kaplan-Meier and Cox regression.

Results: Presence of rs2071748 AA genotype in our recipients was predictive of reduced long-term graft survival, compared to recipients with AG/GG genotypes (log rank P=0.025), with presence of the rs5755720 GG genotype in our recipients showing a borderline association with reduced long-term graft survival, compared with recipients with AG/AA genotype (log rank P=0.048). Multivariate Cox regression, including donor and recipient transplant variables, confirmed association of rs2071748 AA genotype (P=0.006, HR=2.25; [95% CI=1.26-4.02]) and rs5755720 GG genotype (P=0.018, HR=2.08 [95% CI=1.14-2.08]) with long-term graft function. *HMOX1* donor genotype did not show any association with long-term graft function.

Discussion: Our results show, for the first time, preliminary evidence for *HMOX1* pancreas transplant recipient genotype in long-term pancreas graft function. Replication in a larger cohort is necessary to confirm these results alongside functional analysis to determine if these risk genotypes contribute to decreased long-term graft function through disrupting *HMOX1* cytoprotective mechanisms.

Variation in beta cell dysfunction genes *TCF7L2* and *KCNJ11* does not predict long-term graft outcome in pancreas transplantation

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Introduction: Pancreas transplantation is an established treatment option for some patients with diabetes. However, overall graft attrition rates remain high with 24% of patients returning to exogenous insulin by 3 years. Whilst clinical indicators of transplant outcomes have informed donor selection, it is currently unknown whether these organ donors harbour genetic variants that predispose to future beta cell dysfunction. With recent advances in our understanding of beta cell genes involved in type 2 diabetes (T2D) onset, we aimed to establish whether variants in well-established T2D susceptibility loci, such as *TCF7L2* and *KCNJ11*, play a role in predicting long-term pancreas graft function.

Methods: We genotyped 435 pancreas donors and 430 recipients who had undergone pancreas transplantation at the Oxford Transplant Centre for *TCF7L2* rs7903146 and *KCNJ11* rs5215 single nucleotide polymorphisms. This study had >80% power to detect a hazard ratio (HR)>1.50. Death-censored cumulative events were analysed using Kaplan-Meier analysis.

Results: There were 85 graft failures in 430 recipients. All genotypes were within Hardy-Weinberg equilibrium for both of the genes tested ($p=0.55-0.06$). In the *TCF7L2* rs7903146 group there were 68 donors with the CC genotype, 207 with TT and 197 with CT genotype. For the *KCNJ11* rs5215 polymorphism 60 donors displayed the CC genotype whilst 210 and 238 displayed the TT and CT genotypes respectively. Variation in *TCF7L2* rs7903146 or *KCNJ11* rs5215 in either the donors or recipients did not predict long-term graft function (log rank $p=0.32-0.35$).

Discussion: Variation in the rs5215 and rs7903146 genotypes in our pancreas transplant donors or recipients did not predict long-term graft outcome. However, further screening in larger datasets may determine if they play a smaller role ($HR<1.50$) in predicting long-term pancreas transplant function.

Category: Surgical - Pancreas

P189

Does distance from transplant centre affect outcomes in pancreas transplantation?

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Introduction: The population of Wales served by its transplant centre is around 2.3 million and covers a large geographic area. Some patients therefore undergo long-distance consultation and care, with potentially significant implications to their social life. Indeed, studies have shown that patients living farther from the transplant centre have reduced access to deceased donor transplant. However no studies have evaluated the effect of distance from transplant centre and outcomes from transplantation. The purpose of this study was to evaluate the effect of distance from transplant centre and outcomes in pancreas transplantation.

Methods: The online 'AA Route planner' was used to determine the distance from the transplant centre for 119 consecutive pancreas transplant recipients, transplanted between January 2004 and December 2013 in a single centre. Outcomes measured were rates of acute rejection and graft survival.

Results: Over a 10-year period, 119 pancreas transplants were performed in a single transplant centre. The mean distance (\pm SEM) from the transplant centre was 31.6 ± 2.4 miles. Thirty-five (29.4%) patients experienced at least one episode of rejection following their transplant. The mean distance between patients who experienced rejection and those who did not was 29.9 ± 4.8 and 32.3 ± 2.8 miles respectively ($p=0.65$). Mean graft survival was 49.1 ± 3.2 months, with 5-year graft survival being 83%. Cox regression survival analysis showed that distance from transplant centre did not affect graft survival ($p=0.296$). When distance was analysed using 2 groups, namely '40 miles or less from transplant centre' and 'more than 40 miles from transplant centre', 5-year graft survival was 85% and 73% respectively (log-rank test p -value of 0.122).

Conclusion: This study has demonstrated that distance from transplant centre for pancreas transplantation is not associated with any adverse outcomes. Moreover, such 'centralised' practice for pancreas transplantation continues to be safe. Patients should be encouraged to maintain regular consult with their local physician as well as their transplant centre.

P190

Intra- vs extra-peritoneal implantation of pancreas transplant grafts

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Introduction: A variety of techniques are used for pancreas transplantation without a clear consensus on the optimal approach. One variation is whether the pancreas graft is placed intra-peritoneally through a midline incision, or extraperitoneally using an iliac incision. Adequate exposure to iliac vessels can be obtained by either approach, but there are inherent advantages and disadvantages to each. In this study, we aimed to analyse the short and long term differences from either approach.

We performed a retrospective analysis of 50 consecutive pancreas transplants performed in a single centre over a 6-year period. Sufficient data was available on 44. Intra vs extra. Data was collected on length of hospital stay, number of returns to theatre due to complications and inflammatory response.

Results: The total length of hospital stay was slightly longer in the extra-peritoneal group, but not statistically significant (36.3 vs 46.1 days; t -test, $p=0.5$). There was also no significant difference in peak levels of CRP (250.5 vs 256.7, $p=0.88$) or number of returns to theatre for complications (0.68 vs 0.8, $p=0.72$). However, the peak amylase was significantly higher in the extra-peritoneal group (138.5 vs 263.3, $p=0.02$). The long term survival of the grafts was not statistically significant with 63% of intraperitoneal grafts vs 46.7% of extraperitoneal grafts functioning at last follow up. Median follow up was 45.5 months.

Summary: There are no major significant differences in outcome between intra- and extra-peritoneally placed pancreas transplant grafts. There was an increased peak amylase level in the extraperitoneal group which may represent increased localised inflammatory response often observed in extraperitoneal grafts, which may be a reason to favour intraperitoneal placement. However, surgeon and institutional experience is undoubtedly a factor in choice of technique, as there are no significant differences, this is likely to remain the case.

P191

Use of ex vivo normothermic perfusion for quality assessment of discarded human donor pancreases

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Introduction: Approximately 50% of pancreases retrieved for transplantation are deemed unsuitable and are discarded. This is primarily due to concerns about graft quality and the associated risk of complications, particularly those related to graft pancreatitis. However, at present this decision is subjective and some of these declined grafts may be suitable for transplantation. *Ex vivo* normothermic perfusion (EVNP) prior to transplantation may allow a more objective assessment of graft quality and reduce discard rates.

Methods: Human pancreases retrieved but declined for transplantation underwent EVNP with ABO-compatible warm oxygenated packed red blood cells for 1-2 hours. Primary outcome measures included blood flow, plasma amylase, insulin secretion and histological assessment.

Results: Five declined human pancreases were assessed using EVNP after a median cold ischaemia time of 16h 35mins (range 13h 14mins to 31h 14mins). Pancreas 1, declined due to retrieval injury, was from a 27-yr old donation after brain death (DBD) donor (BMI 20) and had the highest blood flow and basal and stimulated insulin secretion during EVNP. Pancreas 2 (fatty infiltration; BMI 24), was from a 51-yr old donation after circulatory death (DCD) donor and had the lowest insulin secretion. Pancreas 3 from a 14-yr old DBD donor with duodenal trauma had intermediate insulin and amylase levels. Pancreas 4 (fatty infiltration; BMI 19) was from a 46-yr old DBD donor and had markedly higher amylase levels than others. Pancreas 5 was from a 50-yr old DBD donor (BMI 23), and was declined due to fibrosis. Despite a cold ischaemic time of over 30 hours, amylase levels were not markedly increased compared to the other pancreases and endocrine function was maintained.

Conclusion: This is the first detailed study to assess the perfusion, injury and function of human pancreases using EVNP and demonstrates the feasibility of the approach. Further experiments are planned to investigate influence of donor type, age, BMI and cold ischaemic times on pancreatic function and injury.

P192

Bladder drainage of pancreas transplants alone: friend or foe?

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Introduction: Immunological monitoring of Pancreas Transplants Alone (PTA) remains a challenge and bladder drainage is thought to facilitate early detection of rejection but may lead to significant metabolic complications with uncertain impact on graft survival.

Methods: A single-centre analysis of 30 consecutively performed PTA over a 3 year period by interrogating a prospectively maintained database.

Results: All patients included had DM type I with severe hypoglycemia unawareness. Median age was 46 y (range 28-65) with a median BMI of 23.8 (range 18-32). 37% of the cohort was male. 28 patients had their first PTA. Donor median age was 33 y (range 2-59) with 20 (67%) being deceased brain dead. Immunosuppression included Alemtuzumab induction and maintenance with Tacrolimus with Mycophenolate. Median admission creatinine was 83 mmol/L (range 52-160). All patients had intraperitoneal graft placement with a porto-caval anastomosis and bladder drainage. Median hospital stay was 14 d (range 8-44). At discharge median fasting and two hour blood sugars during an OGTT were 5.2 and 7 mmol/L respectively. Median urinary amylase was 22,630 U/L (range 4,112-78,013). 30 % of patients were reoperated, for bleeding (n=8) or collection (n=2). 10 patients showed partial or occlusive thrombus. All were anticoagulated and only one graft was lost. Graft loss (13.3%) occurred in 4 cases with graft pancreatectomy in 3 of them (10%), at 3 w, 9 m and 15 m respectively. Rejection was treated with steroids in 5 cases (17%). Each recipient was readmitted at least once (range 0-8), predominantly for dehydration (47%). 56.7% of the patients had conversion to enteric drainage at 11 m (range 3.2-25.9). Median follow up (fu) was 16 m (range 0.3-37). One patient died (3%) at 4 m fu with a functioning graft. Median creatinine at fu was 98 mmol/L (range 55-225). One patient needed a kidney transplant.

Conclusion: In our experience, bladder drained PTA results in a temporary decline of native renal function in 50% of the patients. Readmission rates and partial thrombosis were high, but 90% of grafts were saved with anticoagulation. Planned enteric conversion may be reasonable around 12 m.

P193

Routine postoperative cystography following bladder-drained pancreas transplant

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Introduction: Routine postoperative cystogram has been used in our centre to assess for leaks following bladder-drained pancreas transplant, prior to removal of the urinary catheter. This study aims to assess the utility of this protocol.

Methods: We performed a retrospective audit of consecutive bladder-drained pancreas transplants in our centre between January 2011 and October 2014. Data were extracted regarding timing of cystogram, abnormalities reported and volume of contrast used.

Results: Thirty-nine patients received bladder-drained pancreas transplants during the study period – 31 primary pancreas-transplants alone (PTA), 4 second PTAs, 3 pancreas-after-kidney transplants and one pancreas after simultaneous kidney transplant. 35/39 (89.7%) patients underwent routine postoperative cystography at a median of 12 days (range 6-22 days) following surgery. The median volume of contrast instilled into the bladder was 200mls (range 150 to 400mls). Two cystograms were initially reported as demonstrating urine leak. Both reported leaks were subsequently shown to represent contrast refluxing into the duodenal segment (one following CT urogram with 500mls contrast). There were therefore no clinically or radiologically confirmed leaks in this series.

Discussion: No leaks were demonstrated on routine, non-voiding cystography in the present series. This investigation, with the contrast volumes used, may not have much utility in the routine care of postoperative bladder-drained pancreas transplant recipients, and may possibly delay discharge from hospital. Routine removal at day 8-10 postoperatively may facilitate discharge without compromising care.

P194

Laparoscopy assisted pancreas transplantation

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Introduction: Minimally invasive surgical techniques have improved patient outcomes in surgery. Transplant surgery has been slow to incorporate this advance.

Methods: Information was gathered from a prospectively maintained database. The initial part of the operation was laparoscopy directed and included mobilisation of the bowel and dissection of the vessels. The organs were placed intraperitoneally through a standard kidney transplant incision in the right iliac fossa. The pancreas had a portocaval anastomosis with enteric drainage. The renal allograft was anastomosed to the right external iliac vessels.

Results: 3 recipients received either a Simultaneous kidney transplant (SPK) or a pancreas transplant alone (PTA). All patients had Type 1 diabetes mellitus. The mean age of the recipients was 38 years (23 - 54 y) and 2 were female. All donors were deceased brain dead with a mean age was 42.6 y and 67% were female. The mean operating time for the SPK was 302 minutes, while that for the PTA was 208 minutes. All grafts functioned primarily. The mean hospital stay was 9 days (8-11d). The PTA patient lost graft function after 5 months due to rejection. The 2 SPK patients are insulin & dialysis independent. (1- 65 months).

Discussion: The standard SPK is performed through a long midline laparotomy. This has the obvious consequences on post-op recovery, hospital stay and return to work. Minimally invasive surgery has the potential to reduce the surgical insult. Robotic surgery may have the added advantage of shortening the learning curve and allow the entire operation to be performed laproscopically. There are challenges around organ delivery, maintaining temperature, availability and cost.

Conclusion: Laparoscopic assisted transplants appear safe and could in the future become part of a transplant surgeon's armamentarium.

P195

Pancreas allograft thrombosis – revisiting the role of hypercoagulability

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Background: Pancreas allograft thrombosis continues to present a significant problem in the early post transplant period. The role of thromboelastography (TEG) directed anticoagulation and the effect on graft thrombosis is discussed.

Methods: All patients who underwent pancreas transplants at a single centre for 2013 were retrospectively analysed. Primary end point was the incidence of graft thrombosis, correlated with donor variables (pancreas donor risk index PDRI), preservation time, and recipient hypercoagulability as measured using the TEG.

Results: During 2013, 71 pancreas transplants were performed, with 57 SPK, 12 PTA and 2 PAK. During this period, 12 patients (17%) demonstrated evidence of thrombosis on CT / MRI angiography; 7 patients had arterial thrombus (distal SMA), 3 patients the vein could not be demonstrated and presumed to have a thrombus, and 3 patients had both arterial and venous thrombosis. 1 graft (1.4%) was lost to thrombosis. 10 patients received therapeutic anticoagulation with low molecular weight heparin and have functioning grafts. Coagulation index >3 indicating hypercoagulability was associated with 9 thrombosis, whereas 3 occurred in patients with normal coagulation index. There was no correlation between donor age, BMI, cold ischaemia, donor PDRI, preop hypercoagulability and the occurrence of thromboses.

Discussion: Graft thrombosis is multifactorial and the judicious use of anticoagulation directed by TEG as a tool to identify hypercoagulability improves the likelihood of graft salvage.

Category: Renal Transplantation - Outcomes 1

P196

Survival and transplantation rates of the elderly incident haemodialysis population

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Introduction: In 2012, 24.9% of UK haemodialysis patients were older than 70. However, this age group only represented 8% of all patients listed for renal transplant. One reason is the perception that survival in the elderly dialysis population is short. The aim of this work was to investigate the survival outcomes and transplantation rates of our elderly incident haemodialysis population.

Methods: Patients aged 70 or above who commenced haemodialysis from 2005 to 2012 in our hospital were identified from our prospectively maintained database. Data such as age, comorbidities, date of dialysis initiation, duration of haemodialysis and renal transplant date was collected. Kaplan-Meier survival analysis was used to evaluate survival.

Results: 218 patients commenced haemodialysis; 68.3% were male, 67.4% were prescribed anti-hypertensives and 25.2% were diabetic. Only 4 patients from this cohort were transplanted during this interval. One was placed on the waiting list, but died prior to receiving a transplant. 31 patients underwent consideration, but were not listed: 19 were felt to be unsuitable following multi-disciplinary team meeting (reasons for this were not evident on review of patient notes), 9 had medical co-morbidities and 3 declined transplantation. Of the cohort that remained on haemodialysis, survival at 4 years of those aged 70 to 80 and those over 80 years, was 53.7% and 46.3% respectively.

During the study period, of 1180 kidney-only transplants performed at our centre, only 41 (3.47%) recipients were aged 70 or above (24 DCD, 10 DBD, 5 double kidneys, 2 from living donors). At present, there are 268 patients placed on the waiting list for renal transplant, of which 13 patients (4.9%) were over the age of 70 when waitlisted (range 70-74 years).

Discussion: A relatively large number of elderly patients commence dialysis, but few are considered for transplantation, and even fewer actually get transplanted. Our mortality data would suggest that survival rates are better than originally thought. Utilization of an objective assessment tool to determine a patient's physiological age might change clinicians' perceptions of being "too old for transplant".

P197

Outcomes of kidney transplantation from hypertensive living donors

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Introduction: The disparity between donor kidney availability and demand has increased utilization of kidneys from marginal living donors, including hypertensive donors. The aim of this study was to compare kidney graft outcomes of patients after transplantation with kidneys from hypertensive and normotensive living donors.

Methods: Data was prospectively collected on consecutive recipients who underwent kidney transplantation from live donors in 2002-2012. Donors were categorized as hypertensive or normotensive, elderly (≥ 60 years) or younger (< 60 years) and with high Body Mass Index (BMI) (≥ 30) or normal BMI (< 30).

Results: We included 494 patients (300 males, 194 females) who received a kidney from a living donor. 45 donors had pre-transplantation hypertension. Follow up was 73 months (median, range 2-145). 77 patients lost their grafts and 41 patients died. Patients who lost their grafts were more likely to have a hypertensive donor ($p=0.003$) or a donor of Afro-Caribbean (AC) ethnicity ($p=0.022$). There was no association of elderly donors ($p=0.305$) or donors with high BMI ($p=0.348$) with the risk of graft loss. The median eGFR for recipients of kidneys from normotensive donors was 53 ml/min (range 14-93) at 3 years and 48 ml/min at 5 years (range 17-73), whereas for recipients who received kidneys from hypertensive donors median eGFR was 46 ml/min (range 15-90) and 53 ml/min (range 27-90), respectively ($p=0.103$ and $p=0.381$ respectively). In survival analysis, recipients of kidneys from hypertensive donors had reduced graft survival (log rank $p<0.001$) and reduced patient survival (log rank $p=0.042$), but the latter was not significant in multivariate analysis ($p=0.212$). In Cox-regression, AC ethnicity (Hazard Ratio (HR) 2.199, 95% Confidence Intervals (CI) 1.194-4.051, $p=0.009$), rejection (HR 5.212, 95% CI 3.186-8.524, $p<0.001$) and donor hypertension (HR 2.140, 95% CI 1.159-3.953, $p=0.015$) increased the risk of graft failure.

Discussion: Receiving a kidney from a donor with history of hypertension was associated with increased risk of graft loss. Although the group of hypertensive donors was relatively small, this group of donors seems to merit additional study and focus.

P198

UK kidney donor risk index (UKKDRI) at a single institution and its relation to eGFR at 3 years post transplant

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Background: The UKKDRI has been developed to help predict graft survival in deceased donor (DD) kidney transplantation. This system uses donor age, weight, history of hypertension, number of days in hospital and the use of adrenaline. The aim was to establish the UKKDRI at a single centre during a single year, its use in DCD as well as DBD grafts, and to validate these scores against recipient eGFR at 3 years post-transplantation.

Methods: The UKKDRI was calculated for all DDs during 2010. These were then grouped into indexed levels of risk. *Group 1* (lowest risk) represented those with a UKKDRI of ≤ 0.87 , *group 2* represented those with a UKKDRI of 0.85-1.02, *group 3*, a UKKDRI of 1.03-1.34, and *group 4* (highest risk), a UKKDRI of ≥ 1.35 . The UKKDRI for DCD and DBD's were compared with recipients' eGFR at 3 years post-transplant. Intergroup analyses were made to test the sensitivity of comparing recipient eGFR against the predicted level of donor risk.

Results: During 2010, 87 DDs were transplanted with a mean age of 52 years (48% female, 60% DCD). The UKKDRI for the entire cohort was 1.32 ± 0.05 . A UKKDRI over 1.35 was present among 39% of DBD donor grafts and 61% of DCD grafts. There was an inverse linear trend between the UKKDRI and the mean recipient eGFR, 47 ± 2.48 ($p < 0.0001$, $r^2 = 0.23$). An increasing mean eGFR was noted from groups 1 to 4 (*group 1* eGFR = 63.39 ± 4.77 , *group 2* eGFR = 53.8 ± 3.38 , *group 3* eGFR = 44.67 ± 4.19 and *group 4*, 38.14 ± 3.22) ($p < 0.0001$). There were 2 inter group comparisons that were statistically significant, group 1 vs.4 ($p < 0.0001$) and 1 vs. 3 ($p = 0.010$) [1 vs. 2 ($p = 0.317$), 2 vs. 3 ($p = 0.208$), 2 vs. 4 ($p = 0.080$) and 3 vs. 4 ($p = 0.286$)].

Discussion: A greater percentage of DCD grafts have a UKKDRI over 1.35. A strong negative correlation exists between increasing UKKDRI and decreasing eGFR for this single centre data. This further validates the UKKDRI as a useful instrument to evaluate donor related graft outcomes.

P199

Excellent outcome following combined liver kidney transplantation in a patient with primary hyperoxaluria

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Introduction: We report a case of successful outcome of renal allograft following a prolonged period of dialysis requirement post combined Liver Kidney Transplant (LKT) for Primary Hyperoxaluria Type1 (PH1).

Case report: Our patient presented with multiple renal stones at age 3. He had a strong family history; diagnosis was confirmed by genetic analysis. He developed progressive renal disease reaching end stage at age 48. After 4 years of conventional thrice-weekly haemodialysis (HD) he developed systemic oxalosis with high plasma oxalate (POx) levels (80µmol/l). He received a combined LKT from a deceased donor. The hepatic graft functioned immediately but renal graft function was delayed. He received intensive haemofiltration immediately pre and postoperatively followed by daily long (6 hour) dialysis sessions. He had persistent high POx levels due to release from body stores. Serum creatinine (SCr) fell to 300µmol (CrCl <30 ml/min) by two weeks but there was no further improvement. Renal transplant biopsies performed on days 14 and 35 revealed deposition of oxalate crystals and no evidence of rejection. As SCr and POx levels remained high at 250µmol and 20 to 30µmol respectively, he was at high risk for further renal oxalate deposition. To remove his high body oxalate load and keep POx levels low, dialysis (4 hour) was continued for 6 sessions per week for the first 5 months then 5 per week for the last month. When further improvement was noted at 6 months with fall in SCr to 160µmol (CrCl >30ml/min) and oxalate levels to less than 15µmol, dialysis was stopped. Renal and hepatic function remains stable 1 year post transplant

Conclusion: In this patient, measures aimed at maintaining high urine output and oxalate crystallization inhibition (magnesium, phosphate and potassium citrate supplementation) together with removal of plasma oxalate by aggressive prolonged dialysis treatment has resulted in a functioning renal allograft 6 months post combined LKT.

P200

Single centre retrospective analysis of renal transplants done at recipient age of above 70 years

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Introduction: There has been increase in the transplant activity in the recent years for the marginal recipients with recipient's age above 70 years in United Kingdom. We conducted retrospective study in our unit to look at the outcomes for the above group.

Methods: Retrospective single centre study for all the patients transplanted at their age of 70 yrs and above. Transplant activity spanned between December 2007 and April 2014 with follow up ranging between 6 to 80 months.

Results: Total number of renal transplants done was 75. 76% were male recipients. Average age at transplant was 72.8 years (70 to 80 years). Graft survival at 1 year and 2 year was 83% and 77% respectively. Death censored graft survival at 1 year and 2 year was 95% and 93%. Patient survival at 1 year and 2 years was 85% and 79%. 27% of patients died during follow up ranging between 6 to 80 months. 11% had non skin malignancy of which three fourth were gastro-intestinal malignancy. 19% had opportunistic infections. 4 % had post op MI. 8% had cardiac event /failure at 1 year. Delayed graft function was noted in 47% with no increased rate of graft loss or death. Rejection episodes were 17% which is not much different to younger population.

Conclusion: First UK study looking at the outcome of renal transplants after recipient age of 70 yrs. Good graft outcome censored for death even in the older recipients. All patients with cardiac event/failure had abnormal ECHO pre transplant apart from two diabetics. Gastro-intestinal investigation during pre-transplant assessment probably would pick up malignancy at earlier stage.

P201

Long term graft survival in underweight patients following renal transplantation - a single centre ten years experience

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Introduction: Low preoperative body mass index (BMI) is considered a strong marker of poor nutritional status with inferior outcomes in such patients demonstrated across multiple surgical disciplines. Despite this, there is a relative lack of evidence concerning the outcome of underweight recipients following renal transplantation, which is in contrast to the great interest in the effect of obesity. The aim of this study is to compare the long-term graft outcomes for underweight recipients with an age and sex matched cohort of patients with ideal BMI.

Methods: A retrospective single centre paired analysis of consecutive adult patients undergoing renal transplantation between January 2004 and January 2014 at the QE Hospital, Birmingham. Underweight (BMI <18.5 kg/m²) patients were age and sex matched with ideal weight (BMI 18.5–25 kg/m²) counterparts. Data was censored at death, re-initiation of dialysis or an end point of October 2014.

Results: 33 of 1095 (3.0%) patients were underweight of which 60.6 % were females with mean age of 27.0. There was no difference in one-year graft or patient survival between the underweight and matched ideal weight groups. Kaplan-Meier analysis demonstrated no difference in dialysis free patient survival between the two groups (P 0.955).

Discussion: Graft outcomes for underweight patients undergoing renal transplantation in this study were comparable to a matched ideal weight cohort. Therefore low BMI in itself should not be a barrier to renal transplantation.

P202

Outcomes after listing for transplantation in those aged 70 or over

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Background: Low likelihood of listing and subsequent deceased donor transplantation has previously been reported for the elderly with additional concerns about patient frailty, morbidity and mortality in those transplanted successfully. We analysed transplantation and patient survival rates for those aged 70 years or more listed on the deceased donor waiting list (DDWL) between 2004 and 2014. Additional analysis was made of post transplant outcomes.

Methods: We identified adults aged >70 years in a large single UK transplant centre successfully listed on the DDWL June 2004-May 2014. All individuals were followed with analysis made of patient survival, transplantation and wait list status and patient and graft outcomes after transplantation.

Results: We identified 171 patients, mean age 73 years, successfully listed on the DDWL June 2004 to May 2014 and followed for a mean of 36 months (SD 31). At time of last f/up 53 were still active on the WL, 26 (15%) were suspended and 32 (19%) were removed from the WL while 34 (20%) had died. Transplantation occurred successfully in 26 (15%). Overall survival after listing was 74% at 1 year and 23% at 5 years. Transplantation conferred a significant survival benefit ($p=0.014$) with 1 year survival 99% v 92% (WL) and 5 year survival 83% v 60%. Transplanted patients had a mean age at listing of 73 years. Median length of stay post transplant was 9 days (R 6-39) and median GFR at discharge 38.6 ml/min and at 1 year 38.4 ml/min. After a median follow up post transplant of 35 months (R: 1.7-112) 21/26 (81%) patients were alive with functioning grafts, 3 had died and 2 experienced graft failure.

Conclusions: For those aged 70 years and over entering the transplant wait list, subsequent transplantation confers a significant survival benefit to remaining on the waiting list.

Kidney transplantation and atypical haemolytic uremic syndrome: our experience so far

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Atypical haemolytic–uremic syndrome is a rare microangiopathic haemolytic condition characterized by thrombocytopenia and acute renal failure.¹ Atypical HUS (aHUS) defines non Shiga-toxin-HUS and even if some authors include secondary aHUS due to *Streptococcus pneumoniae* or other causes, aHUS designates a primary disease due to a disorder in complement alternative pathway regulation.

The prognosis for patients with atypical haemolytic–uremic syndrome with a factor H mutation is poor; 60% have end-stage renal disease or die within a year.² The expected rate of graft failure due to recurrent atypical haemolytic–uremic syndrome among patients with a factor H or factor I mutation is 80% within 1 to 2 years.³ The incidence of complement-aHUS is not known precisely. However, more than 1000 aHUS patients investigated for complement abnormalities have been reported. In adult-onset HUS following kidney transplantation, the recurrence rate and the incidence of acute rejections are high, resulting in a detrimental graft survival.⁴ Moreover recurrent disease develops early with 60% of cases occurring in the first month after transplantation.⁵

To date our unit has transplanted 5 patients aHUS successfully, with the first one in September 2013. She was thought to have had HUS secondary to E-coli but had recurrence of HUS (biopsy proven) in the transplant graft. The graft was salvaged by treating her with eculizimab. The next patient was a 23 year male with a C3 mutation who underwent a DBD kidney transplant in January 2014. Next was a 43 year female patient who had previously been transplant in 2002 and who was diagnosed with atypical HUS in 2009 which affected her renal transplant graft which eventually failed in 2012. She received a living related kidney transplant from her 42 year husband but had multiple donor specific antibodies. She required a slightly different approach including 10 preoperative treatments with Therasorb and ATG and IVIG on induction. Our most recent experience also happened to have been our longest haemodialysis patient (24 years). We also successfully performed a simultaneous liver-kidney transplant in a 62 year man with aHUS (mutation in complement factor H).

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P204

Long term patient related outcomes following ABO-incompatible kidney transplantation (ABOi-KT)

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Introduction: Graft and patient outcomes following ABOi-KT are good, but little is known about the patient perspective post-transplant. Compared to compatible transplantation, there is increased donor and recipient anxiety relating to pre-transplant antibody removal and increased risk of rejection and graft loss. This study aims to assess the health related quality of life in patients >5 years after ABOi-KT.

Methods: 37 patients had an ABOi-KT performed >5 years ago (transplanted between Jul 2005 and Sep 2009). A telephone questionnaire (based on the SF-36) assessed: health and social life compared to pre-transplant, experience of antibody removal, how worthwhile the transplant was perceived overall and whether they would recommend ABOi-KT to other patients. Graft survival, rejection and infection were correlated with responses.

Results: 3 patients died with a functioning graft and were excluded. 34 patients were approached (including 2 with graft failure). In total 26 patients (76 % of the cohort) responded and mean follow up was 76 months (± 11.8 SD). 92% experienced improved health post-transplant (5 point Likert scale; mean 4.65 ± 0.846). 81 % felt more enabled in terms of time and effort spent on social activities (5 point Likert scale; mean 4.31 ± 0.97). The majority of respondents (73%) found antibody removal only mildly or moderately stressful. When asked 'how worthwhile' they found the experience, on a scale of 1-10, patients were overwhelmingly positive (mean score was 9.38 ± 1.235) and 100% would recommend it (including those with graft failure). 7 respondents had rejection and 11 had infectious complications. Comparing responses between patients with and without rejection and between those with and without infection, there was no significant difference for any of the questions asked (rejection vs not: health $p=0.61$; social $p=0.87$; antibody removal $p=0.96$, infection vs not: health $p=0.59$, social $p=0.86$ and antibody removal $p=0.421$).

Discussion: ABOi-KT not only offers acceptable graft and patient survival compared to compatible transplantation, but is perceived as a positive experience by patients, irrespective of post-transplant complications. Overall, the transplant had improved their health, social life and capabilities despite the process of antibody removal and complications.

Category: Renal Transplantation - Miscellaneous

P205

Patient outcome and time to re-transplantation following renal allograft failure in the UK

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Introduction: With an increasing number of kidney transplants and improved patient survival after transplantation, recipient survival following graft failure is becoming more common. We analysed data from NHSBT to assess this further.

In 2011-12, 1332 kidney transplant recipients died in the UK. Of these, 360 (27%) had suffered graft failure before death. Graft failure was more common in recipients of deceased donor (DD) than living donor (LD) transplants (28.0 vs 21.1%, $p < 0.01$).

When censored for patient death, 49.3% of patients who suffered graft failure in 2008-12 returned to the DD transplant waiting list. The median time before returning to the waiting list was 261 days after starting dialysis. The median wait for a repeat transplant was a further 715 days, meaning the median time to re-transplantation from a DD was 976 days (2.6 years). In patients who received a second transplant from a living donor, median time to repeat transplantation was 313 days (0.86 years).

Results: In the above cohorts, median age at first graft failure was 51.3 +/-14.2 (SD) years for first and 50.2 +/- 11.5 years for second transplants, the discrepancy relating to an increased need for repeat transplantation in paediatric recipients.

Without re-transplantation, the prognosis after graft failure was poor. In a cohort of 259 patients followed from 6 months after graft failure in 2008-12, mean actuarial survival was 18 months if the patient had not been re-entered onto the deceased donor waiting list, and 34 months if the patient had been relisted for transplantation but not transplanted. Less than 20% of patients lived more than 4 years after graft failure unless they had been re-transplanted.

Conclusion: These data demonstrate the survival advantage of prompt re-listing for repeat kidney transplantation, where clinically appropriate.

P206

Angiotensin-2 associates with graft failure and mortality in renal transplant recipients

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Introduction: Angiotensin-1 (Ang1) and angiotensin-2 (Ang2) are involved in stabilizing the vascular endothelium and may play a role in premature mortality and graft failure in renal transplant recipients (RTR). Early identification of RTR at risk could allow for management, possibly via anti-Ang2 therapy. We aimed to investigate the association of Ang1 and Ang2 with graft failure and mortality in a prospective cohort of stable, outpatient RTR.

Since elevated Ang2 levels have been demonstrated in sepsis, which has pathophysiological similarities to the deceased brain dead donor we also separately studied Ang2 associations in RTR transplanted with deceased donor kidneys. Plasma Ang1 and Ang2 next to clinical parameters were measured in 552 RTR and in 86 living kidney donors (LKD).

Results: Ang1 was higher in RTR than in LKD ($p=0.002$), while Ang2 was similar. Surprisingly, in a multivariate analysis, significant associations between Ang2 and heart rate, Nt-pro-BNP or hsCRP were found (all $p<0.001$) while for Ang1, no associations were found. In deceased donor-RTR, Ang2 levels were higher compared to living donor-RTR. After adjustment for potential confounders, Ang2 levels were both associated with graft failure (HR 2.41, 95%CI 1.24-4.71, $p=0.01$) and mortality (HR 1.53, 95%CI 1.03-2.27, $p=0.04$) after deceased donation.

Conclusion: Intervention studies targeting Ang2 to attenuate inflammation are required to provide insight in the mechanism of the Ang/Tie2-system in renal transplantation, especially after deceased donation.

P207

Renal cell cancer in a UK regional renal transplant population – what should be the role of peri-transplant imaging?

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Introduction: There is an increased risk of developing renal cell cancer (RCC) in patients with renal cystic disease, haemodialysis and following renal transplantation. A long time interval between native renal imaging and transplantation could lead to development of denovo tumours pre-transplantation. Our aim was to evaluate the clinical characteristics of RCC with a focus on the timing of renal imaging and tumour development.

Methods: A multicentre retrospective cohort study was performed for all patients receiving a renal transplant between 2002 – 2014. Case identification was via ICD-10 codes and scrutiny of a prospectively maintained transplant database.

Results: Of 1386 patients undergoing renal transplantation 19 developed RCC (1.4%). 17 were in native kidneys and 2 in renal allografts. Mean interval between pre-operative native renal imaging and transplantation was 3.5 years. 6 patients had no documented renal imaging prior to their transplant. Median time from transplantation to diagnosis of RCC was 5 years. 5 patients (26.3%) developed RCC within 6 months of renal transplantation. The histology included nine clear cell RCC (50%), eight papillary RCC (44%), one chromophobe RCC and one sarcomatoid RCC. Mean tumour size on histological analysis was 42.05mm. The majority were pT1 tumours. Median follow-up was 2.59 years. 4 patients died during follow up – three deaths were related to the diagnosis of RCC.

Discussion: Within our renal transplant population we identified a considerable time interval between native renal imaging and renal transplantation. 26.3% of patients diagnosed with RCC were within 6 months of transplantation, suggesting that these tumours were present before transplantation. This raises the question of whether patients should receive up to date renal imaging prior to transplantation. In elective live donor cases, imaging is easy to organise. In emergency cadaveric donation this is logistically more complicated. The incidence of RCC in our population is in keeping with historic series and patient outcomes were good despite immunosuppression regimes.

P208

Donor serum and urine proteomic signatures differentiate between immediate and delayed graft function in kidney transplantation

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Introduction: Despite the persistent shortage of donor organs, paradoxically, many organs obtained from older higher risk donors are deemed unsuitable for transplantation and discarded. The ability to assess the quality of donated organs prior to transplantation is vital. We tested the hypothesis that donor serum and urine proteomic signatures can discriminate between immediate and delayed graft kidney function after transplantation.

Method: Serum and urine samples from living donors (LD), brain dead donors (DBD) and donors after circulatory arrest (DCD) were grouped initially according to donor type and subsequently according to the incidence of delayed graft function (DGF), followed by analysis using a label free quantitative (LFQ) proteomic approach. Proteins in donor samples were precipitated digested and analysed using tandem mass spectrometry (LC-MS/MS, LTQ Orbitrap Velos). Data quantified by the "in house" proteomic pipeline (CPFP).

Results: Initially we showed that the proteomic signature of LDs clustered distinctly from deceased donors. Subsequent proteomic analysis of serum samples when grouped according to the incidence of immediate or delayed graft function classified donors on the basis of post transplantation outcomes. Similar discriminatory proteomic signatures were confirmed in donor urine. Uniquely identified and significantly regulated proteins amongst the two groups (DGF vs IF) were shortlisted ($p < 0.05$ ANOVA, at least > 2 fold change) in serum and urine from donors associated with DGF outcomes. Shortlisted proteins indicated a parallel activation of apoptotic, metabolic, inflammatory and cytoprotective pathways. Interrogation of the proteomic signatures revealed that at the point of sample collection, a systemic state of inflammation was more pronounced in DBD than DCD reflecting the pathophysiological changes following brain death.

Conclusion: This is the first study that describes proteomic signatures in donor serum and urine that classifies donors on the basis of post transplantation outcomes in kidney recipients. Data suggests that donor organ quality is affected by an interplay of proteins related to pathways of apoptosis, metabolic, inflammation and cytoprotection.

P209

Resistive index as a marker of renal function and pathology amenable to medical intervention in renal transplant recipients: a single centre experience

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Introduction: There has been little progress in non-invasive evaluation of renal allografts. Serum creatinine level/glomerular filtration rate (GFR) remain the basis of non-invasive assessment. Where there are concerns of decline in the graft function an ultrasound examination of the transplanted kidney is the initial investigation of choice to exclude a surgical cause of dysfunction followed by a transplant biopsy. The renal resistive index (RI) is a non-invasive ultrasound-based method to assess vascular resistance and compliance. Correlation between RI, and renal allografts dysfunction has been suggested while in chronic disease of native kidneys it has been proposed as a determinant of steroid responsiveness.

Aim: To assess whether resistive index can be used as a marker of renal allograft function and pathology responsive to medical intervention

Methods: We retrospectively reviewed the electronic records of 249 serial day case renal transplant biopsies carried out over a 3 year period (2011 to 2014). The transplant recipient, day zero biopsy (post-implantation) results, the resistive index on ultrasound of the allograft and their protocol or for cause biopsy findings were correlated. The RI was recorded from the ultrasound done at 6- 8 weeks post transplant for protocol biopsies (done at 12 weeks) or within 12 weeks of time of biopsy for longer term for cause biopsies.

Results: We assessed 186 patients, 76 of these underwent multiple biopsies, 26 had 2 biopsies, 13 had 3, 8 had 4, 2 had 5 and 1 had 6. The majority of the biopsies were carried out on male recipients 65% (N= 161) vs female 35% (N=88). The ethnic mix was as follows 66% Caucasian, 17% Indo-Asian, 14% Black, 2% Oriental-Asians. The RI was recorded in 79% (N=196) of the correlating ultrasounds. Out of these 49% (N=96) had RI values within the normal range < 0.7 (Group A) while 51% (N=100) had RI values >0.7 (Group B). The day zero biopsies done in B patients showed more acute/higher degree of chronic damage. The number of normal biopsies were greater in A than B. On comparison allograft biopsies from patients in B showed a higher incidence of rejection (Banff 1A or >) (25.29 % vs 6.87%), increased incidence of Calcineurin inhibitor toxicity (9.57% vs 3.44%), increased incidence of recurrent disease (7.44% vs 3%). B grafts also showed more evidence of chronic changes (21.83% vs 1.06%).

Conclusion: A higher RI of ≥ 0.7 is associated with greater severity of baseline changes in transplanted kidney. It is associated with an increased incidence of rejection, recurrence and CNI toxicity. This raises the question "should earlier biopsies be considered in patients with RI ≥ 0.7 ". This is particularly relevant in curtailing progression of acute rejection where it could be managed at an earlier Banff classification. More detailed radiological examination of the allograft in experienced hands could provide a non-invasive means of diagnosing pathology responsive to medical intervention earlier.

P210

Can the need for graft nephrectomy after late renal transplant failure be predicted?

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Introduction: Graft nephrectomy is universally recommended when graft survival is less than 6 months. In case of later graft failure it is not always necessary to remove the graft. Indications for late graft removal include symptoms of graft intolerance (pain, infection, fever, hematuria), the presence of a tumor, or to create space for retransplantation. We aimed to find predictive factors for graft intolerance, which would allow timely identification of patients that might benefit from elective graft nephrectomy.

Methods: We retrospectively collected data of kidney transplantations performed in our centre between 1980 and 2010 that failed at least 6 months after transplantation. We excluded patients if there was a previous graft in situ, when (planned) graft nephrectomy was performed within 3 months after graft failure, or when follow up was less than 3 months. For every patient undergoing graft nephrectomy, we selected a control with a comparable date of graft failure and duration of follow up who did not require graft nephrectomy. With logistic regression we analyzed which patient and graft characteristics were related to the need for late graft nephrectomy. Markers that were univariately associated with graft nephrectomy were considered for a multivariate prediction rule.

Results: 2643 kidney transplantations were performed, of which 716 have failed. In and - exclusion criteria were met in 289 cases. In 73 cases of graft removal (25%), an appropriate control could be selected. Median interval between graft failure and graft removal was 7.7 months (interquartile range: 4.3-11.9). Factors that were associated with graft nephrectomy in multivariate analysis were acute rejection (OR 4.9, p 0.09) or chronic rejection (OR 5.4, p 0.01) as cause of graft failure, prednisone dose at time of graft failure (OR 2.6, p 0.03) and cardiovascular comorbidity (OR 0.3, p 0.009).

Conclusion: In this retrospective analysis, graft failure caused by rejection (acute or chronic), prednisone dose at time of graft failure, and cardiovascular comorbidity were independent predictive factors for graft nephrectomy after late graft failure.

P211

Why do renal transplants fail? – A Welsh perspective

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Background: Maximising long term renal graft survival is a key aspect of transplant care. It is readily known that a return to dialysis adversely affects patient morbidity and mortality. In 2012, we undertook a study to investigate the factors leading to graft loss in a major transplant centre. This highlighted the issue of non compliance as a significant contributory problem which was particularly prevalent in young patients. We have now extended this study over a different time period and have included hospitals throughout Wales.

Method: A retrospective analysis was undertaken looking at contributory factors leading to graft loss over the the 3 year period from January 2011 to December 2013. Data was collected from 4 hospitals.

Results: 103 graft failures were identified over a 3 year period. The prevalent transplant population in the 4 units is 1616. 72% of the failures occurred in men. Within the group, the median age at the time of transplantation was 42 years (+/- 15) and the median age at the time of graft failure was 47 years (+/- 15). Mean graft survival for the cohort was 8.2 years (+/- 7). The majority of the recipients had at least one biopsy to investigate the cause of graft dysfunction and 34% had a biopsy proven episode of rejection. Of these, at least 25% had a history of non compliance. 67% of these patients were the young recipients of living donor grafts. 28% of grafts failed due to 'chronic graft nephropathy' with recurrent IgA nephropathy also featuring prominently. 72% of patients commenced haemodialysis following transplant failure and 36% of patients were re-listed for a further transplant.

Conclusion: This extended study confirms that non compliance and subsequent immunological graft damage is a major cause of renal transplant loss. Young recipients of living donor kidneys are again emerging as a high risk group and our attention should be focusing on strategies to avoid this potentially avoidable cause of graft failure.

P212

How effective is percutaneous transluminal renal angioplasty in the management of transplant renal artery stenosis?

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Introduction: Transplant Renal Artery Stenosis (TRAS) is a recognised complication following kidney transplantation leading to hypertension and graft dysfunction. Although percutaneous transluminal renal angioplasty (PTRA) is an established method of treating TRAS, there is a paucity of data investigating the relationship between efficacy and baseline glomerular filtration rate (GFR).

Methods: A retrospective analysis of 33 patients from our unit who underwent (PTRA) between 2002 and 2014 for TRAS was undertaken. Renal function (creatinine and eGFR) and blood pressure were monitored from six months before and up to one year after the PTRA.

Results: PTRA was performed once in 30 patients and twice in 3 patients. 68% of our patients were male with a mean age of 51 years (range 23-73). 61% were Caucasian and 27% were of Black ethnicity. PTRA was performed on average 1022 days (range 26-7876) after transplantation for deteriorating graft function (mean eGFR 6 months prior to procedure 44 mls/min v 38 mls/min at the time of procedure, $P < 0.01$). eGFR at 6 months improved after PTRA (eGFR 43 mls/min, $P = 0.02$) and this persisted up to 1 year (mean eGFR 44 mls/min, $P = 0.02$). On further analysis, those patients with an eGFR of < 30 mls/min at the time of procedure did not derive benefit at 1 year (mean eGFR 22 mls/min, $P = 0.57$). However no significant difference was detected in rate of change of eGFR before or after PTRA regardless of eGFR at the time of procedure. There was no significant change in blood pressure one year after PTRA (mean blood pressure 133/77) compared to at the time of PTRA (mean blood pressure 134/78, systolic $P = 0.81$, diastolic $P = 0.79$). There were no complications of PTRA recorded.

Discussion: One year after angioplasty, patients in this study had a significant increase in eGFR compared to at the time of angioplasty but there was no significant change in blood pressure. In addition, in our cohort, improvement in eGFR was only detected in those with an eGFR of 30 mls/min or greater suggesting that below this eGFR, PTRA may not be as beneficial.

Category: Renal Transplantation - Waiting List

P213

Trends in repeat kidney transplantation in the UK

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Introduction: As more patients return to ESRD following renal allograft failure, we investigated trends in repeat transplantation rates over time in the UK (table):

Year/transplant number		1 st	2 nd	3 rd	4 th	Total	Repeat transplants as % of total transplants
2008	LD	803	73	8	3	887	9.5%
	DD	1390	143	25	4	1562	11.0%
2009	LD	819	89	24	1	933	12.2%
	DD	1384	136	27	4	1551	10.8%
2010	LD	859	98	10	0	967	11.2%
	DD	1452	157	14	1	1624	10.6%
2011	LD	864	85	13	3	965	10.5%
	DD	1452	170	26	5	1653	12.2%
2012	LD	872	78	16	0	966	9.7%
	DD	1621	161	25	1	1808	10.3%
Total	LD	4217	423	71	7	4718	10.6%
	DD	7299	767	117	15	8198	11.0%

Results: From 2008-12, the percentage of repeat kidney transplants has remained steady at ~11% of the total transplant number. The ratio of deceased (DD) and living donor (LD) repeat transplantation is unchanged, the latter comprising 485/1384 (35%) of repeat transplants. Third and subsequent kidney transplants remain ~1.6% of the transplant total, although absolute numbers are small.

Conclusion: Repeat kidney transplantation represents a small proportion of overall transplant activity in the UK. Despite patients surviving longer and more patients losing graft function, repeat transplantation rates are stable and are not responsible for increased waiting time for DD transplantation.

P214

Simple measures can improve rates of pre-emptive listing for renal transplantation

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Introduction: Pre-emptive renal transplantation positively impacts allograft and patient survival and is considered the gold-standard therapy for patients with end-stage renal disease. A relatively low rate of pre-emptive listing was noted in the region served by our transplant centre. We aimed to show that this could be rectified with the introduction of simple changes in practice.

Methods: Two interventions were introduced in January 2012. Firstly a regional recipient assessment tool was introduced to standardise the work-up process. Secondly recipient co-ordinators undertook regular visits to referring units to expedite listing of potential recipients. Patient data were collected from a regional database. All patients activated on the deceased donor transplant list or who received a pre-emptive living donor transplant were included. Two cohorts were compared: 1) pre-intervention group, listed from 2009-2011 and 2) post-intervention group, listed from July 2012–December 2013. This allowed a 6 month period to assess the impact of the changes in practice.

Results: 378 patients were included in the pre-intervention group, 140 (37%) of whom were listed pre-emptively. 133 patients were included in the post-intervention group, 76 (57%) of whom were listed pre-emptively. The electronic records of patients in both groups who were not listed pre-emptively were reviewed. The commonest reason for not listing pre-emptively was an avoidable delay in commencing work-up. However there was a substantial reduction in the proportion of patients for whom work-up was delayed following the changes in practice (48% pre-intervention vs. 28% post-intervention).

Discussion: The introduction of simple measures such as a regional recipient assessment tool and expedition of recipient work-up by co-ordinators can reduce delays and increase pre-emptive listing rates for renal transplantation.

P215

An audit of practices regarding temporary suspension from the waiting list for deceased donor kidney transplantation

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Introduction: The availability of organs is the most important limiting factor in the provision of kidney transplantation for those with end-stage renal failure. The shortfall between supply and demand for deceased donor kidneys means that it is important to keep all practices in the allocation of organs continually under review, in order to ensure equity of access to all potential recipients. One aspect of maintaining the waiting list is managing the temporary suspension of individuals from the list if they are unavailable or unsuitable for transplant for a period of time. We therefore conducted an audit of practices regarding the suspension of individuals from the deceased donor waiting list.

Methods: We audited all patients (N=287), either active or suspended, on the deceased donor waiting list for kidney transplant at our hospital over a six-month period from June to November 2014. Data were obtained from our hospital's electronic patient records and from the UK transplant network database.

Results: Patient demographics (gender, age, ethnicity, blood group, dialysis status) were comparable between the suspended and active lists. The mean suspension length was 543 days and the longest was 3,057 days. Most suspensions (67%) were on-going at the end of the study period. These were longer on average than terminated suspensions (206 versus 708 days). The most common reasons for suspension were medical issues, living donor in work-up, and travel. The most common medical reasons were cardiac issues, infection and malignancy. We also reviewed in detail all suspensions for travel in this cohort; our data indicate these may continue unnecessarily long after the patient's return. There are striking similarities between our data and published data from the USA.

Discussion: We propose ways in which suspensions, particularly those for travel, may be minimised for the benefit of all patients on the deceased donor waiting list.

P216

Using simple patient variables to “predict” kidney waiting list registration and transplantation

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Introduction: Our previously published prediction model for patients 90 days on renal replacement therapy (RRT), either dialysis or transplantation was able to give an adequate prediction of 10 year survival. The parameters were: age of the patient at the start of RRT, primary renal disease, treatment modality, and sex. Our hypothesis is that RRT patients with the lowest risk scores have best survival probabilities, due to both better health and being transplanted more often. To test this hypothesis we analyzed the relation between patient risk groups and waiting list registration and transplantation rates.

Methods: We analyzed data from 9887 patients aged 18-70 years being on dialysis at 90 days after starting RRT (period 1999-2009) from the Dutch Renal Replacement Registry and Eurotransplant. Based on their survival prediction, we divided 9594 patients into 5 risk groups; 293 patients with missing data were excluded. Differences in waiting list registration, transplantation and waiting times were analyzed with chi square test and ANOVA.

Results: Registration rates on the waiting list were 94% and 90% in the lowest risk groups, 80% in the middle group and 58% and 32% in the highest risk groups ($P < 0.001$). After registration, the number of transplanted patients varied from 92% and 86% in the lowest risk groups till 65% and 55% in the highest risk groups ($p < 0.001$), mainly due to the higher rates of living donor transplants in the lowest risk groups. Death on, and removal from, the waiting list varied from 5% and 2% respectively in the lowest risk group, till 35% and 10% in the highest risk group ($p < 0.001$).

Discussion: The prediction model can be used to “predict” waitlisting and transplantation chances. Patients with high risk scores are less likely to be registered and transplanted.

P217

Exploring variation in the practice patterns of assessing patient suitability for renal transplantation in the United Kingdom

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Background: The Access to Transplant and Transplant Outcome Measures (ATTOM) study is the largest UK transplant study to date exploring equity in access to renal transplantation. In conjunction with ATTOM this national survey aimed to investigate whether centre variation existed in the assessment of patients for deceased donor renal transplantation in the UK.

Methods: Thematic analysis of 43 qualitative interviews with key stakeholders conducted across 9 renal centres in the UK informed the development of an online survey distributed to the Clinical Directors of all UK renal centres. This survey measured differences in centre assessment processes including their evaluation of cardiovascular disease (CVD) and explored local decision making processes.

Results: All 71 renal centres (100%) in the UK responded. Of these, 82.7% reported seeing pre-dialysis patients in a low clearance clinic, 8.6% of which were nurse led. 14 centres had a dedicated transplant assessment clinic whilst 28% did not have a formal assessment protocol. Age was used as an exclusion criterion in 3 centres (max: 75 years). In contrast, 83% of centres excluded patients with a high BMI, median 35 (range 30-40), whilst there was considerable variation in the investigation of CVD. Cardiac investigations were risk-stratified in 90% of centres, with three centres opting for coronary angiography as first line in high risk patients. Surgical involvement in assessing suitability varied across the UK with 11.3% of centres listing patients for transplantation without any formal surgical review. Decisions regarding listing were made using an MDT in 76.1% of centres, whilst 62% did not have any formal protocol in place to re-evaluate listed patients.

Conclusions: There is marked variation in the assessment of patients, delivery of care and decision making processes for listing across the UK. Research is on going to investigate if any unit factors influence listing independently of patient factors in a prospective cohort in ATTOM using a hierarchical statistical model.

P218

Is a tight control of the National Kidney Transplant Waiting List (NKTWL) necessary?

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Introduction: According to NHSBT annual statistics, for the 5th year running the number of patients on the NKTWL list has declined. However, the same report shows that some transplant units confirm an increase in the waiting list, despite increasing the number of renal transplants. In this observational study, we analysed our own performance and compared it to the national trend.

Method: We extracted data from our prospectively maintained database at our local tissue-typing lab. We looked at the number of patients that were activated on the kidney waiting list per financial year from 2009/2010 to 2013/2014. In addition, we obtained figures on the number of new activations nationally from NHSBT.

Results: Our local figures show that despite a high transplant rate our waiting list time is broadly static with a sharp rise in the last financial year.

Year	Total on National Waiting List	Patients suspended	New Activations on National Waiting List per year	Total N. of Renal Transplant in the UK per year
2009/10	7997	2297	3256	2376
2010/11	7800	2529	3103	2388
2011/12	7636	2594	3160	2472
2012/13	7332	2728	3267	2699
2013/14	7026	2874	3436	2929

Historically, there was a steady decrease in the number of patients on our local waiting list despite a constant incidence of patients requiring RRT. However, in the last few years we have increased our local waiting list to it's highest ever level (n=390); of them 190 new activations in last financial year with the highest number of renal transplants performed (n=149).

Conclusions: These figures demonstrate that the number of patients added to the national waiting list is constantly increasing. This is in keeping with what we have observed locally. We believe this is due to an improved activation pathway and more aggressive policy of placing new starters on the waiting list at our unit. The apparent success in reducing the national waiting list should be treated with caution and may not be accounted for by just a rise in number of kidney transplants. Also, the number of pre-emptive transplants should be taken into consideration. In our opinion it is time to consider a national permanent audit on patients awaiting transplantation at each unit in order to support national data analysis.

P219 - WITHDRAWN

Category: Renal Transplantation - Complications

P220

Cardiovascular changes during and following kidney transplantation: an observational pilot study

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Background: Delayed graft function (DGF) is associated with adverse outcomes following renal transplantation (RTx). Recipient perioperative haemodynamic status is a key modifiable risk factor in the development of DGF. The aim of this study was to investigate the perioperative haemodynamic changes in RTx.

Methodology: A prospective observational cohort study of 20 patients undergoing cadaveric RTx was performed. Cardiovascular parameters (mean arterial blood pressure (MABP), cardiac index (CI), stroke volume index (SVI), total body water (TBW), systemic vascular resistance index (SVRI) and oxygen delivery (DO₂I)) were measured intra-operatively and for the first 24 hours post-operatively using thoracic bioimpedance technique (NICCOMO™, Medis GmbH, Germany) and pulse contour analysis (Nexfin™, BMEYE, Netherlands). Mixed venous blood gases, serum BNP and N-GAL (CardioRenal Panel, Alere, USA) were monitored in addition to routine haematological and biochemical parameters.

Results: Mean recipient age was 46.7±12.7 years; mean donor age was 57.7±13.2 years. 55% of donors were extended criteria. 40% of patients had DGF. There were no early graft losses. One patient died post-operative day 12. Mean values at time of reperfusion were as follows: MABP: 55.2±13.4mmHg, CI: 3.1±1.2L/min/m², SVI: 42.5ml/m², SVRI: 1878±367dyn/sec/cm⁻⁵/m². Mean ΔCI at time of reperfusion was -0.35±0.28 L/min/m². Absolute ΔCI at time of reperfusion was not associated with DGF. However all 4 patients with ΔCI >-0.5 L/min/m² had DGF. Mean SvO₂ was 65.3±8.7% at reperfusion and 69.8±6.7% immediately post-operatively.

Conclusions: Non-invasive cardiac output monitoring provides valuable information regarding perioperative fluid status and haemodynamic parameters in patients undergoing RTx. It is more accurate than existing strategies of CVP monitoring and avoids damaging vessels for future vascular access as is the case with invasive monitoring.

P221

Obesity and renal transplantation

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Background: Morbid obesity is generally considered a relative contraindication to renal transplantation. Locally, we have adopted an inclusive approach to renal transplantation. We aim to describe our outcomes with reference to BMI.

Methodology: A retrospective analysis of all renal transplants performed at in our institution over a 10-year period was performed (n=1005). Data were collected on graft and patient outcomes, peri- and post-operative complications and weight change in the year following transplantation. The association between these factors and BMI at time of transplantation was assessed.

Results: Mean recipient BMI at time of transplantation was 25.9±4.8kg/m². 15.5% (n=100) had BMI 30-34.9kg/m² and 4.3% (n=28) had BMI ≥35kg/m². There was no significant change in mean BMI year-on-year between 2003 and 2013 however the numbers of patients with morbid obesity (BMI ≥35kg/m²) has increased. Mean weight gain in the first year post-transplantation was 3.5±1.4kg. Patients with BMI <20 demonstrated the greatest weight gain (p<0.001). BMI had no significant impact on 1-year graft or patient survival. Patients with BMI <20kg/m² had a significantly higher eGFR than patients with BMI ≥20kg/m² at 90, 180 and 365 days (p=0.001). There was no significant relationship between BMI and eGFR at higher BMI. Wound complications (and more severe wound complications [Clavien Dindo classification]) were more likely in patients with higher BMI (p<0.001). Patients with higher BMI also spent significantly longer in hospital post-transplantation (p=0.02). There was no association between BMI and the development of NODAT.

Conclusions: These results indicate that renal transplantation in the obese and morbidly obese is safe with comparable 1-year graft and patient outcomes to the general population. Based on this evidence, patients with high BMI should not be excluded from transplantation. High rates of wound complications and longer length of hospital stay may have implications for resource allocation in transplantation of the obese patient.

P222

South Asians have a higher risk of post-transplantation diabetes mellitus (PTDM) and death after renal transplantation

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Introduction: South Asians (SA) have a higher risk for cardiovascular disease and diabetes than the general population, but in renal transplant recipients, data are limited and controversial. The purpose of our study was to investigate the impact of SA ethnicity on PTDM incidence and patient survival following renal transplantation.

Methods: In this retrospective single centre study, the largest of its kind, we report the outcomes of 1184 patients (733 males, 451 females), mean age 48.3 ± 13.1 years, range 18-78, mean follow up 56.6 ± 30 months), receiving a steroid sparing, tacrolimus based regime after monoclonal antibody induction. Steroids were stopped 7 days post - transplantation and only introduced to treat rejection.

Results: 591 patients were Caucasians (49.9%), 330 patients were of SA ethnicity (27.9%) and 143 were Afro-Caribbeans (12.1%). There was no difference regarding gender among the ethnicities ($p=0.701$), but SA patients were less unlikely to undergo pre-emptive kidney transplantation ($p<0.001$) and to receive a kidney from a live donor ($p<0.001$). In addition, they were older at transplantation ($p=0.001$). SA patients were more likely to be diabetic before transplantation ($p<0.001$) and to develop PTDM ($p<0.001$). There were more deaths in the SA group, but this did not reach significance ($p=0.059$) in univariate analysis.

In survival analysis, there was a trend for increased mortality for SA patients (log rank $p=0.059$). SA ethnicity increased the risk of PTDM (log rank $p<0.001$). In Cox-regression analysis, older age at transplantation ($p=0.025$), months on dialysis ($p=0.028$), SA ethnicity (0.037) and pre-transplantation diabetes ($p=0.003$) increased significantly the risk of death. Similarly, older age at transplantation ($p<0.001$), steroid use ($p<0.001$), SA ethnicity ($p<0.001$) and Afro-Caribbean ethnicity ($p=0.004$) increased the risk for PTDM.

Discussion: SA ethnicity is an independent risk factor for PTDM and death. This group of patients merits additional study and focus to reduce these risks.

P223

A single-centre experience of biopsy proven recurrent and *de novo* immunoglobulin A nephropathy in transplant recipients

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Introduction: IgA nephropathy (IgAN) frequently recurs following renal transplantation, but the risk factors for severe disease are poorly understood.

Methods: Recipients found to have biopsy-proven IgA nephropathy of their renal transplants were identified for a five year period via an electronic histopathology database. They were analysed according to whether their graft function stabilised (FU) or progressively declined with return to dialysis (FA), to identify factors predictive of poor outcome. All patients were maintained on baseline immunosuppression with tacrolimus and a mycophenolic acid derivative, 9 were also taking prednisolone.

Results: Twenty two patients (all Causasian; 15 male; age 49 ± 15 years) were identified with transplant IgAN.

Table 1: Features of transplant IgAN according to outcome

	LD: DD	Time from transplant to biopsy (years)	BP (mmHg)	Cr at biopsy (□mol/l)	P:CR at biopsy (mg/ mmol)	On steroids at biopsy (%)	Biopsy features*	With additional cellular rejection (%)	Number on RAS blockade after biopsy	Time from biopsy to follow up or failure (years)
FU (N=12) 8M;4F Age: 50 ± 15 years 2 re-grafts	4:8	5.4 ± 3	SYS: 146 ±18 DIAS: 79 ±10	197±112	305±217	50%	GS: 16% IF: 75%	33%	4	2.5 ± 2.3
FA (N=10) 7M; 3F Age: 47 ± 13 years 3 re-grafts	6:4	4.8 ± 4.8	SYS: 138 ±16 DIAS: 77 ±10	212±77	295±253	30%	GS: 12% IF: 70%	20%	6	2.2 ± 2.5

Unless stated, data are mean ± s.d. Abbreviations: LD, live donor; DD, deceased donor; BP, blood pressure; Cr, creatinine; P:CR, protein:creatinine ratio; GS, glomerulosclerosis; IF, interstitial fibrosis; RAS, Renin Angiotensin System. * GS was stated as mean % GS on biopsy; IF was defined as % of biopsies where IF was present, regardless of severity. Four patients with crescentic IgAN received pulsed cyclophosphamide, three of whom had initial stabilisation of renal function. There were no significant differences in characteristics between those whose grafts continued to function and those that failed.

Conclusion: Transplant IgAN is a serious condition - almost half of our patients experienced graft failure within two years of diagnosis. Our Unit now plan to compare this cohort with patients without recurrent disease to identify risk factors.

P224

The effect of lifestyle management on obesity and metabolic risk after kidney transplantation: a pragmatic randomised controlled trial

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Introduction: Post-transplant weight gain is a common and worrisome problem. Use of corticosteroids, adverse dietary habits and low physical activity can contribute to muscle atrophy and accumulation of fat. These unfavorable changes in body composition are associated with increased cardiovascular risk and graft failure. We aimed to combat the occurrence of post-transplant weight gain by setting up an intervention study, Active Care after Transplantation (ACT). ACT is a randomized-controlled, pragmatic, lifestyle intervention that evaluates the effects of an exercise and nutritional intervention on quality of life and the development of obesity and metabolic risk in the first year after renal transplantation.

Methods: From three hospitals in the Netherlands, we will include 219 renal transplant recipients (RTR) with a recent kidney transplantation (<1year ago). RTR will be randomized over three groups: standard care, exercise program and combined diet-and exercise program. The exercise intervention will consist of 3 months exercise rehabilitation followed by 12 months of lifestyle counselling. The combined intervention will consist of the exercise program supplemented with 15-month nutritional intervention. The lifestyle counseling is based on the theory of behavioural change. Motivational interviewing will be used to improve self-management skills of the participants. Primary outcomes will be quality of life and post-transplant fat-mass. Secondary outcomes will include nutritional intake, physical activity, aerobic capacity (VO₂max), cardiometabolic risk factors (including blood pressure, lipid profile, glucose homeostasis, waist circumference) and barriers and success factors for intervention. Health economic modelling will be applied to estimate potential cost-effectiveness of the intervention. Information on medication, hospital admissions and disease complications will be extracted from patient files.

Discussion: ACT will provide formal evidence for the role of lifestyle management in post transplant risk management to achieve improvement in long-term graft and patient survival.

P225

Recurrent IgA nephropathy in kidney transplant recipients receiving a steroid sparing immunosuppression protocol

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Background: Steroid sparing immunosuppression is increasingly used in order to avoid the many well-known side effects of steroids. It has been argued that steroid use is strongly associated with a reduced risk of IgA Nephropathy (IGAN) recurrence post transplantation. In this study we investigate the incidence of recurrent IgA Nephropathy (IGAN) and its effect on outcomes in kidney transplant recipients receiving a steroid sparing immunosuppressive regime.

Methods: We retrospectively reviewed the medical records of 135 (102 male, mean age 44,1 +/-11,7 years) kidney transplant recipients with biopsy proven IGAN as their primary diagnosis, transplanted in our centre between September 2002 and August 2013. All the patients received a steroid sparing immunosuppressive regime (7day course) with Alemtuzumab induction and tacrolimus monotherapy or IL2 induction with Tacrolimus and MMF. Steroids and MMF were only introduced to treat rejection. The diagnosis of recurrent IGAN was based on case and/or protocol renal biopsies.

Results: 53 (39.3%) (41 male, mean age 44,7 +/-11,3 years) out of 135 patients developed biopsy proven recurrent IGAN. Mean follow up was similar between the patients with 56,9 (+34.6) and without recurrence 51,6(+32.2) months (p=0.36). There were no significant differences in recipient age, gender, ethnicity, induction and type of transplant between the two groups, except for older donor age in the recurrent IGAN cohort.(44,+15 vs 49,9+11,8 years, p=0,002) Mean time from transplantation to recurrence was 20.4 (+20.2) months). A multivariate Cox regression model, adjusted for donor and recipient sex, age, recipient race and gender, type of transplant (live/deceased donor, ABOi), and induction immunosuppressant medications, revealed older donor age (HR:1.03, p=0,006) and retransplantation as significant risk factors for recurrence. (HR: 1.01, p=0,035) During the follow up period, 11 grafts were lost. Recurrence of IGAN did not have an effect on graft survival on multivariate analysis. (p=0.11)

Conclusion: Recurrent IGAN in patients receiving a steroid sparing immunosuppression protocol appears to have an incidence within the range reported in the literature. In this medium term data series, recurrent IGAN does not appear to affect graft outcomes.

P226

New onset diabetes after transplantation - is it a big deal? Risk factors and impact after kidney transplantation: a single centre experience

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Introduction: New Onset Diabetes after Transplantation (NODAT) has been recognised to effect graft and patient survival following renal transplantation. But there's lack of evidence in its effect on ethnic minority; in particular transplant patients from Indian sub-continent (ISC). We have reviewed our experience to address this issue. We focused on the incidence, risk of cardiovascular consequences of NODAT and its effect on graft and patient survival.

Method: The data was collected from a prospectively collated database from a single centre between April 2007 to February 2013. The data collected donor variables- age, sex, type of donor, co-morbidities, cold ischemia time and recipient variables- age, sex, ethnicity, BMI, cause of renal failure, type of dialysis, immunosuppressive medications, CMV mismatch, graft and patient survival. A univariate and multivariate analysis were performed using SPSS.

Results: A total of 639 patients were included in this population, 294 (46.1%) Caucasians and 345 (53.9 %) non-Caucasians with a mean age at transplant of 45.6 ± 12.3 . During a mean follow-up of 4.55 years, 62 (9.7%) of the patients had NODAT, 16 (25.8%) were Caucasian and 43 (69.4%) were non-Caucasian.

The significant risk factors are recipient age, from Indian sub-continent, deceased donors and recipient body mass index and no significant difference was found in Co-variables - Rejection, CMV mismatch, BK viraemia, immunosuppressive agents, and delayed graft function. There was no difference in the graft and patient survival. 1 patient (1.6%) with NODAT died from a cardio-vascular event.

Conclusion: Increased incidence of NODAT was found in the renal transplant patients from ISC and despite published evidences; there is no significant effect on the graft and patient survival following transplantation. However, further research is needed.

P227

Absence of low-grade proteinuria is associated with improved outcomes in patients with worse 3 month graft function in renal transplantation

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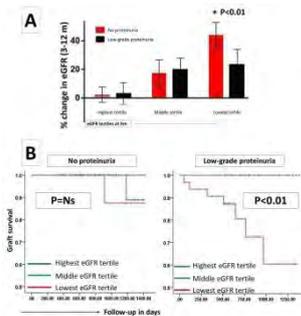
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Introduction: Low-grade proteinuria has been shown to be associated with adverse outcomes after renal transplantation. However most patients with proteinuria have worse eGFR and this interaction may potentially contribute to the adverse outcomes noted so far. In this study, we have analyzed low-grade proteinuria at 3 months post-transplantation with emphasis on early renal function.

164 patients who were transplanted between 2011-13 were included in the analysis. Low-grade proteinuria was defined as urinary protein creatinine ratio >25 (250mg/day). Patients were also divided into tertiles based on their eGFR at 3 months. Percentage change in eGFR was calculated between 3 and 12 months for the tertiles of GFR stratified by the presence of proteinuria. Also graft survival was analysed over a mean follow-up of 800 days.

Results: Of the 164 patients included in the analysis, 65 had early low-grade proteinuria. These patients had significantly worse overall graft survival (hazard ratio 8.303, 95% CI 1.356 to 37.27, $p = 0.02$). When patients with and without proteinuria were stratified into tertiles by their eGFR at 3 months, absence of proteinuria was associated with a significant improvement in eGFR from 3-12 months post-transplantation in those within the lowest eGFR tertile group (worse renal function) when compared to patients with proteinuria (Fig-1A). In addition, when graft survival was examined within the eGFR tertiles, low 3 month eGFR (lowest tertile group) was associated with significantly worse graft survival only in patients with low-grade proteinuria (Fig-1B).

Conclusion: In conclusion, low-grade proteinuria risk stratifies patients with early renal dysfunction. Importantly absence of proteinuria is associated with a significant improvement in eGFR by 12 months post-transplant a finding which may potentially explain the improved graft survival noted in this group of patients despite early poor renal function.



Category: Renal Transplantation - Outcomes 2

P228

Making every kidney count – accelerating renal transplantation research

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Introduction: On average, patients wait for a kidney transplant for 1,000 days and one person dies every day while waiting for a transplant they can't get. The session will describe our progress in facilitating a step change in renal transplantation research, through a discrete fundraising appeal and open call.

Methods: In 2012, the organisation conceived an appeal to raise £3million for research into renal transplantation. The ambition was to fund several larger programme grants (£750,000) which collectively would accelerate knowledge across a number of research areas - tackling rejection of transplanted kidneys, making transplanted kidneys last longer and making more kidneys available for transplantation. Preference would be given to inter-institutional applications and co-partnering with other funding bodies and/or industry. An initial call was made for expressions of interest, to which there were 33 responses, followed by the formal application process, under the organisation's well established and robust governance.

Results: The organisation recruited senior and influential figures to form a development board and produced fundraising collateral to engage major supporters in the issue. Fundraising commenced and in 2014 we were able to release the first £750,000 to proceed to the first open call. 14 submissions were received and following peer review, the first programme grant was awarded which will be announced before the end of 2014. The aims of this first programme will be explored in the presentation.

Discussion: This is an ambitious plan to accelerate research in renal transplantation with the potential to deliver early patient benefit. It has engaged the organisation's supporters to enable the delivery of a series of programme grants which encourages inter-institutional and industry collaboration. With the first programme grant selected, the potential already exists to raise further funding to award the next programme grant. Latest developments will be explored at the conference.

Where does it end? Outcome of the rejected kidney offers for potential renal transplant and their outcome: a single centre experience

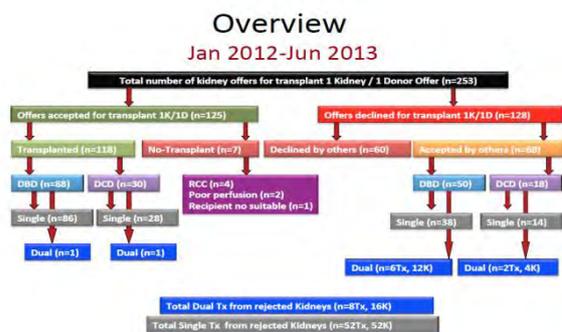
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Background: Worldwide there are no uniformly acceptable deceased donor selection criteria for renal transplantation. There are national and international guidelines available based on which most of the units make their own locally agreed policies depending on their recourses and expertise.

Materials and methods: In this present study we have reflected on our deceased donor selection criteria for organ transplantation by looking into the offers that we have rejected for renal transplantation but got accepted by other centres during Jan 2013 to June 2013. We recorded donor demographics, retrieval information, and reasons for decline by our centre. We then recorded outcome of those kidneys after transplant from other centres.

Results: During this 18 months period we declined 68 donors offers for potential renal transplant. They included 18 Donation after Cardiac Death (DCD) and 50 Donation after Brain Death (DBD) offers. Out of 18 DCD rejected kidneys 72% were working at 1 year after transplant at other centre. From 78 DBD offers 86% were working at 1 year. Combination of age more than 60 with hypertension accounted for 26% (N=18) rejected offers, addition of diabetes to above combination accounted for 12% (N=8). 20% (N=14, DCD=4, DBD=10) donors were above 70 years of age. A total of 8 dual kidney transplants were performed 2 from DCD pairs and 6 from DBD pairs. 6 pairs were from donors above 70 years.



Conclusions: Learning from these outcomes and with availability of resources we have successfully developed a dual kidney program in addition to further relaxing our criteria for expanding criteria donor.

P230

The spectrum of renal allograft failure

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Introduction: Reducing “late” kidney transplant failure is become a major challenge in kidney transplantation, with a prevailing view that antibody mediated rejection is the major cause of late graft loss. But previous studies are limited as they are either selected for stably functioning grafts which then experience dramatic deterioration in renal function (often non-adherence) or limited follow-up.

Methods: We evaluated the clinical, histological and immunological data in all, nonselected transplant failures occurring between 2008 and 2014 in patients under the long-term care of a single transplant centre, thus allowing detailed analysis of DSAs and evaluating histological findings using the latest BANFF criteria with from time to graft failure spanning to beyond 15 years. Of note, histological characteristics were only considered diagnostic when obtained “proximal” to graft failure (i.e. distant biopsy lesions were not classified as “causal”)

Results: In total, 171 patients experienced graft failure (return to dialysis or retransplantation). Early failures were exclusively due to primary non function (n=33). Later, aetiologies became more heterogenous; ABMR was a major contributor at all timepoints (n=27) and was associated with nonadherence in approximately 50% of patients, particularly when active lesions were evident. C1q-binding DSA was seen in 30% and was associated with a shorter time to graft failure; But IFTA in the absence of inflammation or infection was also common, particularly in graft failing beyond 5 years, and was the commonest classification of failure beyond 10 years. A proportion was associated with low grade infiltrates (not meeting criteria for rejection) on the background of late rejection and nonadherence. But the majority either showed no inflammation or inflammation restricted to scarred areas, which was not associated with such prior occurrences.

Conclusion: This study affirms the importance of ABMR as a cause of late graft loss, refining the immuno-clinico-pathological. It also highlights that for cases of true “late” graft failure, progressive IFTA in the absence of an alloimmune process represents an important pathway to graft loss, and target for intervention.

P231

Obstetric and long-term pregnancy outcomes in renal transplant recipients: a 40 year single-centre study

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Introduction: Fertility rapidly returns to women after successful kidney transplantation. The aim of this study was to analyse obstetric and kidney outcomes among all renal transplant recipients in our centre who have had pregnancy.

Methods: All female renal transplant recipients who had a pregnancy were identified through our prospectively maintained electronic patient record and case notes between January 1, 1973 and February 28, 2013. We retrospectively analyzed 40 years of outcomes from 138 pregnancies reported from 89 renal transplant recipients. A nested case controlled study was also performed by identifying 83 pairs of pregnant and non-pregnant controls matched for age, sex, transplant period and transplant function. Patient and graft outcomes were analysed from the time of delivery.

Results: Mean ages at the time of transplantation and pregnancy were 25.2 years and 30.3 years respectively. Median duration of follow up from the first pregnancy was 8.2 years (interquartile range: 3.8, 16.9). There were live births in 74% of pregnancies with high prevalence of prematurity (61%), preeclampsia and low birth weight. The only significant predictors of the composite adverse obstetric outcome (1st or 2nd trimester loss [n=34], stillbirth [n=2], neonatal death [n=2], very preterm birth [<32 weeks] [n=6] or significant congenital anomaly [n=3]) by univariate analysis were reduced eGFR (per mL/min) and increased urine protein:creatinine ratio (per 100mg/mmol) at the time of conception (odds ratio [OR] 0.98; p=0.05 and OR 1.86; p=0.02 respectively). There was no significant association between age, time since transplant, primary renal diagnosis, decade of transplant, living donor transplant or calcineurin inhibitor (CNI) use and obstetric outcome. Reduced eGFR (OR 0.98; p=0.04), increased urine protein: creatinine ratio (OR 1.50; p=0.04) and living donor transplant (OR 0.35; p=0.02) were the only significant predictors of $\geq 20\%$ loss of eGFR 1 year after delivery by univariate analysis. There were no significant independent predictors for either obstetric or renal outcomes by multivariate analysis. In the nested controlled study there was no significant difference in eGFR at 6, 12, 60 and 120 months after study entry in pregnant women and non-pregnant controls; mean eGFR fell from 53.9mL/min to 24.9mL/min over the 10 years in pregnant women compared to 53.6mL/min to 30.6mL/min in non-pregnant controls. There was no significant difference in patient survival, overall graft survival or graft survival censored for death with function by Kaplan Meier analysis.

Conclusion: This analysis provides reassuring information about the long-term effects of pregnancy on kidney transplant function. In addition, it confirms previous information about the relatively high rates of obstetric complications in renal transplant recipients and emphasises the influence of transplant function and proteinuria on the obstetric risks.

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Patient and graft outcomes following 3rd, 4th and 5th renal transplants – a single centre comparative study

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Introduction: For patients who have lost their first renal graft, a second kidney transplant is widely accepted as the next best therapeutic option (due to similar graft survival rates). This study investigates patient and graft outcomes following 3rd, 4th and 5th renal transplants.

Methods: We reviewed all transplants performed between 2000 and 2014 at our Unit. 1st and 2nd transplants (Group 1) were grouped together and compared with 3rd, 4th and 5th transplants (Group 2).

Results: There were 2951 renal transplants during the study period. 2895 were 1st and 2nd transplants (median age 44, IQR 21) and 56 (1.9%) were 3rd, 4th and 5th transplants (median age 43, IQR 17.75). 1150 (39.7%) recipients in Group 1 were female versus 28 (50%) in Group 2. Also 1379 (47.6%) donors in Group 1 were DBD, 427(14.7%) DCD and the rest from living donors. There were 27 (48.2%) DBD, 2 (3.6%) DCD and 27 (48.2%) living donors in Group 2. The 1-, 3-, 5- and 10 year patient survival for Group 1 was 97.5, 95.7, 93.8 and 89.3% where as the graft survival for the same period was 94.7, 90.8, 83.3 and 32.3%. The 1-, 3-, 5- and 10 year patient survival for Group 2 was 96.3% 94.1% 94.1% and 87.4% where as the graft survival for the same period was 82.6% 80.2% 76.7% and 57.8% (p-values=0.811 and 0.854 respectively). In 43 cases out of 49 (87.8%) where the information was available, at least one of the previous grafts was removed at some point. Moreover, in 21 out of 45 cases (46.7%), the common iliac artery was used for the new arterial anastomosis. In 8 out of 47 cases (17.0%) the new transplant was performed intraperitoneally.

Conclusions: Despite the surgical challenges associated with re-transplantation, performing a 3rd, 4th or 5th kidney transplant is feasible with comparable results in terms of short and long term patient and graft survival compared to patients who had their 1st and 2nd transplant.

P233

Health related quality of life in kidney transplant recipients – does the type of donor matter?

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Introduction: There has been an increase in the proportion of donation after cardiac death (DCD) kidneys, along with an increase in donor and recipient age in recent years. How these factors affect the health-related quality of life (HR-QOL) of kidney transplant recipients is not clearly known.

Methods: This is a pilot cross-sectional study of HR-QOL in kidney transplant recipients using scores from SF-36 questionnaires. All recipients transplanted between April 2013 and March 2014 who were still under follow-up in our unit were invited to fill in the questionnaires during clinic visits. Questionnaires were completed between 14 and 16 months from transplantation. The type of transplant [DCD, donor after brain-stem death (DBD), living donor (LD)] and demographics were recorded. Multiple linear regression (MLR) was used to identify factors affecting SF-36 scores.

Results: The response rate was 68% (54/80), of which 14 were DBD, 15 DCD and 25 LD recipients. LD recipients were younger than the other two groups (mean years 45, DBD 51, DCD 60, $p=0.01$). Both physical (41 ± 11 , 40 ± 13 , 47 ± 10 , $p=0.08$) and mental composite scores (43 ± 10 , 50 ± 8 , 47 ± 10 , $p=0.25$) were similar in the 3 groups- DBD, DCD and LD respectively. On MLR analysis, the number of post-operative days as an inpatient was associated with the physical score ($B = -0.49$, $p=0.02$), and the 1-year eGFR was associated with the mental score ($B= 0.17$, $p=0.04$). Patient age, gender, number of hospital admissions, type of transplant and 1-year haemoglobin level were not associated with SF-36 scores or composites. Scores reported by recipients 16-60 years old were lower in all physical and mental dimensions in comparison to general population age-matched peers. On the other hand, recipients >60 years old reported scores that were similar to age-matched peers.

Conclusion: Self-reported HR-QOL was similar amongst DBD, DCD and LD kidney recipients, providing further evidence of equivalent outcomes between DBD and DCD transplants. Older recipients' reported HR-QOL was similar to that reported by their general population peers. A prospective study would help to delineate further the effect of age, waiting time and the various types of transplants on HR-QOL.

P234

Cognition in kidney transplant recipients: a systematic review and meta-analysis

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Introduction: We aimed to summarise how kidney transplantation affects cognition.

Methods: We searched databases (November 2014) for studies measuring cognition in kidney recipients, extracted study quality and cognitive test scores, and synthesized results using random effects, expressed as standardized mean differences (SMD) with 95% confidence intervals (CI).

Results: 7 studies (847 participants) compared recipients' cognition to other people and 7 (149 participants) compared change in cognition within people from before to after transplant. 58 different tests were used 1m-7yr after transplant. Study quality was poor, particularly cross-sectional studies which did not adjust for potential confounders. Recipients had better cognition than people with end-stage kidney disease (ESKD, 3 studies, 337 participants, SMD-0.43, CI-0.56 to -0.30), specifically orientation (3 studies, 337 participants, SMD-0.41, CI-0.55 to -0.27), memory (2 studies, 304 participants, SMD-0.66, CI-0.92 to -0.40) and motor skills (2 studies, 304 participants, SMD-0.50, CI-0.89 to -0.11). Compared to healthy people, recipients had worse cognition (6 studies, 320 participants, SMD+0.36, CI+0.19 to +0.53), specifically orientation (6 studies, 320 participants, SMD+0.40, CI+0.20 to +0.59) and reasoning skills (2 studies, 94 participants, SMD+0.61, CI+0.19 to +1.04). Comparing changes within people, cognition improved from before to after transplant (7 studies, 149 participants, SMD-0.49, CI-0.62 to -0.37), particularly orientation (7 studies, 149 participants, SMD-0.50, CI-0.71 to -0.30), perception (1 study, 21 participants, SMD-0.49, CI-0.71 to -0.28), memory (4 studies, 111 participants, SMD-0.58, CI-0.79 to -0.37) and reasoning skills (2 studies, 41 participants, SMD-0.37, CI-0.54 to -0.20).

Discussion: Cognition improves after transplant but recipients still have specific cognitive deficits compared to healthy people. Transplant education, medication and lifestyle management interventions should be delivered appropriately to help recipients participate in shared clinical decision-making.

P235

Fatigue, anxiety and depression in kidney transplant recipients, haemodialysis patients, lymphoma patients and healthy controls

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Introduction: Fatigue, anxiety and depression are common symptoms in patients on haemodialysis (HD) and result in a lower quality of life. It is not known how these symptoms change after transplantation and how they compare to other patient groups and healthy controls.

Methods: We conducted a cross-sectional cohort study in 140 patients: HD patients, patients one year after kidney transplantation, lymphoma patients receiving chemotherapy, lymphoma patients in remission for one year and healthy controls. All participants completed the RAND-36 quality of life survey, the Checklist for Individual Strength (CIS) fatigue questionnaire and the Hospital Anxiety and Depression Scale (HADS).

Results: 53% of HD patients and 50% of patients on chemotherapy were severely fatigued, compared to 33,3% of transplanted patients, 23% of lymphoma patients in remission and 20% of healthy controls ($p=0,011$). HD patients and patients on chemotherapy were more likely to have a depressive disorder (23,3% and 20% vs. 13,8% of transplanted patients and 13,3% of lymphoma patients in remission, $p=0,032$). HD patients are probably also at higher risk for anxiety disorder (23,3% vs. 13,8%/15%/16,7% of transplanted patients/patients on chemotherapy/patients in remission, $p=0,087$). Both anxiety and depression were less common in healthy controls (3,3% and 0%, $p=0,051$ and $0,014$). Transplanted patients reported the largest health gains of all groups ($p=0,00$), but still had a lower overall quality of life than healthy controls (average score 51,2% vs. 72,5%, $p=0,00$).

Discussion: Fatigue, depression and anxiety are very common in HD patients, resulting in a lower quality of life, comparable to lymphoma patients on chemotherapy. Transplanted patients do better, with scores similar to lymphoma patients in remission, but still have a lower quality of life than healthy controls.

Category: Renal Transplant Surgery - Vascular

P236

Kidney retransplantation in the ipsilateral iliac fossa: a surgical challenge

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Introduction: The aim of this study is to review the surgical outcome of kidney retransplantation in the ipsilateral iliac fossa in comparison to first kidney transplants by performing a case-controlled study.

Methods: Our hospital database was screened for retransplantations between 1995-2013. Each patient that underwent a kidney retransplantation in the ipsilateral iliac fossa was matched with 3 patients with a first kidney transplantation. Matching was based on recipient gender and age, year of transplantation and type of donor (deceased vs. living). Demographic characteristics, surgical outcome, surgical re-interventions and long-term graft survival were compared. Follow-up was until July 2014 for all cases and controls.

Results: We identified 99 patients that received a retransplantation in the ipsilateral iliac fossa. There was significantly more blood loss and longer operating time in the retransplantation group. The number of urological complications did not differ significantly. However, the number of vascular complications, like thrombosis or venous laceration, was higher in the study group, respectively 8% vs 2%. Surgical re-interventions due to bleeding, to solve urological complications or otherwise did not differ significantly between the study and the control group. The number of graft nephrectomies within 1 year was significantly higher in the study group: 16 patients (16%) vs. 14 patients (5%) with a first transplant. The Kaplan-Meier graft survival curve shows that the majority of graft failures in the study group were within the first month after transplantation and due to cellular rejection or thrombotic events. After one year, graft survival curves were almost parallel. The graft survival rates at 1 year and 3, 5 and 10 years were 76%, 67%, 61% and 47% in the study group vs. 94%, 88%, 77% and 67% in the control group.

Discussion: Kidney retransplantation in the ipsilateral iliac fossa is surgically challenging and associated with more vascular complications and graft loss within the first year after transplantation. Patients should be informed about these complications and the higher surgical risk during informed consent.

P237

Anatomical variations in living kidney donors: the importance of radiological assessment in renal transplant planning

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Introduction: Pre-operative radiological assessment is an essential part of surgical transplant planning. Joint guidelines from the British Transplantation Society (BTS) and Renal Association provide clear detailed recommendations for this radiological workup in healthy kidney donors. The objectives of this study were to assess local compliance with these imaging guidelines, and highlight the prevalence of anatomical variants in living donors of relevance for operative success.

Method: Pre-operative imaging of 111 living kidney donors (70 female, 41 male, mean age of 53.8 years) that had open/laparoscopic nephrectomy were reviewed retrospectively against the BTS guidelines. Incidental anomalies in renal anatomy were also recorded.

Results: All 111 donors were compliant with BTS guidelines for pre-operative radiological assessment, which included ultrasound, radionuclide investigations and CT. 77% (85/111) of donors showed anatomical variants that were important for pre-operative planning. Most of these donors (64%, 71/111) had renal vasculature anomalies. Other variations included cystic kidneys, calculi, bifid renal pelvis, duplex collecting systems, and aberrant kidney locations (pelvic kidney).

Conclusion: The high frequency of anatomical variability in our cohort of healthy kidney donor population underscores the importance of thorough radiological assessment prior to transplant. In our centre, complete compliance with the BTS guidelines allowed identification of relevant anatomical variants prior to successful transplantation.

P238

Night time renal transplant surgery is associated with less technical failures

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Background: To minimize cold ischemia time, renal transplantations from deceased donors are regularly performed during the night. However, sleep deprivation of those who perform the transplantation may have adverse effects on cognitive and psychomotor performance and may cause reduced cognitive flexibility. We hypothesize that renal transplantations performed during the night are associated with an increased incidence of technical failure.

Methods: A retrospective survey of the Dutch Organ Transplant Registry concerning all transplants from deceased donors between 2001 and 2013 was performed. Night time surgery was defined as the start of the procedure between 8 PM and 8 AM. The primary outcome measure was technical failure, defined as graft failure within 10 days after surgery without signs of (hyper) acute rejection.

Results: 4.519 renal transplantations in adult recipients were performed, of which 1.480 renal transplantations during the night. The incidence of technical failure was 1.0% for procedures started during the night *versus* 2.6% for daytime surgery ($p=.001$). In a multivariable model, correcting for relevant donor, recipient and graft factors, daytime surgery was an independent predictor of technical failure ($p<.001$).

Conclusion: When renal transplantations are performed during the night, the incidence of technical failure is significantly lower. Further research is required to explore factors that may positively influence the performance of the surgical team during the night.

P239

Is the reluctance for the implantation of right donor kidneys from living donors justified?

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Introduction: The general opinion is that the implantation of renal allografts with shorter renal veins is technically more challenging and therefore prone for technique related vascular complications. Therefore, many surgeons prefer left kidneys for transplantation because of longer renal veins. For living donor kidneys, most centers prefer the selection of left kidneys. We hypothesize that the implantation of right kidneys from living and deceased donors is associated with more technical graft failures as compared to left kidneys.

Methods: Two consecutive cohorts of adult renal allograft recipients from living (n=4.412) and deceased (n=5.387) donor kidneys between 1st January 2000 to 1st January 2013 were analyzed. Data were obtained from a prospectively maintained electronic database of the Dutch Organ Transplant Registry. Technical graft failure was defined as removal of the renal allograft within 10 days without signs of acute rejection.

Results: In the living donor kidney transplantation cohort, the implantation of right donor kidneys was associated with a higher incidence of technical graft failure in a multivariable model (p =.03). In the deceased donor kidney transplantation cohort, right kidneys were not significantly associated with a higher risk of technique related graft failure (p=0.12).

Conclusion: Our data show that the implantation of right kidneys from living donors is associated with a higher incidence of technique related graft failure as compared to left kidneys.

P240

Doppler ultrasound scans after renal transplantation: too much of a good thing?

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Introduction: Ultrasound remains the principle imaging technique in the post-operative period for renal transplant patients. No definitive guideline currently exists to govern the frequency and interval for these scans. Historically in this regional transplant unit, recipients had a daily Doppler ultrasound scan for the first five days after transplantation. We proposed that a reduction in frequency of this investigation could be safely introduced.

Method: All consecutive renal transplant recipients between December 2012 and March 2014 were included in this study. Patient's data were retrieved from the electronic care records and radiology database, including number of scans performed, scan interval, indications and graft outcomes. The change in practice from routinely scanning recipients on day 1 to 5 (pre-intervention group 1) to day 1 and 3 only (post-intervention group 2) was made on 1st August 2013.

Results: 125 patients were identified of whom 57 (45.6%) were in group 1. The mean number of Doppler ultrasound scans was reduced after the intervention from 4.7 to 3.3 per person. The mean number of scans fell in both living donor and deceased donor recipient groups, although the latter group had more 'for cause' scans reflecting the higher early post-operative complications in this cohort. Length of stay was comparable in both groups 1 and 2.

Discussion: The reduction in routine post renal transplant Doppler ultrasound scanning from 5 to 2 scans did not compromise patient safety or outcomes and was associated with more appropriate use of resources.

P241

Predictive value of postoperative C reactive protein and white cell count in kidney donors experiencing surgical complications

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Introduction: Patients undergoing donor nephrectomy are fit and well individuals. Despite this, 1 in 5 will suffer a perioperative complication causing significant morbidity. Recent published data has highlighted the importance of the predictive value of early postoperative C reactive protein (CRP) rises for complications in similar abdominal surgical procedures. We therefore assessed the predictive value of CRP (and other markers of the systemic inflammatory response to surgery) for clinically significant postoperative complications in this unique but growing patient cohort.

Methods: 746 patients undergoing laparoscopic donor nephrectomy between 2003 and 2013 were analysed. Data was collected on 30 day perioperative complications stratified by the Clavien-Dindo classification and then separately for the common infective complications of wound, urine and respiratory infections. Predictive values of days 1,2,3 CRP levels and white cell count (WCC) were evaluated by receiver operating characteristic (ROC) curves.

Results: 147 clinically significant surgical complications occurred in 746 patients. 142 were of an infective aetiology. Early peak CRP was not a sensitive marker of postoperative infections (AUC 0.59, 95% CI 0.5 - 0.65). WCC was also an inaccurate predictor (AUC 0.60, 95% 0.53 – 0.66). For the prediction of major (clavien 3 / 4) complications Day 1 WCC AUC was 0.7 (95% CI 0.5 – 0.87) and neutrophil:lymphocyte ratio (NLR) subset was 0.75 (95% CI 0.69 – 0.88).

Conclusions: This is the largest surgical cohort study to date examining the relationship between the CRP, WCC and postoperative outcomes. Early postoperative CRP is an overall poor predictor of surgically relevant complications. Day 1 WCC and specifically its NLR subset provide some clinical value in stratifying those at risk of serious postoperative complications. However, overall predictive accuracy remains suboptimal using current parameters. Given the significant incidence of postoperative donor nephrectomy complications; new biomarkers of infectious complications require urgent evaluation.

P242

The impact of renal transplantation on lower limb perfusion

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Introduction: Given the dramatic benefits of renal transplantation, the previously strict criteria for inclusion have been extended to include older, more comorbid patients. Currently, those with peripheral vascular disease are often excluded due to the theoretical risk of post transplantation limb ischemia, where the donor kidney diverts blood away from an already under perfused leg. The aim of this study was to determine if renal transplantation affects lower limb perfusion.

Methods: Eighteen patients had lower limb perfusion measured before and after transplantation using two techniques; strain gauge plethysmography (SGP) and ankle brachial pressure index (ABPI). Perfusion change in the ipsilateral leg was compared to the change in the contralateral leg, giving an internal control for each patient.

Results: SGP: There was no significant postoperative blood flow change in either the ipsilateral leg ($-0.63 \pm 0.63 \text{ cm}^3/100\text{cm}^3/\text{min}$) or the contralateral leg ($-0.15 \pm 0.60 \text{ cm}^3/100\text{cm}^3/\text{min}$), nor was there any significant difference between the legs ($p=0.379$). ABPI: There was no significant ABPI change in either the ipsilateral leg (-0.02 ± 0.03) or contralateral leg (0.02 ± 0.02), nor was there any significant difference between the legs ($p=0.718$).

Conclusions: Renal transplantation has no significant impact on lower limb perfusion as measured by SGP and ABPI. It is unreasonable to exclude patients from transplantation based solely on the concern of a postoperative reduction in lower limb perfusion.

Category: Renal Transplant Surgery - Urology

P243

Retention of transplant ureteric stents: an audit of practice and outcomes

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Introduction: Routine ureteric stenting during renal transplantation plays a major role in preventing Major urological complications (MUCs). However, it also is at a disadvantage of increasing the risk of Urinary tract infections post-transplant if stents are not removed in a timely fashion; this might jeopardise graft function. This audit sought to determine compliance with our unit protocol to remove ureteric stents by six weeks after transplantation.

Methods: A retrospective audit of patients receiving a kidney transplant in our centre between 01/01/2013 and 31/12/2013 was conducted. Transplant to ureteric stent removal interval was calculated and the reason for stent removal being delayed was determined. To complete an audit cycle, data were compared with a previous year's audit (01/01/2012 to 31/05/2012).

Results: Ninety patients were transplanted in the period studied. All received a single transplant JJ stent. The median time to stent removal was 39.8 days (range 15-122 days) compared to 64.6 days during the previous audit period. Seventy Three recipients (81.1%) had their stent removed within the 6 week protocol period (19.3% in the previous audit). Those exceeding the 6 week threshold had delayed removal due to patient morbidity (n=15), unknown reasons (n=1), lack of theatre capacity (n=1).

Conclusion: Sequential audits in our unit have highlighted deficiencies in the timely removal of transplant ureteric stents. However, this audit shows the majority of recipients adhered to our 6 week threshold for removal. As a result of last year's audit, a policy of default listing of patients for stent removal was adopted; rather than a 'reactive' policy requiring recognition of the presence of a stent. It has been a major factor in improving adherence to our 6 week protocol, reducing the burden of stent related morbidity and the number of delayed stent removals.

P244

The utility of routine ultrasound imaging after elective transplant ureteric stent removals

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Introduction: Ureteric stent insertion at the time of graft implantation is widely practised, aiming to reduce the incidence of major urological complications (MUCs) (e.g. ureteric stenoses or leaks). MUCs are rare but often become apparent soon after stent removal. We evaluated whether routine post-stent removal graft ultrasound imaging (PSRGU) was useful in detecting MUCs before they became clinically or biochemically apparent.

Methods: A retrospective analysis was undertaken to identify elective transplant ureteric stent removals from adult single renal transplant recipients (sRTRs) at our centre between 2011-2013. Data were collected on donor and recipient variables, ultrasound findings and subsequent clinical outcomes.

Results: Elective ureteric stent removal was performed for 340 sRTRs (mean (SD) donor age 46.0 (15.4) years; mean (SD) recipient age = 45.2 (13.3) years; SPK = 63; live donor = 140) of whom 20 returned to their local hospital for follow-up. Of the remaining 320 patients, 217 had routine PSRGU (median (IQR) days post-stent removal = 17 (11-29)), 75 had urgent PSRGU (50 for a rise in creatinine), 12 had other urgent imaging (e.g. CT) and 16 had no further renal imaging. Of the 217 patients who underwent routine PSRGU, 205 (94.5%) had no change of management due to the ultrasound scan, 3 (1.4%) required repeat imaging only with no intervention, and in 8 patients (4%) incidental (non-ureteric) findings were identified. One patient (0.4%) had nephrostomy insertion after routine PSRGU but no ureteric stenosis was identified and no further ureteric intervention was performed. Of 75 patients having urgent PSRGU, 3 patients required ureteric reimplantation. No urine leaks were identified post-stent removal. The estimated cost for routine PSRGU over 3 years was £13,671.

Conclusion: At our centre, routine PSRGU has a low yield for MUCs that are not clinically or biochemically apparent. MUCs are more likely to present with a rise in creatinine, and be confirmed on urgent PSRGU. Routine PSRGU provides no added value to intense clinical and biochemical monitoring post-transplant.

P245

Ureteral length in living donor kidney transplantation; does size matter?

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Introduction: The aim of this study is to evaluate the effect of ureteral length on urological complications, like ureter strictures or urinary leakage.

Methods: Data were collected from the INEX registry, a prospective study performed between October 2010 until December 2012, in which 200 recipients of a living donor kidney transplant were included to compare the intra- to the extravesical ureteroneocystostomy. Ureteral length was measured in 198 patients and used to divide recipients into 3 categories: Short ureters(<8.9cm), medium ureters(9.0-10.9cm) and long ureters(> 11cm). Urological complications between the categories were compared and a risk factor analysis was performed.

Results: Fifty recipients were allocated to the short ureter category, 98 to the medium category and 50 recipients to the long ureter category. The mean follow-up of all recipients was 27 ± 10 months. A univariate risk factor analysis for gender, arterial multiplicity and for type of ureteroneocystostomy showed no differences in outcome for the whole group of 198 recipients. However, a subgroup analysis revealed that male recipients in the short ureter category had a significant higher risk for urological complications ($p=0.038$) as well as recipients in the long ureter category with an arterial reconstruction ($p= 0.043$).

Discussion: In case of a male recipient or an arterial reconstruction, ureteral length does influence the number of urological complications.

P246

Umbilical vein catheter versus double J stent for ureteric anastomosis in renal transplantation: a single centre, open label, randomized trial

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Introduction: Double J (DJ) stents are used routinely in renal transplantation to prevent ureteric complications. A recent Cochrane review of literature showed that routine prophylactic stenting reduces the risk of major ureteric complications.

Aim: The aim of the study was to compare the use of Umbilical Vein Catheter (UVC) to DJ stents in renal transplants. Primary end point was ureteric complication rate. Secondary end points were UTIs, re-operation or radiological interventions, and cost effectiveness.

Methods: 300 patients were randomized using a sealed envelope technique. 151 to DJ stents & 149 to UVC. There was a significant conversion rate from UVC to DJ stent, intra-operatively (30%). Eventually 187 DJ stents & 98 UVCs were included in final analysis. Intention to treat (ITT) and per protocol (PP) analysis were done. Fishers' exact test was used for two-sided p values. Absolute risk with 95% confidence interval (CI) & number need to treat (NNT) were calculated.

Results: Patient demographics were similar in both groups. Both ITT & PP analyses showed no significant increase in ureteric complications with the UVC ($p=0.1194$ & 0.1286 , respectively; AR 3.5%; 95%CI=-1.22% to 8.21%; NNH=29). Regarding UTIs, ITT showed a significant increase in DJ stent group ($p<0.0001$) with AR 21.6%, 95% CI=11.5 to 31.7; NNT=5. However, the PP analysis failed to show any significant difference between the 2 groups ($p=0.5937$; AR 3.56; 95% CI= -7.71 to 14.84; NNT=29). There was a significant cost difference between the 2 groups with DJ stents costing £848 per patient (cost of stent itself plus day surgery procedure of flexible cystoscopic removal) and UVCs costing just £0.80. This resulted in a savings of over £83,000 in this study.

Conclusion: This prospective randomized trial showed that UVCs are comparable to DJ stents in terms of ureteric complications. However, ITT analysis showed a higher risk of UTIs with DJ stents. But there was a significant conversion rate, making per protocol analysis insignificant. UVCs need to be evaluated further in future trials, to tap the potential huge cost benefit.

P247

External or internal stenting in renal transplantation

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Introduction: In renal transplantation, urological complications (UC) are accountable for a proportional amount of morbidity and mortality. Previous studies demonstrated that stenting of the ureterovesical anastomosis reduces the incidence of UC. Multiple techniques of ureteral stenting are available, and there is no consensus on which technique of stenting is best. The aim of this study was to compare an external stenting technique with an internal stenting technique on the incidence of UC.

Methods: Retrospective analysis of 216 renal transplantations performed between July 2009 and July 2012. Until 2011, 93 patients received an external stent that is placed through the neoureterocystostomy and through a suprapubic bladder puncture (SP stent). Since 2011, 123 recipients received an internal JJ stent. The primary outcome is UC, defined as the need for percutaneous nephrostomy drainage or surgical revision of the ureterovesical anastomosis.

Results: The rate of UC for SP stents was 17,2%, compared to 4,9% for JJ stents ($p = 0,003$). All patients with UC received nephrostomy drainage. No difference in surgical ureter revision rate was observed between the groups (4,1% vs. 5,4%; $p = 0,65$).

Discussion: Internal stenting with a JJ stent results in a significant decrease in UC rate compared to external stenting through the SP technique. There was no difference in surgical revision rate.

P248

Current management of ureteric stenosis following renal transplantation

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Introduction: Ureteric stenosis is well recognised as a major urological complication of renal transplantation. Following initial antegrade decompression, definitive treatment options include long term ureteric stenting, endoscopic stricture management or ureteric re-implantation. There is minimal current data in the literature to help guide patient choice or define why patients opt for particular treatment strategies. Therefore we aimed to characterise the outcomes of up to date current management for ureteric stenosis.

Methods: A retrospective cohort study was performed for all patients following renal transplantation who required treatment for ureteric stenosis between August 2008 and August 2014. Case identification was via a prospectively maintained database on all renal transplant patients and ICD procedure codes. Data was abstracted from clinical records.

Results: 21 patients were identified as having developed ureteric stenosis during the study period. 11 patients underwent early open ureteric re-implantation, 2 had endoscopic management with successful balloon dilatation, 1 had proximal ureteric stenosis managed with pyeloureteroplasty and 7 had long term ureteric stents. Mean length of time between elective stent changes was 4.2 months (range 1-12 months). One patient opted for re-implantation after stenting. Renal function in endoscopic/stent patients was preserved except for one patient with graft failure due to drug non-compliance. Of the 12 patients having open re-implantation one had re-stenosis managed with long term stenting and 91% had satisfactory renal function. Recorded incidence of urinary tract infection was more prevalent in the long term stent cohort.

Conclusion: In our current series endoscopic, open reconstruction and long term stenting can all provide satisfactory outcomes. In some situations surgical and clinical factors impact the choice of treatment. Patient choice also plays a significant role. Unfortunately in some cases it was unclear from clinical note review why patients had opted for particular treatments. Although this study has provided up to date information to aid counselling patients, further work is warranted to assess what variables affect patient informed choice and what the cost efficiency of open vs. long term stenting is.

P249

Prostatic assessment in male renal transplant recipient patients: compliance with the european association of urology renal transplant guidelines

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Introduction: Prostatic assessment in the evaluation of male renal transplant recipients can be useful not only to assess for overt malignancy, but also for benign prostatic conditions affecting bladder function. This is even more so as older patients are assessed for transplantation. The European Association of Urology renal transplant guidelines recommend all male recipients over 50 years of age should undergo a digital rectal exam (DRE) and PSA blood test at the time of transplant assessment (BTS guidelines do not comment on this).

Methods: A retrospective cohort study was performed for the 3 year period 2011-2013. Case identification was via analysis of a prospectively maintained regional renal transplant register. 407 renal transplants were performed with 263 (65%) males and 148 (56%) patients were aged >50. Males >50yr seen in the renal transplant surgical clinic at the time of first assessment were included in the study.

Results: Of the 148 patients in the study population mean age was 61 years (range 51 years to 78 years). 5% (7/148) of patients had a documented DRE performed at the assessment clinic. 6 of these were performed by a urology registrar involved in the surgical renal transplant assessment clinic. No PSA tests were requested without a DRE or on the basis of benign feeling DRE. 1 patient had a PSA test performed prior to being seen in the assessment clinic. 2 patients were referred to urology for further evaluation of lower urinary tract symptoms.

Discussion: Our audit demonstrated that 95% of male patients over 50 did not have a DRE as part of prostatic assessment when seen in the surgical renal transplant assessment clinic. This was almost 100% when patients were assessed by non-urological surgeons. There is little evidence base for the development of guidelines on this matter and it may be that transplant surgeons feel that a DRE adds little to the transplant assessment. PSA screening in potential renal recipients is controversial and further work is required to assess its role. Recent large European studies have suggested that PSA screening may not be warranted but did not analyse patients about to receive immunosuppression after transplant.

P250

Short and long term outcomes after balloon dilatation for ureteric stenosis after kidney transplantation

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Introduction: Ureteric obstruction occurs in 2-10% of patients, usually in the first few months after renal transplantation. Prompt diagnosis and intervention are vital to prevent graft loss. Percutaneous nephrostomy tube insertion is considered to be the first-line treatment. The present study evaluated the short & long term impact of nephrostomy for ureteric stenosis.

Methods: In this 19-year retrospective study of 1476 consecutive kidney transplants, we assessed the short term success, complication rate and the long-term impact on allograft and patient survival of ameliorating ureteric stenosis by percutaneous nephrostomy, minimally invasive balloon dilatation and stenting (PCN). Outcomes were compared to NHSBT survival data for our centre.

Results: Ureteric stenosis occurred in 52 patients (3.5%), which was early (≤ 6 months) in 34 and late (> 6 months) in 18. Characteristics for these patients: 69% male; mean age 47 years; 73% deceased donor transplants; mean cold ischaemic time 15 hours; mean donor age 50 years; 28% ≥ 2 arteries. PCN was universally successful initially. Recurrent stenosis occurred in 10 patients (19%) - 5 were treated by surgical revision and 5 maintained on long-term ureteric stenting. 3 patients had significant bleeding episodes after the initial PCN insertion. 7 patients were treated for uncomplicated urinary infection after PCN. 10-year graft survival was 67.6% and 53.1% and mean creatinine at 1 and 10 years was 222 & 164 and 241 & 448 $\mu\text{mol/L}$ for those with early and late ureteric stenosis respectively. In those with late ureteric stenosis, transplant loss was universally attributed to biopsy-proven chronic allograft nephropathy (CAN) whereas transplant loss in early ureteric stenosis was due to different reasons including primary recurrent disease, infection and infarction. None were lost due to urological complications.

Discussion: Our data suggest that PCN to treat ureteric obstruction is safe and effective both short and long term with a 20% restenosis rate. All allografts lost in those with late ureteric stenosis were due to CAN suggesting an association between the two that would require further evaluation to confirm.

Category: Renal Transplant Surgery - Miscellaneous

P251

Inter-centre variation in the peri-operative management of transplant recipients in the UK

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Background: Anecdotally there appears to be substantial variation in the peri-operative care of kidney transplant recipients. However this has not been studied in detail. Our aim was to conduct a review of the peri-operative management of renal transplant recipients in the UK to establish what variation in practice exists.

Methods: This was a qualitative questionnaire based study of UK renal transplant units. The clinical lead in each UK renal transplant unit was approached regarding participation. A telephone questionnaire was then carried out with a transplant nephrologist or surgeon representing each centre. Questions related to routine clinical practice. Questions focussed on a number of key areas including intra-operative drug administration, peri-operative fluid management, management of immunosuppression, graft rejection, and postoperative hypertension. Once completed, the questionnaires were sent electronically to each unit for review to ensure the accuracy of the data.

Results: Twenty of 23 (87%) adult renal transplant units in the UK participated in the study. Seventeen questionnaires were completed by a consultant and 3 by a registrar. There was wide variation in practice across all areas studied. Striking examples of this variation included 9 different perioperative antibiotic regimes, 7 different postoperative fluid regimes with variation both in fluid type and quantity and no two units had identical immunosuppression protocols.

Conclusion: We have confirmed the anecdotal impression of a wide variation in practice in UK renal transplant centres. There appears to be clinical equipoise in many aspects of peri-operative renal transplant care which require further study.

P252

Peri-operative anticoagulation in renal transplant recipients

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Introduction: There is no standard approach to Anticoagulation (AC) in early post transplant period. Many centres use Intravenous unfractionated heparin (UFH). Subcutaneous Low molecular weight heparin (LMWH) has not been reported widely because of risk of accumulation or under coagulation with changing renal function. We report outcomes of our experience with UFH and LMWH.

Methods: A retrospective review (2000-13) of electronic and paper records of patients requiring therapeutic post-op AC, including patients on oral AC pre-op and patients with an immediate post-op indication. Haemorrhage was defined as a symptomatic bleed requiring blood transfusion.

Results: 22 patients of 700 transplants had postoperative AC. Mean age 53 yrs (27 – 74yrs), 18 were on HD. 15 patients were on AC pretransplant [3 previous thromboembolic (VTE) events, 2 Anti-phospholipid syndrome, 5 prosthetic cardiac valve, 5 atrial fibrillation] whilst 7 started post-op AC (4 new VTE, 3 grafts at high risk of thrombosis). Mean time to post-op AC was 36h (1-192 h). 11 (50%) received LMWH and factor Xa monitored in 2. 11 (50%) received UFH, monitored by APTT. APTT was checked 4 hourly during first 12h then 12 hourly. Supra-therapeutic levels required dose reduction and APTT recheck in 2 hours. Four developed haemorrhage with 1 mortality. All bleeders were on UFH (36% v 0%, p 0.027) and had high APTT ratio (4 to 9) before bleed. Even with timely monitoring, APTT ratio fluctuated above and below desired range (0.75 – 9). Mean time to bleed was 101h post-transplant (12 – 144h). A mean 1.75 units were transfused after haemorrhage. 1 patient required re-operation. There was no death-censored graft loss although 2 developed DGF. 2 VTE events occurred (1 LMWH, 1 UFH).

Discussion: It is difficult to keep patients on UFH within therapeutic range after transplant. Bridging protocols for anticoagulation in patients with normal renal function are based on LMWH. No bleeding was observed on LMWH but was common on UFH with similar thrombotic events. Despite complexity of using LMWH with changing GFR post transplant it appears safer approach than UFH.

P253

Metabolic phenotyping the renal transplant surgical journey

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Originally defined as 'the quantitative measurement of the time-related multi-parametric metabolic response of living systems to pathophysiological stimuli or genetic modification', metabonomics has recently been proven as a successful, pragmatic and exciting application for clinical and surgical environments. The value of employing a metabolic profiling approach in transplantation, to characterise both kidney and liver transplants in terms of associating graft outcome to biological sample analysis by nuclear magnetic resonance (NMR) and/or mass spectrometry (MS), despite still being in its infancy, has shown promising potential.

To complement, a unique study has been established to metabolically phenotype prior to (24 h) and post (days 1–5) surgery living donor renal transplantations, performed at the Imperial College NHS Trust Renal & Transplant Centre (London, UK). Using an advanced multi-platform analytical strategy (i.e., combined NMR, MS and chemometrics), donor and recipient (n = 100) urine and plasma metabolic profiles were obtained, and subsequently integrated and modelled, with the ultimate aim to devise an objective means of characterising renal function post-transplantation and to stratify patients on the basis of likelihood of complications (such as delayed graft function, rejection episodes or disease recurrence).

The focus of this presentation will be directed towards the real-life, successful application of an exhaustive metabonomic approach in clinic and surgery, exemplified through key cases from initial untargeted exploration (hypothesis generating) to targeted analysis (hypothesis testing), for both healthy donors and ill recipients. The implementation of advanced chemical techniques (NMR and MS) for urine and plasma metabolite profiling will be described, along with the subsequent multivariate approaches necessary to successfully interpret and correlate markers or patterns that define particular class information. Both unsupervised, such as principal components analysis (PCA), and supervised, such as partial least squares (including potential orthogonal signal correction) regression and discriminant analysis ([O]-PLS[DA]), chemometric techniques will be demonstrated as a means to stratify sub-populations attributed to numerous causes, both endogenous and exogenous, for example, from underlying physiology, to clinical comorbidities and even therapeutic drug administration. Finally, multimodal data integration with conventional clinical parameters will briefly be discussed.

P254

Multi-disciplinary management of renal transplant trauma in a major trauma centre

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Introduction: Trauma of the urinary tract has been shown to occur in approximately 10% of trauma cases with renal injuries being the commonest. Trauma to a transplanted kidney is rare so there remains debate regarding the optimal management of these cases. We discuss the management of trauma to a transplanted kidney at a Major Trauma Centre.

Methods: We report on 2 separate cases of trauma to a renal transplant. Case notes were examined for clinical information, biochemistry results and imaging.

Results: The first patient received a renal transplant from a deceased donor in 1996. The transplant was sited in the right iliac fossa. The patient was riding a motorbike at approximately 40mph and skidded and collided with a tree. The patient sustained an isolated upper pole laceration with associated perinephric and retroperitoneal haematoma (grade III)¹ to the transplanted kidney. He was managed conservatively and had a repeat CT abdomen and pelvis 3 days post-trauma which showed a stable injury and unchanged haematoma. The patient was successfully discharged following this with a stable creatinine.

The second patient received a kidney and pancreatic transplant 2 years ago. The patient sustained the injury after falling 2 floors from scaffolding. The CT scan identified an expanding haematoma with active haemorrhage from the transplanted kidney. The patient also sustained a left frontal brain contusion which required intubation. This patient was managed jointly between transplant surgeons, urologists and interventional radiologists where the decision for super-selective embolization of the upper pole of transplant kidney was made. The patient subsequently had a Doppler ultrasound kidney, which showed good global vascularity of the transplant kidney. The serum creatinine also recovered to a similar level as prior to the trauma and embolization.

Discussion: Both these patients were managed jointly by transplant surgeons, urologists and interventional radiologists. All cases were also discussed in a multi-disciplinary meeting attended by the above specialities. In both situations the native kidneys did not sustain an injury highlighting the susceptibility of transplant kidneys to abdominal trauma. The other concerns are the lack of the normal confines of the retroperitoneum which contain haemorrhage and abnormal renal function which limits contrast usage (and early repeat imaging). Despite these concerns, the transplant kidneys were preserved through the use of conservative measures and super-selective embolization. This is in line with the modern management of renal trauma in trauma centres.

1) Adapted from American Association for the Surgery of Trauma (AAST) renal trauma severity scale.

P255

Compliance over the first 12 months following the 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 an event 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 examined 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 after formal introduction of the new checklist were included. A retrospective analysis was made of patients' notes and the electronic patient record (EPR). The endpoint was the presence of the new completed checklist in the notes or on EPR. Results were collected and audited after each period of 4 months. Members of the surgical and theatre teams were then educated about use of the checklist using short presentations to small groups.

Results: 185 patients were transplanted at our centre over 12 calendar months following introduction of the transplant-specific WHO checklist. Overall, at the end of the 12 months, the new checklist could be identified in 118 patients' records (67%). An audit after the first 4 months (Sep-Dec) revealed the checklist to be present in 53% of patients' notes. During the subsequent months, the checklist was found in 69% (Jan-Apr) and then 80% (May-Aug) of patients' notes. There were no adverse events reported.

Conclusions: The suboptimal overall compliance with the new checklist reflects poor understanding and uptake in the early stages following implementation. Regular education and encouragement as part of an ongoing audit process has led to vast improvements in compliance with the checklist. This is an important step towards improving patient safety in contemporary transplantation.

P256

Organ retrieval for adult multivisceral and small bowel transplantation

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Introduction: Multivisceral and intestinal transplantation (MVIT) is increasingly viewed as the treatment of choice for irreversible intestinal failure and complications of parenteral nutrition. It is a highly specialised service, currently offered to adults by two UK adult transplant centres. Given the low numbers and technical complexities of the procedure, retrievals are not part of the national organ retrieval service and each centre procures their own organs for MVIT. This can provide challenges in minimising cold ischaemia, the limit of which is generally accepted as 6 hours for small bowel. This study reports the experience of one centre in providing the nationwide adult MVIT retrieval service.

Methods: All retrievals for MVIT between January 2009 and November 2014 were included. Data were collected from the unit's prospectively maintained transplant database, which includes retrieval and implant data.

Results: During the study period 50 retrievals for MVIT were completed, all of which were performed by a Consultant Transplant surgeon. The mean distance from base hospital to donor hospital was 143 miles (range 0-452 miles) and the mean travel time of 2hrs 9mins (range 0-6hrs 10mins). Overall, the travel zone for retrievals covered approximately 175,000 square miles. Travel was by aeroplane in 16 cases. The warm dissection phase was completed in a mean time of 4hrs 20mins (range 2hrs 30mins – 9hrs 20mins) and the mean overall operative time was 5hrs 51mins (range 4hrs 4mins – 10hrs 28mins). This was in part dictated by progress in the recipient explant procedure, which often necessitated delay in cross clamp to minimise unnecessary cold ischaemia. The mean cold ischaemic time was 4hrs 35mins (range 2hrs 27mins – 6hrs 50mins). There was no organ damage requiring surgical repair in any of the retrievals.

Conclusion: This study demonstrates that it is logistically feasible to provide a MVIT organ retrieval service with nationwide cover, with very acceptable cold ischaemic times. However, the resources required are significant in terms of personnel, travel costs and theatre usage in the donor hospital.

P257

Single centre experience of the use of aortohepatic conduit in liver transplantation

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Introduction: The use of aortohepatic conduit in orthotopic liver transplantation (OLT) is occasionally required, especially when the native arterial supply is compromised. Aortohepatic conduits have been described to confer a higher risk of post-operative complications, especially hepatic arterial thrombosis. Our study investigates the outcomes of the use of aortohepatic conduits in OLT.

Methods: This is a retrospective single centre analysis of prospectively collected data from our institution's electronic database. All patients that had OLT with the use of an aortohepatic conduit, between January 2003 and October 2014, were included. Patient and graft outcomes and complications were investigated with descriptive statistics. The Kaplan-Meier method was used to estimate patient and graft survival.

Results: During the time interval mentioned, 891 patients who underwent OLT were identified. Eighty-seven (9.7%) patients received 92 liver grafts using aortohepatic conduits. The male to female ratio was 54:33 (62%:38%) and the median age was 48 years (range: 19-69). Median follow-up was 45 months (range: 0-144). 20 patients died during the follow-up period, with patient survival at 12 years being 65.4%. Three (15%) deaths were directly attributed to a conduit-related complication. During the follow-up period 19 grafts failed, 10 (53%) out of which due to a conduit-related complication. Graft survival at 12 years was 72.3%. Overall, complications were recorded in 31 (34%) cases, with 14 (15%) cases being directly related to the conduit (thrombosis, bleeding, stenosis). Other complications included bleeding due to other causes, portal venous thrombosis and stenosis, caval stenosis, biliary leak and stricture, bowel obstruction, wound dehiscence, infected intra-abdominal collections, abdominal organ infarction.

Conclusion: The use of aortohepatic conduit is a useful technique in OLT with acceptable patient and graft survival, despite the increased risk of post-operative complications.

P258

Use of the embedded peritoneal dialysis catheter - experience and results from a tertiary renal transplant unit in the UK

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Introduction: The Moncrief-Popovich technique of peritoneal dialysis catheter (PDC) embedment is purported to offer several advantages in facilitating timely commencement of peritoneal dialysis including reduced peri-procedural morbidity and lower leak rates. The purpose of this study was to report our experience of the utility and effectiveness of the technique in a large consecutive series.

Methods: A retrospective case note review was performed on all embedded PDCs performed in our unit over a 4 year period (2009-2013). Follow-up data was available until November 2014. Data was abstracted on patient demographics, operative technique and outcomes. The primary outcome was proportion (%) of cases commencing PD successfully. Secondary outcomes included index procedure morbidity, PD complications and re-interventions needed due to embedding/externalisation.

Results: 63 PDCs were inserted laparoscopically and embedded over the study and follow-up period. The median age was 65.9 years (IQR 52.6-76.2), 60.3% were male and the median creatinine at embedding was 413 micromol/L (IQR 339-472). 79.4% of cases were performed by a Consultant and 20.6% were performed by a trainee.

38/63 (60.3%) PDCs were externalised at a median 10.5 months (IQR 5-19) after embedding. 3/63 (4.8%) patients died and 7/63 (11.1%) were transplanted prior to externalisation. Of the externalised PDCs, 18/38 (47.4%) were immediately functional and 15/18 were ultimately utilised for PD. 20/38 (52.6%) PDCs did not function after externalisation and remedial re-intervention was attempted for 18/20 (90%). These re-interventions were successful in 15/18 (83.3%) cases. 15/63 (23.8%) PDCs remain embedded as of November 2014.

Discussion: In our experience, just over half of embedded PDCs were ever externalised and, of these, only half worked. The remainder required additional remedial procedures to restore functionality. Our experience has led us to question the cost-effectiveness and utility of the Moncrief-Popovich technique.

Category: Renal Transplant Surgery - Nephrectomy

P259

Is robot-assisted donor nephrectomy the future?

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Background: Laparoscopic donor nephrectomy has become the gold standard for live kidney donors. We expanded our surgical armamentarium with the da Vinci[®] robot to evaluate the multiple technical advantages during LDN in order to maximize donor safety.

Methods: Between January 2012 and May 2014 40 robot-assisted donor nephrectomies were performed by two DaVinci[®] certified surgeons. Operation time, complications, length of hospital stay, and donor- and recipient outcomes were registered. These data were compared with all laparoscopic donor nephrectomies of both surgeons during the same period.

Results: There were significant differences between the robot- and laparoscopy group in BMI (median 23,8 (17,9-38,0) versus 26,1 (18,5-37,0) (p 0,001)), warm ischemia time (median 3,5 min (1-9) versus 3 min(1-6), (p<0,001)) en operation time (median 191,0 min (114-282) versus 165,0 min (85-241), (p 0,032)). The operation time and docking time in the robot group significantly decreased over time, p 0.002 and p<0.001 respectively. There was no significant difference in operation time in the robot group between single or multiple vascular anatomy. Postoperatively there were more complications in the laparoscopy group, however with no relation to the operation. After three months of follow-up there was no significant difference in donor kidney function and survival of the transplant and recipient.

Conclusion: The robot-assisted donor nephrectomy demonstrated no superiority after three months of follow-up compared with the standard laparoscopic donor nephrectomy.

P260

A comparison of technique modifications in laparoscopic donor nephrectomy: a systematic review and meta-analysis

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Introduction: To compare the effectiveness of different technique modifications in laparoscopic donor nephrectomy.

Design: Systematic review and meta-analyses.

Study design: All cohort studies and randomized controlled trials comparing fully laparoscopic donor nephrectomy with modifications of the standard technique including hand-assisted, retroperitoneoscopic and single port techniques were included.

Data-extraction and analysis: The primary outcome measure was the number of complications. Secondary outcome measures included: conversion to open surgery, first warm ischemia time, estimated blood loss, graft function, operation time and length of hospital stay. Each technique modification was compared with standard laparoscopic donor nephrectomy. We pooled data with a random effects meta-analysis using odds ratios, weighted mean differences and their corresponding 95% confidence intervals. To assess heterogeneity, we used the I^2 statistic. First randomized controlled trials and cohort studies were analyzed separately, when data was comparable, pooled analysis were performed.

Results: 31 studies comparing laparoscopic donor nephrectomy with other technique modifications were identified, including 5 randomized controlled trials and 26 cohort studies. Since data of randomized controlled trials and cohort studies were comparable, these data were pooled. There were significantly less complications in the retroperitoneoscopic group as compared to transperitoneal group (OR 0.52, 95%CI 0.33-0.83, $I^2=0\%$). Hand-assisted techniques were associated with shorter first warm ischemia and operation times.

Conclusions: Hand-assistance reduces the operation and first warm ischemia times and may improve safety for surgeons with less experience in laparoscopic donor nephrectomy. The retroperitoneoscopic approach was significantly associated with less complications. However, given the, in general, poor to intermediate quality and considerable heterogeneity in the included studies, further high-quality studies are required.

Registration: The review protocol was registered in the PROSPERO database before the start of the review process (CRD number 42013006565).

P261

Preoperative CT-angiography predicts *ex vivo* vein length for right kidneys after laparoscopic donor nephrectomy

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Introduction: Implantation of a kidney with a short renal vein is technically more challenging and therefore prone for technique related complications. It remains unclear whether preoperative computed tomography angiography (CTA), to assess vascular anatomy of the donor kidney, can be used to predict renal vein length.

Methods: We assessed right and left renal vein lengths, measured in an oblique-coronal plane multiplanar reconstruction (MPR) image, of 100 consecutive kidney donors in whom *ex vivo* vein lengths were measured after recovery of kidneys. In a second retrospective cohort of 100 consecutive kidney donors, donating a right kidney, preoperative CTA vein length measurements were correlated to anastomosis time and early graft outcome.

Results: Left and right renal vein lengths, measured on CTA, were 43.2 mm and 30.0 mm respectively. No correlation was found between CTA and *ex vivo* measurements for the left renal vein ($p=.610$), whereas a significant correlation was found for the right renal vein ($p=.021$). In the retrospective cohort, right renal vein length correlated significantly with the anastomosis time, but not with early graft outcome.

Conclusions: We conclude that the length of the right renal vein after kidney recovery can be predicted by preoperative CTA, but this does not hold for the left renal vein.

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10 year experience of pure laparoscopic donor nephrectomy in a tertiary UK transplant centre

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Introduction: Pure laparoscopic donor nephrectomy (LDN) can be a challenging procedure. Preservation of donor safety is paramount whilst undamaged renal parenchyma and good length of intact renal vessels is required for optimal recipient outcomes. Our aim was to review surgical safety outcomes.

Methods: A prospectively maintained database of 455 consecutive patients from 2003 (when LDN was introduced) to 2014, was analysed. LDN is performed fully laparoscopically with the kidney removed through a non-muscle cutting Pfannensteil incision. Hem-o-lock clips were used for the artery until 2013, when Endo TA stapling has been utilised. Patients were reviewed at 3 months

Results: Of the 455 LDN 98.4% were left and 1.6% right, due to the recipient surgeons preference for left sided allografts. Patients had 1 artery, 2 arteries, 3 arteries and 4 arteries in 70.3%, 25.7%, 3.3% and 0.7% of cases respectively. There were no conversions to open nephrectomy and no returns to theatre before discharge. Median blood loss was 50 mls (0-2000) and median operative time 150 mins (105-290). Median warm ischaemia time and length of stay was 4 mins (2-10) and 3 days (1-16) respectively. Transfusion rate was 0.9% and mean reduction in haemoglobin post-op was 1.7g/dl. Clavien III-IV complication rate was 0.9% (no clavien IV) and overall complications (clavien I-IV) were seen in 17%. Intraoperative complications included 1 splenectomy and 1 diaphragm injury, both repaired laparoscopically. There was 1 delayed splenectomy at 4 weeks. There were no episodes of dislodged Weck clips from the renal artery or vein.

Discussion: Our results compare extremely favourably with historic series in the literature with no conversions, small transfusion rate, minimal complications and preserved donor safety. LDN in our institution is performed by urological surgeons with significant experience in renal laparoscopy and an interest in renal transplantation. There have been no issues using Weck clips, which may be due to surgeon familiarity with their application. We believe that pure LDN undertaken by experienced laparoscopic renal surgeons represents the gold standard for donor nephrectomy in 2015.

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Readmission following hand assisted laparoscopic donor nephrectomy

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Background: Hand assisted laparoscopic donor nephrectomy (HALDN) has become one of the established ways of removing living donor kidney. It is associated with low morbidity, mortality, low conversion rate and readmission rate. This is a review of one centre's experience focusing mainly on readmission within 30 days of discharge.

Methods: This is a retrospective analysis of prospectively collected data on all HALDN performed at our institution between August 2007 and October 2014.

Results: A total of 154 (median age: 51 yrs (range: 49-75) donors underwent HALDN during the study period. Sixteen donors (10.4%) were re-admitted to hospital within 30 days following nephrectomy. Overall re-admission rate was 11.7%. There was no difference in the median (4 days) and mean hospital stay between the whole and re-admitted group (4.31 vs. 4.76 days). There was also no difference in the median age between both groups. Reasons for readmission include: intra-abdominal collection (n=3, 18.8%), chest infection (n=2, 12.5%), wound infection (n=2), perforated appendicitis and pulmonary embolism (n=1, 6.25%), acute appendicitis (n=1), perforated duodenal ulcer (n=1), acute cholecystitis (n=1), incisional hernia (n=1), vomiting and diarrhoea (n=1), and non-specific abdominal pain (n=3, 18.8%). Five patients required surgery - two for appendicitis, one each for perforated duodenal ulcer, repair of incisional hernia, and removal of non-functioning renal autograft.

Conclusion: The overall readmission rate following HALDN is high compared to published data. The reasons for readmission were unrelated to nephrectomy in 33% with over 15% requiring surgery for complications unrelated to nephrectomy. Living donors should be fully informed about the risks including the possibility of complications unrelated to HALDN.

P264

An enhanced recovery after surgery programme maintains physiology in patients undergoing hand-assisted laparoscopic donor nephrectomy

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Introduction: An Enhanced Recovery After Surgery (ERAS) programme reduces perioperative morbidity, length of stay and improves patient outcome by limiting the physiological stress response to surgery. The aim of this study was to compare physiological and biochemical parameters of an ERAS programme with standard care in live kidney donors.

Methods: A sequential cohort study was performed on patients receiving a hand-assisted laparoscopic donor nephrectomy. An enhanced recovery protocol was developed using guidelines from the ERAS Group. Standard perioperative care (SPC) involved preoperative overnight fasting and administration of 1L 0.9% saline IV followed postoperatively by 3L of 0.9% saline IV, intravenous morphine via a Patient Controlled Analgesia (PCA) device and a return to diet with removal of the urinary catheter after 24 hours. The ERAS group consumed a carbohydrate drink at 8 and 2 hours pre-operatively without IV fluid administration. Intraoperatively, they received a rectus sheath nerve block followed by insertion of an indwelling rectus sheath nerve catheter containing 0.25% bupivacaine administered at 5ml/hr. ERAS group patients had their urinary catheter removed in the theatre recovery area, received no postoperative IV fluids and were encouraged to eat, drink and mobilise on the evening of surgery.

Results: One hundred patients received either SPC (n=50) or the ERAS protocol. There were no differences in patient demographics (Mean age SPC 46.1yrs v ERAS 45.1yrs; Male 18/50 each). In theatre recovery, the diastolic BP was higher in the ERAS group (Mean SPC 70.6mmHg v ERAS 74.1mmHg p=0.040). Day 2 postoperative reductions in albumin and haematocrit were more attenuated in the ERAS group (Mean SPC -7.7g/L v ERAS -6.0g/L p=0.016; Median SPC -5% v ERAS -4% p=0.029 respectively). Changes in weight were smaller in the ERAS group (Median SPC +1kg v ERAS -0.6kg p<0.001). The increase in creatinine was higher in the ERAS group (Median SPC +38micromol/L v ERAS +45micromol/L p=0.039). There were no differences in graft outcome.

Conclusion: An ERAS programme appears to maintain homeostasis in the HALDN population compared to standard care.

P265

Multiple renal arteries in live donor transplants-radiological estimation of volume of kidney supplied by each artery compared with intra-operative assessment and graft outcome

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Aim: Multiple renal arteries occur in 25% of donor kidneys. Pre-operative imaging (either CT or MRI) can identify accessory arteries with >98% accuracy, but the fractional renal volume supplied has not been studied. We studied the accuracy of three radiological parameters (diameter, cross-sectional area of artery and segmented renal volume) for predicting volume of kidney supplied and compared with intra-operative assessment during implantation.

Methods: 4 donors undergoing laparoscopic nephrectomies with multiple renal arteries were assessed. Pre-op contrast enhanced arterial phase CT was evaluated blindly. On MIP projections, maximum diameter and cross sectional area of each artery was recorded. Volume of renal tissue supplied was calculated by manual segmentation of arterial territory using proprietary volumetric software. Intra-operatively the surgeon estimated the area of kidney supplied by each artery independent of radiologist readings. Graft outcome was recorded at Day 7 and 30.

Results: Main arterial diameter (Art 1) was 5mm (4.8-5.3mm), accessory artery (Art 2) was 2.95 mm (1.6-3.9). Mean CT estimate of kidney supplied by main renal artery was 76% (62-85%). % Volume supplied by each artery showed no statistically significant difference between the CT and intra-operative estimation. Positive correlation between CT volume and intra-operative volume supplied ($r = 0.95$; $p = 0.04$). The recipient's mean serum creatinine/e-GFR at day 7 was 99.8 (>60) and at day 30 was 101(>60).

Table 1: % kidney supplied (R= Radiologist, S=Surgeon) *Wilcoxon Signed Ranks Test $p > 0.05$

	Art 1 (R)%*	Art 1 (S)%*	Art 2(R)%*	Art 2(S)%*
1	85	80	15	20
2	76.6	70	23.4	30
3	81	75	19	25
4	62	50	38	50

Conclusion: Pre-operative fractional segmentation on CT studies can help predict the volume of kidney supplied by each artery. This may help in deciding which accessory artery can be potentially sacrificed without affecting the graft outcome.

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Multiple renal arteries in kidney transplantation: a systematic review and meta-analysis

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Background: The influence of the use of grafts with multiple renal arteries (MRA) in renal transplantation is not clearly established.

Objectives: To compare outcomes between MRA and SRA in terms of 1- and 5-years graft survival. Secondary outcomes were patient survival, complication rates, creatinine levels and WIT.

Data sources: A systematic literature search with predefined search terms was performed using the databases PubMed, EMBASE and the Cochrane Library.

Study eligibility criteria: All studies after 1985 and with more than 50 MRA grafts included were assessed for eligibility. Exclusion criteria were non-English language, non-human trials, no available full text or only supplements and studies reporting on patients <18 years.

Results: Recipients who received a graft with MRA showed significant higher complication ratio (13.8% vs 11.0% in SRA group, fixed OR 1.393, $p < 0.0001$), higher DGF (10.3% vs 8.2 % in SRA group, fixed OR 1.333, $p = 0.022$) and is associated with a significant lower 1-year graft survival (93.2% vs 94.5%, fixed OR 0.819, $p = 0.034$). Both creatinine levels as WIT were significant higher in MRA but showed high heterogeneity (98% in WIT and 70% in creatinine levels) However, the long term outcomes were similar in terms of 5-year graft survival (81.4% vs 81.6%) and 1- and 5-year patient survival (95.4% and 89.6% in MRA group and 95.4% and 87.0% in SRA group)

Limitations: No randomized controlled trials were included. WIT and 1 and 5 year creatinine levels showed heterogeneity. Only studies with >50 MRA were included.

Conclusion: Grafts with MRA are associated with higher complication ratio compared to SRA. However, the outcomes after 5 year are comparable in terms of graft and patient survival.

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Intra-operative use of implantable doppler probe could potentially reduce renal graft loss from vascular complications

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Introduction: Renal vessel thrombosis is a common cause of early graft loss. Implantable Doppler probes (IMDP) are already routinely used to monitor free flaps in plastics and maxillofacial surgery. We looked at our own series of patients with an IMDP.

Methods: We retrospectively analysed prospectively collected data of all renal transplants that had IMDP from April 2011 until October 2014 within our institution.

Results: 112 patients with a median age of 52.5 years were identified. Ten (8.9%) patients returned to theatre post-operatively. Five (4.4%) returned due to an abnormal IMDP signal and two of these required revision of the vascular anastomoses, which normalised the signal. A third patient had normal findings on re-exploration, but required a transplant nephrectomy 48 hours later due to venous thrombosis. Re-exploration was normal in the remaining two patients. A further three patients required re-exploration before skin closure due to an abnormal IMDP signal. All three had revision of the vascular anastomoses. Mesh closure was performed in one patient to increase space. All three were discharged without further complication.

Discussion: Detecting thrombotic complications after renal transplantation relies on clinical changes and ultrasound (US), both may lead to diagnostic delay. In this series the IMDP has probably improved the outcome in five patients. In all these cases the problem was identified quickly, indeed three problems were identified before skin closure. In conclusion, IMDP can potentially allow early diagnosis allowing prompt graft saving treatment.

P268

Vascular multiplicity should not be a contra-indication for live kidney donation and transplantation

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Introduction: Careful consideration is warranted in the selection process of potential living kidney donors. Whether vascular multiplicity should be considered as relative contra indication and therefor an 'extended donor criterion' is still under debate.

Methods: From 2006 to 2013, data from all live kidney donors in our center (n = 951) was collected, and retrospectively reviewed. Vascular anatomy as imaged by MRA, CTA or other modalities was compared with intraoperative findings. Furthermore, the influence of vascular multiplicity (both arterial and venous) on outcome of donors and recipients after live donor nephrectomy and live donor kidney transplantation was studied.

Results: CTA is a superior modality compared to MRA regarding renal vascular anatomy assessment. Specifically sensitivity, negative predictive value and accuracy are higher for CTA. Regarding outcome of live donors with vascular multiplicity, warm ischemia time (WIT) and skin-to-skin time were significantly longer if arterial multiplicity was present (5.1 vs. 4.0 minutes, p = 0.02 and 202 vs. 178 minutes, p < 0.001). Skin-to-skin time was significantly longer in donors with venous multiplicity (203 versus 180 minutes, p = 0.03). Analysis of renal transplant outcome in recipients showed a significantly increased WIT (30 vs. 26.7 minutes, p = 0.002) and lower creatinine drop values (279 vs. 291 mmol/L, p = 0.02) on the first postoperative day in patients receiving a donor kidney with arterial multiplicity compared to donor kidneys with singular anatomy. No differences were found in other outcome measurements, both in donors as in recipients, specifically graft- and patient survival.

Discussion: CT-scan proves to be superior to MRA regarding correct pre-operative anatomical imaging of a live kidney donor. Although significant differences were found in WIT and skin-to-skin time, we conclude that vascular multiplicity should not be considered as a contra-indication to donation, since it has little impact on clinical outcome in the donor (kidney function, complication rate and length of stay). Furthermore, renal transplant recipients receiving a donor kidney with multiple vascular anatomy have excellent outcome.

Category: Viral Infections

P269

CMV disease prophylaxis in transplantation: Importance of using the correct eGFR for dosing of valganciclovir

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Introduction: Increased use of intensive immunosuppressive regimes has increased the likelihood of opportunistic infections such as cytomegalovirus (CMV). Dosage of valganciclovir (for CMV prophylaxis) is dependant on renal function, which is adjusted according to the estimated glomerular filtration rate (eGFR). Most commonly utilised method to calculate eGFR is the Modification of Diet in Renal Disease (MDRD) formula. However this has the limitation of not taking into account patient weight, which is a rough approximation of volume of distribution of the drug. A more accurate method to estimate eGFR is needed in order to achieve adequate dosing of valganciclovir. The aims of this study were to evaluate the incidence of CMV in patients following kidney and Pancreas transplantation; and to assess the adequateness of prophylaxis in these patients.

Methods: A retrospective review was conducted of all patients who had kidney and/or pancreas transplant at one national transplant unit between 1st April 2009 and 31st March 2014. Patients diagnosed to have CMV infection were identified and their data were collected. Valganciclovir dosing was determined by 2 methods of calculating eGFR: MDRD and Cockcroft-Gault, a method that takes into account patient weight.

Results: 62 (9.8%) patients out of 633 developed CMV post-transplantation. 18% and 45% of patients were under-dosed for CMV prophylaxis according to eGFR calculated using MDRD formula and Cockcroft-Gault formula respectively.

Discussion: CMV continues to be a significant problem in transplantation and this study raises important questions about the method used to estimate renal function as it has significant implications for dosage of CMV prophylaxis. We advocate the Cockcroft-Gault method to determine estimate renal function in the context of drug dosage such as valganciclovir.

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A primary cytomegalovirus infection post-transplantation has a significant impact on circulating T cells and renal allograft function

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Background: Cytomegalovirus (CMV)-infection may profoundly affect the peripheral T-cell compartment and is associated with T-cell ageing and generation of cytotoxic CD4⁺CD28null T cells. We investigated the effect of a primary CMV-infection post-Kidney transplantation (KTx) in CMV-seronegative recipients receiving a kidney from a CMV-seropositive donor (D+/R-) on peripheral T cells under immunosuppression and valganciclovir prophylaxis.

Methods: Within the first year post-KTx, the presence of CMV-specific T cells and T-cell differentiation status were monitored. In addition, as ageing parameters we measured the T-cell receptor excision circle (TREC)-content, CD31⁺ naïve T-cell numbers and the relative telomere length (RTL). The D+/R- KTx-recipients were compared to recipients of a D+/R+ combination.

Results: In 12 out of 23 D+/R- KTx recipients CMV viremia was detected within the first year post-KTx whereas 3 other patients showed a serological response to CMV without a viremic episode and detectable CMV-specific T cells. Only in the viremic patients a significant impact of CMV-infection on T cells was observed. They developed CMV-specific, (IFN- γ -producing) CD137-expressing CD4⁺ and CD8⁺ T cells and their T-cell compartment shifted towards more differentiated memory cells with expansion of CD4⁺CD28null and CD8⁺CD28null T cells. One year post-KTx the total CD8⁺ T-cell count was almost doubled in this group compared to non-viremic D+/R- and D+/R+ recipients. Both the TREC-content ($p < 0.05$) and CD31⁺naïve CD4⁺ ($p = 0.01$) and CD8⁺ ($p = 0.05$) T-cell numbers were significantly decreased at 12 months post-KTx. The RTL of CD8⁺, but not CD4⁺ T cells significantly ($p = 0.02$) declined in the D+/R- KTx-recipients post-KTx. The viremic D+/R- patients had a significant ($p < 0.01$) lower glomerular filtration rate compared to D+/R+ KTx recipients at 12 months post-KTx.

Conclusion A primary CMV-infection significantly decreases thymic output, increases the number and differentiation status of peripheral T cells and negatively affects renal allograft function.

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Boosting the adaptive immune response prevents the high incidence of herpes zoster after lung or heart transplantation

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Introduction: Primary varicella zoster virus (VZV) infection causes varicella and may reactivate leading to herpes zoster (HZ). We reported that VZV-reactive memory T cells are significantly lower in transplant recipients compared to controls. We investigated the incidence of HZ post-transplantation and questioned whether the VZV-specific T and B cell memory responses are recovered after VZV reactivation.

Methods: Records of patients after lung (LuTx: n=120) and heart transplantation (HTx: n=222) between Jan 2000 and Mar 2014 were analysed for VZV-PCR DNA up to Aug 2014. VZV-specific B and T cell memory responses before and after HZ (n=5) were compared to patients without HZ (n=5).

Results: VZV infection was clinically diagnosed and confirmed by PCR in 16 LuTx and 38 HTx recipients. Three patients who were VZV IgG negative pre-transplantation, developed primary VZV infection 1.2 years post-LuTx, 4.7 and 7.8 years post-HTx. 15 patients developed HZ post-LuTx: two had systemic dissemination, of which one died 6 days later, and 13 had uncomplicated cutaneous HZ (≤ 3 dermatomes). 36 patients developed HZ post-HTx: 2 had systemic dissemination, 5 had cranial nerve involvement and 29 had uncomplicated cutaneous HZ. Incidence of HZ post-LuTx (37.1 cases/1000 PY) or HTx (30.8 cases/1000 PY) was significantly higher than an age-matched healthy population (7-8 cases/1000 PY). In 4 patients the number of VZV-specific IgG producing B-cells increased after HZ to higher frequencies than those without HZ ($p=0.06$). The percentage of VZV-reactive CD4 and CD8 central and effector memory T-cells increased in all patients after HZ to significantly higher frequencies compared to those without HZ ($p=0.03$).

Discussion: HZ is a frequent complication after lung or heart transplantation and increases VZV-specific T and B cell memory responses. Boosting the VZV adaptive immune response by prophylactic VZV vaccination pre-transplantation may limit the incidence of HZ post-transplantation.

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Dissecting the complexity of interferon response that cross talks with 4E-BP1 in hepatitis E virus infection

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Introduction: Hepatitis E virus (HEV) infection in organ transplantation patients bear high risk of developing chronic hepatitis. Pegylated IFN- α has been used as off-label treatment. This study aimed to comprehensively investigate virus-host interactions in HEV infection with focusing on the IFN signalling.

Methods: Subgenomic HEV and HCV containing luciferase reporter and full-length HEV and HCV infectious cell culture models were used. HEV viral kinetics of five liver transplant patients treated with Pegylated IFN- α was analyzed.

Results: Screening of a panel of 36 cytokines and chemokines revealed that HEV replication was in general insensitive to these factors, with a notable exception being IFN- α . In contrast to HCV that IFN- α treatment exerted a rapid and potent antiviral activity, it had only a moderate and delayed anti-HEV effect in cell culture models (41% inhibition, $P \leq 0.01$, treated with 1000 IU/ml for 72 hrs). Consistently, 4 out of 5 chronic HEV patients had only minor fluctuation of viral load in the first four weeks of pegylated IFN- α treatment, although all the patients eventually cleared the virus. In turn, HEV was able to counteract the antiviral IFN response via attenuating STAT1 phosphorylation, a hallmark of IFN signalling, and suppressing IFN- α -induced transcription of interferon stimulated genes (ISGs; 18 genes tested). Surprisingly the basal IFN pathway was more effective in restricting HEV than HCV infection. More interestingly, 4E-BP1, the key downstream element of mTOR pathway, can restrict HEV infection and mediate the anti-HEV effects of IFN- α . Using RNAi gene silencing and lentiviral overexpressing approaches as well as mouse embryonic fibroblasts generated from 4E-BP1 knockout mouse, we found that 4E-BP1 cross-talks with IFN signalling to modulate the transcription of ISGs.

Discussion: This study has shed new light on the molecular insight of HEV-host interaction, which also bears significant implications in management of chronic HEV patients and future therapeutic development.

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Combined prophylaxis and surveillance to prevent CMV infection

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Introduction: Guidelines support either prophylaxis or surveillance/pre-emptive therapy to reduce the risk of cytomegalovirus (CMV) infection. In UK practice, prophylaxis with Valganciclovir varies in length (100 v. 200 days). We describe a hybrid approach with prophylaxis and surveillance.

Patient and methods: We conducted a retrospective analysis on the incidence of CMV infection in our centre between Jan 2006 and Dec 2008 with 1 year follow-up. D+/R- patients received 100 days of Valganciclovir. All patients underwent surveillance with CMV PCR. Testing was weekly until follow-up less frequent, thereafter determined by frequency of clinic visits. Surveillance was for 100 days minimum, 200 days in those receiving prophylaxis.

Results: 159 patients were initially included in the analysis. Prophylaxis was indicated in 37 patients (23%). A total 2515 CMV PCR tests were requested. In the first 3 months, 1490 (59%) tests were requested (23.7% in patients on prophylaxis). Overall, 10.8% of tests were positive with a median peak viral load of 5886 in surveillance group and 59000 in the prophylaxis group. None of the patients on prophylaxis developed viraemia before 3 months. Further results for the two groups are summarised in the table:

	Test/pt	Viraemia (%) patients)	Median time to peak(mth)	CMV disease(% patients)
Prophylaxis(35)	21	17(48.5%)	5	11(31.4)
Surveillance(124)	14.2	37 (30%)	2	7(5.6)

Overall, 30% of all patients received Valganciclovir treatment. Average duration of treatment was 68 days and median interval to commencing treatment was 151 days (prophylaxis) and 55 (surveillance).

Discussion: Surveillance whilst on prophylaxis is not justified and if prophylaxis is limited to 100 days, more intense surveillance is required to allow pre-emptive treatment in advance of CMV disease. Given the amount of testing required, and the high rate of subsequent treatment, it may be more cost effective to give prophylaxis for 200 days without surveillance in high risk patients.

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Cost of pre-emptive cytomegalovirus (CMV) therapy post high risk donor positive, recipient negative kidney transplantation compared with 100 and 200 days valganciclovir prophylaxis.

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Background: Human cytomegalovirus (CMV) is an important opportunistic pathogen that is associated with significant morbidity post solid organ transplantation. Both pre-emptive therapy and prophylactic anti-viral therapy are recognised strategies for improving outcomes in patients at risk of CMV. Although clinical outcomes for each strategy are similar, the comparative costs have not been addressed.

Methodology: We analysed the cost of managing donor CMV positive to recipient negative patients at our institute with pre-emptive therapy (PT) when compared to patients undergoing both 100 days and 200 days of valganciclovir (VGC) prophylaxis, according to the Impact trial. In the PT group, we included the actual cost of blood testing, PCR analysis and dispensed VGC therapy up to 1 year post transplant. In the prophylactic group, we estimated the cost of treating the same cohort of patients with renal dose adjusted VGC for 100 and 200 days. We also estimated the cost of VGC treatment within either group associated with the 36.8% and 16.1% CMV disease rate after the end of prophylaxis reported in the Impact trial. We did not include costs for diagnosis or monitoring of CMV treatment in the prophylaxis groups.

Results: Forty-seven patients received a kidney alone transplant between 2009 and 2013. In the PT group, 38 (81%) developed CMV viraemia requiring VGC treatment. The average cost of monitoring and treatment per patient for the whole group was £5,346.18. In the prophylaxis group, the average cost was £3,479.21 for 100 days and £6,958.42 for 200 days of VGC. When the additional treatment costs of CMV disease post prophylaxis were included, the average cost per patient rose to £5,526.93 for 100 days and £7,854.29 for 200 days of prophylaxis.

Discussion: Although the clinical outcomes for PT versus prophylactic therapy are similar, our data suggest that PT is associated with a similar overall cost to 100 days of prophylaxis but 200 days of prophylaxis is associated with additional cost per patient.

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Norovirus infection in renal transplant recipients – clinical severity and genotype identification

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Introduction: Norovirus (NoV) is increasingly recognized as causative agent of gastro-enteritis in renal transplant recipients.

Methods: We performed a retrospective study (2003-2012) to investigate the clinical significance and viral genotype of Norovirus (NoV) infections in renal transplant recipients. The clinical significance was defined in a 6-point score, allocating one point for each: diarrhoea, vomiting, nausea, IV fluid administration, changes in immunosuppressive agents, and antibiotic treatment. NoV genotypes distribution in part of the cohort (54/79) was compared to part of a control group of non renal transplant patients (67/177) and to the Dutch population (RIVM).

Results: There had been 332 NoV positive samples in our hospital in the period studied. 141/332 positive samples were from 79 renal transplant patients. Mean age was 46.3±19.6 years, with male/female ratio 47/32, and mean time after transplantation of 3.6±4.7 years. Mean increase in serum creatinine was 91±102 umol/l with a range of 0-439 umol/l. In most patients serum creatinine returned to baseline. 57 patients required hospitalization for their infection. 48.1% of the patients scored 4 or more points and were considered to have severe NoV infection. 191/332 NoV positive stools were from 177 non renal transplant patients. 101/177 (57%) NoV positive patients turned out to be immunocompromised: other organ transplant (heart, liver, lung, bone marrow), malignancy, HIV, systemic diseases. 34/177 (19%) other diseases. 20/177 (11%) no severe somatic disease and 21/177 (12%) unknown. In renal transplant patients' stool samples 74% tested genotype GII.P4 compared to 63% in controls. The GII.4 variant trends in the hospital reflect that in the general Dutch population. Of all NoV positive patients 180/256 (70%) was immunocompromised.

Conclusion: Renal transplant recipients with NoV infection may develop severe disease that may lead to (reversible) graft dysfunction. NoV genotype in these patients is similar to genotypes in controls and in the Dutch population. In our hospital population 70% of NoV positive patients were immunocompromised.

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Dealing with the deficit: seropositive-to-seropositive organ transplantation in patients with HIV

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Introduction: With the introduction of HAART, survival has improved in patients with HIV. A new ageing population has emerged with chronic conditions, such as kidney and liver failure, necessitating the need for organ transplantation. Organ transplantation in seropositive patients has shown comparable patient and graft survival to seronegative patients. But the donor pool is limited.

Methods: Medline, Embase and PubMed databases were systematically searched from inception to September 2014 using key words 'HIV positive, recipient, donor, transplantation, kidney, pancreas' in English. Additional references from relevant papers were hand searched from pertinent publications.

Results: 23 articles were identified from the literature search. Over 60% of seropositive individuals were agreeable to organ donation with 55% open to receiving organs from seropositive patients. Concerns of infection, quality of organ and confidentiality were barriers to seropositive-seropositive organ transplantation. Limited data exists evaluating the viability and potential of seropositive-seropositive transplant. To date 14 seropositive-seropositive renal transplants, using anti-thymocyte globulin induction therapy have been reported with good graft function and dialysis-free at 12 months. Uncertainty and stigma still exist around performing transplants in recipients with HIV among professionals who consider transplantation to be a contraindication. Transplant practitioners are often reluctant to use seropositive donors for seropositive recipient but would use a Hepatitis C positive donor for a Hepatitis C positive recipient.

Conclusion: Transplantation of seropositive organs increases the donor pool and provides benefit in resource-limited settings for patients with HIV. Several theoretical concerns exist of 'Trojan horse' effect of transplanted organs super-infecting the recipient with other infectious diseases such as tuberculosis, cytomegalovirus, recombinant HIV of different clade or resistant form. Prospective trials are needed to evaluate the safety and effectiveness of seropositive-seropositive organ transplantation.

Category: Viral Infections (BKV and HIV)

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Polyoma (BK) virus nephropathy – a growing problem in the last ten years

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Introduction: Polyoma (BK) virus nephropathy has become an emerging problem in renal transplantation in recent years with reported incidence of 1-10% and graft loss up to 50%.

Methods: We retrospectively analysed the incidence of BK viraemia, viruria and nephropathy and graft and patient loss in a single adult kidney transplant centre in the last 10 years. Data was collected from microbiology and histopathology database. Data was validated from Proton database and patient notes.

Results: 618 kidney transplants were performed from January 2004 to March 2014. 37 patients in total (6.0%) had BK virus detected in blood or urine. Of these 25 patients (4%) had BK viraemia. 12 (1.9%) patients had only viruria but no viraemia (excluded). The incidence of BK viraemia is increasing since 2010 (2010=1, 2011=5, 2012=6, 2013=13). Patients were analysed in 3 groups: Group A: PCR<10,000(13), Group B: PCR 10,000-1,000,000(8) and Group C: PCR >1,000,000(4). 4 patients in group A and 3 patients in Group C had high tacrolimus levels. The 25 cases are evenly distributed between 30 and 70 years. There were 19(76%) male and 6(24%) female patients. 36%(9) of the cases were in CMV DR+ to DR- patients. While 2 patients got viraemia very late (50 and 52 months post-transplant), the majority of the patients were affected between 3-6 months following transplant. 3 patients had simultaneous rejection with viraemia. All patients were treated with reduction of immunosuppression. 9 patients received Ciprofloxacin and 1 patient got Leflunomide. Majority of patients in all three groups had stabilisation of serum creatinine and eradication of virus. There were 5 graft losses out of the 25 patients affected (20%). There were three deaths unrelated to BK viraemia.

Discussion: Early diagnosis of BK viraemia and immunosuppressant dose reduction in renal transplant recipients can reduce graft loss and maintain good function. Greater vigilance and suitable surveillance/screening for BK viraemia should be considered.

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Reducing allograft rejection in patients with HIV: immunosuppressing the immunocompromised

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Introduction: We live in the HAART-age, where HIV has become a treatable condition. Patients with HIV are living longer and a new population with problems inherent of ageing is emerging, increasing the need for transplantation. Lower graft survival, function and increased rejection rates have been observed in seropositive patients. We explore the significance of allograft rejection in the immunocompromised surgical patient.

Methods: Multiple databases were systematically searched (inception to October 2014) using key words: HIV-positive, recipient, donor, transplantation, kidney, liver, rejection. relevant reference lists were hand-searched for pertinent publications.

Results: 37 articles explored rates of rejection, immunosuppressant use and immunological rejection in HIV-seropositive patients vs. seronegative controls. Seropositive recipients demonstrated comparable and favourable outcomes in patient survival (85-100%, 1 year and 82-100%, 3 years) and graft survival (75-100%, 1 year and 71-96% 3 years). Liver transplants in seropositive patients reported acceptable outcomes in patient survival (70-100%, 1 year and 50-100%, 3 years) and graft survival (83-100%, 1 year and 64-83%, 3 years). However, HIV status was significantly associated with reduced patient and graft survival, and higher rates of treated acute rejection ($p < 0.001$) with rejection rates $> 40\%$. Seropositive patients were found to have higher incidence of C4d positivity in renal biopsies ($p = 0.001$) and raised incidence of DSA positivity ($p < 0.001$).

Conclusion: Seropositive patients appear to mount a strong immunological response despite their immunodeficiency. Preliminary evidence suggests cross-reactivity between donor-alloantigen and HIV-antigen may explain the heightened rejection in some HIV+ patients. More potent immunosuppression at induction and appropriate maintenance are required for graft survival and improved surgical outcomes in this group of patients experiencing growing demands for organ transplantation.

UK guidelines for kidney and pancreas transplantation in patients with HIV infection

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Introduction: The advent of highly active antiretroviral therapy in 1996 heralded a marked decrease in mortality in human immunodeficiency virus (HIV)-infected patients. In parallel, morbidity from kidney, liver and heart disease and other chronic conditions has increased. This is partly a natural consequence of ageing, and partly due to the higher risk of solid organ failure in HIV+ individuals. This higher risk is due to the co-morbidities associated with HIV infection and to the metabolic consequences of anti-viral drug therapy. HIV+ patients are at particular risk of developing chronic and end-stage kidney disease, which, as in the general population, substantially increases the risk of cardiovascular events and death. Consequently, there is growing interest in kidney transplantation in HIV+ patients and a steady increase in both the number of transplants and in the number of transplant centres serving this population.

These are the second guidelines on this subject published by the British Transplantation Society (BTS) and reflect the growing evidence base from published data on several hundred carefully selected HIV+ kidney and pancreas transplant recipients. They provide a comprehensive summary of all aspects of assessment, selection and management of the HIV+ transplant candidate.

Methods: The guidance was written under the auspices of the BTS Standards Committee and produced in line with BTS Clinical Practice Guidelines and the recommendations of NHS Evidence. The co-authors are UK clinicians involved in kidney and pancreas transplantation and in the management of HIV+ patients. A systematic review of the relevant literature and synthesis of the available evidence was undertaken. Where available, the guidelines are based upon published evidence, and, with the exception of descriptive studies, the evidence and recommendations have been graded for strength. A small number of conference presentations have been included where relevant. The publication 'cut off' date for evidence was September 2014. It is anticipated that the guidelines will next be revised in 2018.

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Lymphopaenia associated with the development of BK nephropathy in kidney and simultaneous pancreas-kidney transplant recipients

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Background and aims: BK virus is a polyomavirus that establishes latent infection in the uroepithelial cells of most adults. Post-transplant, the virus can reactivate, leading to viraemia in 10-15% renal transplant recipients and tubulointerstitial nephritis in a subset of these. In a single centre study, 755 subjects were routinely screened by PCR (blood samples obtained at 1,2,3,6,9,12,18 and 24m post-transplant) from 2009-13. We sought to determine:

1. The frequency of BK viraemia and nephropathy in kidney (K, n=675) and simultaneous pancreas-kidney transplant recipients (SPK, n=80).
2. Risk factors for the development of BK viraemia and nephropathy.
3. The effect of viraemia or nephropathy on 12 month allograft function.

Of note, all patients with viraemia and allograft dysfunction underwent a transplant biopsy. Variables considered included donor type, donor/recipient age, cold ischaemic time (CIT), CMV mismatch, HLA mismatch, lymphocyte count and induction therapy.

Results: Overall, 19% of K recipients and 23% of SPK recipients developed BK viraemia (p=ns). In K transplants, the frequency of viraemia did not significantly differ between living, DBD, and DCD donors (15%, 24%, 19% respectively, p=0.1). Mean time of onset of viraemia was 18 weeks, mean duration 220 days, and mean peak viraemia 3.8×10^5 copies/ml. The peak viral titre positively correlated with duration of viraemia (p=0.0015). 62% of patients with viraemia underwent a transplant biopsy and of these 26% had SV40+ BK nephropathy (5% of all patients). Patients with viraemia had a significantly lower lymphocyte count at 1 and 3 months post-transplant compared to non-viraemic subjects (p=0.018 and 0.006 respectively). Prolonged CIT, and older donor and recipient age were not associated with viraemia or nephropathy. At 12 months post-transplant, renal function was significantly worse in patients with BK nephropathy (p=<0.0001). The presence of viraemia alone did not impact graft function.

Conclusion: BK nephropathy contributes to long-term graft dysfunction. Lymphocyte count may be a risk-stratification tool that allows pre-emptive reduction in immunosuppression.

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Incidence and outcome of BK replication in a prospective, multi-centre, open-label randomized controlled trial with renal transplant patients receiving duo-immunosuppressive therapy versus patients receiving triple therapy

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Background: It remains unclear whether the overall degree of immunosuppression or a combination of immunosuppressives are mainly responsible for the increased risk of BK infection in renal transplant patients.

Methods: A prospective, multi-centre, open-label randomized controlled trial in 361 *de novo* renal transplant recipients was performed. Patients were randomised at t = 6 months into three treatment groups with duo therapy consisting of prednisolone with either cyclosporine A (CsA) group, everolimus (E) group or mycophenolate sodium group. A high incidence of acute rejection, resulted in the addition of CsA to the treatment regime in the prednisolone/MPS group (MPS/CsA). At different timepoints, urine and serum samples were collected and at time point 6 and 24 months a renal biopsy was performed. BKV DNA was measured in all samples. Primary outcome was incidence of BK viraemia, BK viremia and BK nephropathy during 2 years of follow up.

Results: In total, 65 of the 271 renal transplant recipients (29.0%) tested positive for BK replication. Viraemia could be detected in 27.2%, viremia was found in 13.8% of the patients. Incidence of BK viraemia in the MPS/CsA group was significantly higher than in the other groups ($p=0.03$) BK nephropathy was diagnosed in 3 patients. These patients were all treated with prednisolone, MPS and CsA.

Longitudinal data analysis showed a significant lower viral load from t = 6 to 24 months post transplant in the CsA group compared to the MPS/CsA group and the E group. Furthermore a significant better clearance of BK viraemia in patients treated in the CsA group was found compared to treatment with MPS/CsA group. BK replication in the MPS/CsA group was significantly associated with a higher incidence of post BK acute rejection.

Conclusions: This study shows that the optimal treatment against BK replication is tapering of immunosuppression in duo therapy with prednisolone and CsA in the first 2 years post transplant, in a low risk transplantation cohort this is not associated, with increased the risk of graft loss, or allograft rejection.

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Incidence and management of BK virus associated nephropathy: a national study

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Introduction: BK virus associated nephropathy (BKVAN) is an important cause of allograft failure and the optimal treatment remains uncertain. The aim of this collaborative study was to describe differences in clinical practice between all renal units in Scotland to determine the impact, if any, on incidence of BKVAN and graft function.

Methods: We included all patients diagnosed with BKVAN after receiving a kidney or kidney pancreas transplant in Scotland between 1st January 2009 and 31st December 2013. We detailed clinical action and outcomes including; graft survival, GFR (mean±SD) and blood viral PCR (copies/mL) at diagnosis and one-year follow-up.

Results: 43 patients were diagnosed with BKVAN during a period when 1078 renal transplants were performed giving an overall incidence of 4%, ranging from 1.4% to 8.5% between centres. Lowest incidence was observed in the only centre with a screening programme. Median time to diagnosis was 8 months (interquartile range 17-4). Mean eGFR was 52±16 mL/min at one month from transplant falling to 32±14 mL/min with a median viral load of 115,000 copies/mL at diagnosis.

All patients were treated with reduction of immunosuppression and 22 were also treated with antiviral agents (leflunamide, ciprofloxacin, cidofovir). 53% of patients either cleared the virus or had <1000 copies/mL at one year from diagnosis. eGFR stabilised or improved in 70% of cases but four grafts failed within 12 months due to BKVAN. Factors influencing stable or improved graft function were; stopping mycophenolate mofetil and the absence of moderate to severe interstitial fibrosis and tubular atrophy on biopsy. Addition of anti-viral therapy did not significantly impact on viral clearance or GFR.

Discussion: The incidence of BKVAN in Scotland is 4% with a lower incidence of transplant failure than previously published studies. This study demonstrates the utility of a collaborative approach to better inform clinical practice.

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Incidence and outcomes of Polyomavirus infection in 639 kidney transplant recipients: are high immunological risk characteristics more relevant than specific induction or maintenance immunosuppressive regimens?

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Introduction: Polyomavirus-associated nephropathy (PVAN) is now recognized as an important cause of graft dysfunction and early kidney transplant loss. Over-immunosuppression is the main risk factor for the development of PVAN. Donor and recipient characteristics do play a role but conclusive evidences are still lacking.

Methods: In this single centre cohort study performed analysing data retrieved from a prospectively collected database we evaluated incidence, outcomes and risk factors of Polyomavirus infection in 639 consecutive kidney transplants performed between 2007 and 2013.

Results: During a mean follow up of 4.5 years, viremia was detected in 54/639 patients (8%); 26/639 recipients (4%) had biopsy-proven PVAN. Death-censored graft loss rate was significantly higher in patient with PVAN compared to recipients with no viremia: 42% (10/24) vs. 14% (76/523), respectively ($p < 0.05$). After immunosuppression reduction, 43/54 patients (80%) effectively managed to clear the virus with preserved renal function; 4 patients (7%) experienced biopsy-proven acute rejection. Two cases (4%) of ureteral stenosis were observed. The risk factors for Polyomavirus active infection were: higher recipient BMI, Afro-Caribbean recipient, older donor age, higher HLA DR and overall mismatch, lack of CMV prophylaxis, and biopsy-proven rejection ($p < 0.05$). Induction (ATG vs. anti-IL-2 receptor antagonists) and baseline immunosuppression (Tacrolimus vs. Cyclosporine) did not affect Polyomavirus viremia or PVAN rates.

Conclusions: Our results show that PVAN significantly reduces kidney allograft survival and identifies a need for post-transplant aggressive screening, prompt reduction of the net state of immunosuppression and possibly use of more reliable tools to assess virus-specific immune response. It also supports our hypothesis that high immunological risk characteristics are more relevant than immunosuppressive regimens.