



19th Annual BTS Congress 2016

**24 to 26 February
SECC, Glasgow**

Abstract Book

Medawar Medal
11:00 Thursday 25 February
Lomond Auditorium

M001

Variation in the Type 2 Diabetes susceptibility gene *HHEX* may 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 success have informed donor selection, it is currently unknown whether these organ donors harbour genetic variants that predispose to future graft failure. With recent advances in our understanding of beta cell dysfunction genes involved in the development of type 2 diabetes, we wanted to establish whether variation in these genes in donor organs could play a role in predicting long-term pancreas transplant function.

Methods

The most associated SNPs from nine T2D susceptibility loci shown to affect beta cell function were screened. These were genotyped in 435 pancreas donors and 430 transplant recipients who had undergone pancreas transplantation at the Oxford Transplant Centre. Death-censored cumulative events were analysed using Kaplan-Meier and Cox regression. This study had >80% power to detect a hazard ratio (HR)>1.50.

Results

There were 85 graft failures in 430 recipients. The presence of *HHEX* rs1111875 CC genotype in pancreas donors was predictive of reduced long term graft survival (log rank P=0.02) with a median survival time of 97 months compared to those with the CT and TT genotypes who had 113 and 114 months median survival time. Multivariate Cox regression (adjusted for donor and recipient factors) confirmed the association of rs1111875 (P=0.02, HR=1.92;[95% CI=1.02-3.63]) with long-term graft function. Variation in 8 other genes in either donors or recipients did not predict long-term graft function (log rank P=0.18-0.91).

Discussion

This is the first study to provide preliminary evidence for donor *HHEX* genotype and variation in donor beta cell function genes in predicting long-term pancreas graft function. Screening of *HHEX* in other datasets is now required to confirm these results.

M002

No survival benefit of simultaneous pancreas and kidney compared to live donor kidney transplantation in patients with Type I Diabetes: a UK transplant registry study

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Background

Treatment options for patients with type I diabetes and end-stage renal disease include dialysis, deceased donor kidney (DDK) transplant, live donor kidney transplant (LDK) and simultaneous pancreas kidney (SPK) transplant. There is reasonable evidence in the literature of a survival advantage for SPK and LDK over DDK, but the best option for those patients with a live kidney donor remains unclear. The aim of this study was to compare outcomes between LDK and SPK for type I diabetes in the UK.

Methods

Data on all SPK and LDK transplants for type I diabetes performed between January 2001 and December 2014 were obtained from the UK Transplant Registry. Patients undergoing pancreas after kidney transplant were excluded. Unadjusted patient and kidney survival were calculated using the Kaplan-Meier method and compared using the log-rank test. Multivariate analysis of kidney and patient survival was performed using Cox proportional hazards regression.

Results

1739 SPK and 385 LDK transplants were performed in the study period. Both LDK donors and recipients were significantly older and had a significantly higher BMI ($P < 0.0001$). There was no significant difference in mean patient survival (SPK 4087 ± 51 days vs. LDK 3949 ± 117 days, $P = 0.435$) or kidney graft survival (SPK 4060 ± 50 days vs. LDK 4164 ± 117 days, $P = 0.204$). On multivariate analysis there was no association between SPK/LDK and patient survival (HR 0.71 (0.47-1.06), $P = 0.05$). However, LDK was associated with a lower risk for kidney graft failure (HR 0.60 (0.38-0.94), $P = 0.025$). There was no significant difference in serum creatinine in functioning kidneys at 3 months, 1, 5 or 10 years post-transplant between SPK and LDK ($P = 0.885$).

Conclusion

This study suggests that SPK does not confer a survival advantage over LDK for patients with type I diabetes and end-stage renal failure. Indeed, LDK was associated with a lower risk of kidney graft loss. Further studies are required to investigate differences in quality of life and treatment satisfaction between SPK and LDK which may influence the choice of transplant offered to these patients, and to evaluate the longer term outcomes of SPK and LDK transplantation.

Acknowledgements

The authors would like to thank NHSBT for providing the data for this study.

M003

HLA-Bw4 antibodies in HLA-Bw4 expressing renal transplant patients – an analysis combining paired epitopes and electrostatic potential assessment to reveal antigenicity

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Introduction

Exposure to mismatched HLA antigens frequently provokes humoral responses to epitopes which are not present upon self HLA molecules. In our routine assessment of potential renal transplant recipients we identified two patients who expressed HLA-B*13 as their only Bw4 positive HLA antigen. In the SAB HLA class I Luminex assay the patients' sera reacted with all Bw4+ve alleles with the exception of B*13. The characterisation of HLA epitopes using physiochemical modelling of regions within 3 angstroms of polymorphic residues and in relation to their electrostatic potential (EP) has recently led to an improved definition of epitope reactivity. We have investigated the presence of Bw4 antibodies in Bw4 +ve patients using reported physiochemical modelling techniques.

Methods

We obtained high resolution X-ray crystallography resolved HLA class I structures from the protein data bank, which served as templates for structural models of the Bw4+ alleles within our SAB assay. We then utilized Swissmodeller and Swissviewer to generate models of these alleles. The EP was calculated using the Poisson Boltzmann equation.

Results

The 'classical' Bw4 epitope, 82LR, is present on all Bw4 antigens including B*13 and can be considered self in the context of these two patients. EP modelling of the 82LR region demonstrated a consistent EP on reacting and non-reacting alleles. We examined areas within 6-15 angstroms of the 82LR epitope to assess the contribution of previously reported paired epitopes. Comparison of positive and negative reactivity on the SAB assay identified the 144QR/QL region; specifically 144QL present on B13 alleles (considered self) and 144QR region on reactive alleles (non-self). Assessment of the EP in this region demonstrated a higher EP upon non-reacting alleles when compared to that of reacting alleles.

Discussion

The EP data may explain the observed Bw4 reactivity in these patients and illustrates a novel physiochemical analysis of self and non-self paired epitopes. These two cases represent all of the patients on the active transplant list at our centre who have B*13 as their sole Bw4 expressing antigen and are known to have been exposed to an alternative Bw4 antigen. Given the EP variation observed, and the previously reported relationship between EP and Bw4 antibody production, this data suggests that the 82LR+144QR paired epitope may be particularly immunogenic in individuals whose only Bw4 antigen is B*13. The risk of becoming sensitised to the common Bw4 epitope may merit consideration when transplanting these individuals or when weaning immunosuppression after allograft failure.

M004

Short UK dialysis does not significantly impact on live donor kidney allograft survival

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Background

The survival advantage of pre-emptive transplantation (Pre-empTx) in live donor kidney transplantation (LDKTx) was reported by Meier-Kreische (Kidney International, 2000). Dialysis practices differ internationally and immunosuppressive regimes have advanced. The aim of this study was to examine the effect of dialysis time on allograft survival in UK LDKTx, including an assessment of allograft survival (GS) between compatible (CTx) and antibody incompatible transplants (AiT) donors.

Methods

Data from NHSBT for LDKTx recipients in the UK were analysed between 2001 and 2013 including 9755 patients, from 8970 were adults and had available dialysis data. These data were analysed for both GS and composite outcomes (combined death or graft failure). No meaningful differences were found in using a competing risk regression model. Dialysis time (DiT) was categorised into Pre-Tx, <1yr, 1-2 yrs, and >2yrs dialysis. AiT (n=946) were grouped as HLA incompatible (HLAi, n=473) and blood group ABO incompatible (ABOi, n=473). Paired Exchange recipients (PrEx, n=278) and CTx (n=7746) were also analysed in this study.

Results

Transplant groups differed significantly with respect to donor age, recipient age, calculated reaction frequency at transplant, HLA mismatches. The risk of graft failure (GF) of LDKTx compared to Pre-empTx increased with more DiT, but only after 1 year of dialysis in the whole cohort (<1yr DiT HR 1.05, p=0.73, 1-2yr HR 1.25 p=0.12, >2yr HR 1.74 p<0.01). Overall Death Censored GS at 5yr was Pre-empTx 92.7%, 0-1yr 92.3%, 1-2yr 90.0%, 2-4yr 87.2% and >4yr 83.6%. In multivariate Logistic Regression adjusted risk of GF compared to CTx, ABOi and PrEx were at no increased risk of GF (HR 1.02, p=0.89 and HR 0.70, p=0.13 respectively), however HLAI had a HR 1.46 (p<0.01) increased risk of graft failure. Death Censored GS at 5yr was ABOi 88.5%, HLAI 78.3% and CTx 91.1%.

Conclusion

A short time (<1year) on dialysis does not reduce GS in LDKTx in the UK. Compared to CTx, AiT recipients have lower graft survival, however reduced dialysis time was associated with improved GS in ABOi and HLAI. These data help clinicians make informed decision on timing of LDKTx, particularly with AiT recipient: donor pairs.

M005

Donor physiology and the renal micro-environment determine anatomical and functional specialisation of tissue resident mononuclear phagocytes in human kidney

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Introduction

Transplanted organs contain a variety of tissue-resident immune cells, including dendritic cells and macrophages (mononuclear phagocytes, MNPs). MNPs respond rapidly to local immune stimuli including cell damage and microbes, and contribute to renal allograft pathology such as ischaemic injury, alloimmunity and ascending urinary tract infection (UTI). A number of functionally specialised MNP subsets have been described in murine kidneys, however kidney-resident MNPs in humans remain largely uncharacterised. Moreover, the steep interstitial sodium gradient generated to concentrate urine creates a unique environment in which MNPs function, and may influence their phenotype.

Methods

Using human kidneys donated for transplantation but unsuitable for implantation, we investigated the position, function and migration of human kidney MNPs with flow cytometry, confocal microscopy, transcriptomic analysis and rt-PCR. We interrogated the effects of high extracellular sodium, as found in the renal medulla, on phagocytosis, cytokine and chemokine production, particularly in the context of uropathogenic *E. coli* (UPEC) infection. We confirmed the *in vivo* significance of our observations using murine models and human kidneys obtained from organ donors with diabetes insipidus (DI).

Results

We observed an asymmetrical distribution of MNP subsets within the human kidney, with a significant enrichment of MHC II+/CD11c+/CD14+ cells in the medulla compared to cortex. This positioning was orchestrated by renal tubular epithelial production of chemokines CX3CL1 and MCP1 in response to high extracellular sodium in the medulla. This effect was dependent on TonEBP, a transcription factor required for cellular adaptation to hyperosmolality. We hypothesised that the positioning of CD14+ MNPs in the medulla conferred a functional advantage, as this is the region most vulnerable to ascending UTI; indeed we found that CD14+ MNPs avidly phagocytosed UPEC and promoted neutrophil recruitment via the production of interleukin (IL) 8, IL6 and Tumour Necrosis Factor (TNF) alpha. Increased extracellular sodium also optimised the anti-bacterial function of MNPs such that developmental or pharmacological disruption of the intra-renal sodium gradient in mice resulted in abnormal MNP localisation and susceptibility to pyelonephritis. In kidneys from organ donors with DI, we demonstrated reduced CX3CL1 and MCP1 expression in the medulla, aberrant positioning of CD14+ MNPs and a higher frequency of positive ureteric microbiological cultures.

Discussion

Our work provides novel insights into the mechanisms by which the renal micro-environment influences the position and function of kidney-resident MNPs. This has implications for our understanding of local immune responses in kidney transplantation and beyond; suggesting that donor DI and the urine-concentrating defect affecting many renal allografts may alter immune responses in infection, ischaemic injury and alloimmunity. More broadly, we identify a unique paradigm where an evolutionary adaptation essential for homeostasis is used as a cue to optimise local tissue defence.

M006

Young, Caucasian, better educated and less socially deprived patients are more likely to be transplanted with a living donor kidney in the UK

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Introduction

Living donor kidney transplantation (LDKT) has significant benefits over deceased donor kidney transplantation (DDKT) in terms of improved survival and timely access to transplant. There is scope to increase the living donor pool in the UK, but there are limited data regarding the factors that enable patients to receive an LDKT. We investigated the recipient factors associated with LDKT in the UK as part of the Access to Transplantation and Transplant Outcome Measures (ATTOM) study.

Methods

1777 incident kidney-only transplant recipients aged 18-75 years were recruited into the ATTOM study between 2011-2013 from all 72 UK renal units. Of these, 1077 received DDKT and 700 received LDKT. Extensive clinical, socio-demographic and comorbidity data were collected at the time of transplantation. Differences between groups were analysed by Chi-square and Wilcoxon tests. A multivariate logistic regression model was built in a step-wise process to analyse factors predicting the likelihood of receiving LDKT versus DDKT. 1-year graft and patient survival were calculated using the Kaplan-Meier method. All data were analysed using SAS®9.4 and p-values<0.05 were considered significant.

Results

409 (58.6%) LDKTs were from blood-related living donors, of which 192 (47.1%) were parent/child, 177 (43.4%) sibling and 39 (9.6%) other relatives. A significantly higher proportion of LDKTs were pre-emptive compared with DDKTs (38.5% vs 12.6%, p<0.0001). LDKT recipients were younger than DDKT recipients (median age 46.5 vs 53.1, p<0.0001), a higher proportion were female (39.7% vs 35.1%, p=0.048) and Caucasian (87.6% vs 79.4%, p=0.0003). At the time of transplant, 50.5% LDKT recipients had ≥1 comorbidity compared with 59.6% DDKT recipients (p<0.0001). The mean Charlson Comorbidity Score of LDKT recipients was significantly lower than that of DDKT recipients (0.37±0.89 vs 0.60±1.15, p<0.0001). LDKT recipients had a lower prevalence of diabetes (10.3% vs 15.7%, p=0.0005), coronary heart disease (6.8% vs 9.7%, p=0.02), congestive heart failure (1.2% vs 2.7%, p=0.03), cerebrovascular disease (2.9% vs 5.9%, p=0.002) and peripheral vascular disease (1.7% vs 3.4%, p=0.03). There was significant variation in the ratio of LDKTs to DDKTs performed between the 23 transplant centres in the UK (p<0.0001).

Factors significantly reducing the likelihood of receiving an LDKT included increasing age (per year, odds ratio [OR] 0.96, p<0.0001), Asian ethnicity (OR 0.51, p=0.0003), Black ethnicity (OR 0.61, p=0.039) and being divorced/separated/widowed (OR 0.58, p=0.002). Factors increasing the likelihood of receiving an LDKT included female gender (OR 1.25, p=0.036), GCSE / A-level education (OR 1.31, p=0.041), Degree level education (OR 1.46, p=0.011), car ownership (OR 2.21, p<0.0001) and house ownership (OR 1.35, p=0.022).

One-year graft survival was significantly higher for LDKT (98.1% [95% CI 96.8-98.9]) compared with DDKT (95.7% [95% CI 94.3-96.7]) p=0.0055. One-year patient survival post LDKT was 99.0% (95% CI 97.7-99.5) and post DDKT was 97.6% (95% CI 96.4-98.4) p=0.0548.

Discussion

Living donor kidney transplantation offers better one-year graft and patient survival than deceased donor kidney transplantation. Amongst patients suitable for transplantation, those who are older, male, divorced, from ethnic minority backgrounds, have a lower level of education and greater social deprivation are less likely to be transplanted with a living donor kidney in the UK.

M007

Targeting fibrocytes in the context of antibody mediated rejection may prolong survival of solid organs after transplantation

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Introduction

The association between fibrocytes and fibrotic disease processes has been well documented but the contribution that fibrocytes make to the pathogenesis of chronic antibody rejection (cAMR), the largest barrier to successful long term allograft survival, has not been explored. Transplant arteriosclerosis in association with cAMR is characterised by intimal hyperplasia, the consequence of which is arterial stenosis and ischaemia with resultant interstitial fibrosis and late failure of the transplanted kidney. In murine models of allogeneic transplantation and endoluminal carotid artery injury we have shown that neointimal cells are recipient derived collagen-1 +, CD34+, CD45+ fibrocytes capable of producing α -SMA; and that fibrocyte accumulation within the intima can be prevented by inhibition of the serine protease cascade. We hypothesise that fibrocyte accumulation in the arterial intima contributes to intimal hyperplasia after human solid organ transplantation and that targeted inhibition of these cells may prevent vascular remodelling and prolong survival of solid organ transplants.

Methods

Fibrocytes were expanded *in vitro* from CD14+ monocytes after separation from whole PBMC. Immunophenotyping was performed using immunocytofluorescence (ICC/IF) and flow cytometry. A humanised mouse model of human vessel transplant was developed utilising the BALB/c *Rag2*^{-/-}*Il2rg*^{-/-} mouse strain, into which human vessels were transplanted as aortic interposition grafts. Tissue sections underwent antigen-retrieval prior to immunofluorescence (IF) analysis.

Results

In vitro cultured fibrocytes, defined by co-expression of collagen-1, CD45 and/or CD34, ubiquitously express CD31 and intracellular PAR-1. Intracellular staining was diffusely and strongly positive for IFN- γ and CXCL12. 57.33% of fibrocytes express angiopoietin-2 and 47.25% express α -SMA. IF analysis of cross sections of human coronary arteries acquired from post-mortem cardiac transplants revealed evidence of intimal hyperplasia and co-localisation of collagen-1, CD45, CD34 and CD31 with α -SMA within the cells of the neointima. Human vessel transplantation and injection of human PBMC into a BALB/c *Rag2*^{-/-}*Il2rg*^{-/-} humanised mouse strain results in the accumulation of human cellular material that stains with a pattern consistent with human fibrocyte infiltration.

Discussion

These data acquired from human studies corroborate our data generated in pure murine models. Human fibrocytes differentiated *in vitro*, express cell differentiation markers consistent with other published human data as well as our previously published murine data. Human arteries of solid organs lost to cAMR show evidence of intimal hyperplasia, fibrocyte infiltration and extracellular matrix (ECM) protein deposition. PAR-1 activation by thrombin appears to contribute to human fibrocyte differentiation, at least *in vitro*. Targeted inhibition of this differentiation pathway may limit fibrocyte recruitment to the intima preventing vascular remodelling and prolonging survival of solid organs transplants. A humanised mouse model of vessel transplantation is a promising *in vivo* model which alongside *in vitro* models will serve to dissect the cellular and molecular mechanisms underlying this complex pathophysiology.

M008

The use of kidneys from donors with Acute Kidney Injury (AKI): the good, the bad, and the ugly

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Introduction

The widening gap between supply and demand in kidney transplantation has led to the increased use of kidneys from marginal donors, including those with acute kidney injury (AKI). Despite the organ shortage, donor kidneys with AKI are often declined or discarded. To determine if this policy is justified we have analysed outcomes of AKI in a large UK cohort.

Methods

In a retrospective analysis of the UK transplant registry, adult deceased donors between 2003-2008 were evaluated. Donors were classified as no AKI, or AKI stage 1, 2 or 3 according to the AKIN criteria defined by change in creatinine between admission and donation. Relationship of AKI with DGF/PNF, eGFR and graft survival (GS) at 90d and 1y using risk adjusted Cox regression analysis.

Results

11,244 kidneys were included in the analysis. 35% of AKI kidneys were not accepted or transplanted. There is evidence that the chance of graft failure (GF) at 1y is greater for donors with AKI than for those without (GS 89% v 91%, $p=0.02$; OR 1.20 (95% CI: 1.03-1.41)). The odds of DGF and PNF increase with donor AKI stage ($p<0.005$, $p=0.04$ resp). Analysis of association between donor AKI and recipient eGFR suggests risk of inferior eGFR with increasing AKI stage versus no AKI ($p<0.005$; OR 1.25 (95% CI: 1.08-1.31)).

Discussion

This study shows that a significant number of donor kidneys with AKI are discarded. We report a small but significant reduction of 2% in 1y GS of kidneys from donors with AKI. The 20% increased risk of graft failure due to AKI in the donor is similar to the 17% increased risk of graft failure associated with dialysis vintage of 6 months when compared to pre-emptive transplantation, and is significantly lower than the 37% and 55% increased risk of graft failure when dialysing for longer than 1 or 2 years prior to kidney transplantation (Meier-Kriesche, 2005). In this analysis, over 1500 recipients received a donor kidney with AKI and still had a functioning graft at 1y. We conclude that donor kidneys with AKI stage 1 or 2 should not be discarded as they give comparable outcomes; caution is advised for AKI stage 3 donors.

Basic Science
14:30 Wednesday 24 February
Lomond Auditorium

O001

Endotoxemia is a novel driver of systemic inflammation and endothelial activation in kidney transplant recipients

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Introduction

Cardiovascular disease is the leading cause of death and a major driver of graft loss in kidney transplant recipients (KTRs). Traditional cardiovascular risk factors incompletely explain the increased incidence of cardiovascular events in KTRs. Inflammation correlates with endothelial dysfunction in general and chronic kidney disease populations. In turn, endothelial dysfunction is considered the earliest detectable stage of cardiovascular disease. Although less studied in kidney transplantation, recent evidence confirmed that inflammation is an important and reproducible risk factor for cardiovascular events, all-cause mortality, and graft failure among KTRs. Despite its clinical significance, the factors contributing to inflammation among KTRs remain under-investigated, and it is unclear whether the underlying determinants of inflammation or the inflammatory process itself that leads to such adverse outcomes. A potential source of inflammation and endothelial dysfunction in KTRs may arise through gut-derived endotoxemia. The primary objective of this study was to investigate the role of endotoxemia on inflammation and endothelial activation in clinically stable KTRs, alongside traditional cardiovascular factors, as well as novel risk factors including hypovitaminosis D, hyperuricemia, hypoadiponectinemia, and high dietary intake of fructose.

The secondary objective was to explore the determinants of endotoxemia in this setting.

Methods

This single-centre cross-sectional study enrolled 128 clinically stable KTRs. Fasting serum samples were collected for measurements of high-sensitivity C-reactive protein (hsCRP), soluble E-selectin (sE-selectin), endotoxin, 25-hydroxyvitamin D, adiponectin, urate, full lipid profile, and estimated glomerular filtration rate. Dietary intakes were determined by 3-day food diary. Body composition was measured using bio-impedance based body composition monitor. Central obesity was assessed using waist circumference.

Demographic, nutritional and clinical predictors of inflammation (hsCRP), endothelial activation (sE-selectin), and endotoxemia (endotoxin) were assessed using univariate and multivariate regression analyses.

Results

Endotoxemia ($\beta=0.18$, $p=0.03$), reduced vitamin D ($\beta=-0.20$, $p=0.04$), high fructose intake ($\beta=0.11$, $p<0.001$), decreased dietary fibre intake ($\beta=-0.16$, $p<0.001$), and increased waist circumference ($\beta=0.05$, $p=0.002$) were associated with hsCRP independently. Endotoxemia was also associated with raised sE-selectin ($\beta=0.04$, $p=0.007$) independently of inflammation ($\beta=0.50$, $p=0.02$). Other independent predictors of elevated sE-selectin levels include low adiponectin levels ($\beta=-0.04$, $p=0.004$), increasing waist circumference ($\beta=0.30$, $p=0.005$), male ($\beta=0.07$, $p=0.01$), and elevated mean arterial pressure ($\beta=0.30$, $p=0.006$). Determinants of endotoxemia include reduced vitamin D ($\beta=-0.11$, $p<0.001$), raised triglycerides ($\beta=0.06$, $p<0.001$), increased fructose intake ($\beta=0.10$, $p=0.01$), and increased waist circumference ($\beta=0.20$, $p=0.01$).

Discussion

Endotoxemia in KTRs contributes to both systemic inflammation and endothelial activation. The association between endotoxemia and endothelial activation independently of inflammation suggests a possible non-inflammatory mechanism of endothelial activation. Targeting endotoxemia may serve as a potent upstream intervention for endothelial activation in KTRs, thereby improving cardiovascular outcome in this population. This study demonstrates potential targets for intervention, and sets the scene for future interventional research and therapeutic strategies.

O002

TGM – A novel Helminth-derived immunomodulatory molecule that ameliorates allograft rejection

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Background

Immunosuppression for transplantation is associated with considerable morbidity. Helminth parasites have evolved to effectively suppress immune responses whilst ensuring the wellbeing of their hosts. This project investigated the potential of helminth-derived proteins as novel therapeutic agents.

Methods

Allogeneic (BALB/c to C57BL/6) skin grafts were performed alongside *Heligmosomoides polygyrus* infection, or insertion of a minipump infusing *H. polygyrus* excretory-secretory products (HES). Allografts were monitored for rejection and draining lymph nodes were harvested for analysis by flow cytometry. HES was assessed for TGF-beta activity (MFB-F11 bioassay) and capacity to induce the regulatory transcription factor, Foxp3, in T cells. Finally candidate proteins within HES were produced as recombinant molecules in HEK293 cells.

Results

Infection of allograft recipients (n=28) with *H. polygyrus* prolonged the median survival of fully-allogeneic skin grafts by 40% compared to controls (n=26; p < 0.0001). Similar allograft protection was achieved with HES (n=13; allograft survival of 14 days vs. 10, p < 0.0001). In comparison to control animals, *H. polygyrus* infection induced modest increases in Foxp3+ Treg abundance within allograft-draining lymph nodes (+18.1%, p = 0.0028), as did HES (+16.2%, p = 0.0034). Expression of the (Th1 and Th17) effector T cell transcription factors Tbet and ROR-gt returned to baseline in infected and HES-treated allograft recipients and the cytokines IFN-g and IL-17 were also suppressed upon alloantigen restimulation. HES was shown to induce *de novo* Foxp3 expression in human and mouse CD4+ T cells via the TGF-beta receptor. Active candidate molecules within HES were then identified and expressed as recombinant proteins. Of these, TGM has emerged as a novel TGF-beta homologue that can recapitulate the effects of HES including prolongation of allograft survival.

Discussion

TGM is a novel immunomodulatory molecule (patent pending) that prolongs murine allograft survival *in vivo*, is biologically active in human T cells and may lead to a long-overdue alternative to current immunosuppression options.

O003

B-Cell populations and signatures of operational tolerance are markedly affected by immunosuppression in long-term renal transplant recipients

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Introduction

European and American consortia have independently proposed immune phenotypes ('signatures') which may discriminate RTR who demonstrate operational tolerance (stable allograft function in the absence of pharmacological immunosuppression) from those who are maintained under a variety of immunosuppressive regimens. The identification of renal transplant recipients (RTR) under immunosuppression who also display these 'signatures' may enable safe and targeted drug minimisation. We hypothesised that immunosuppression itself may have an impact upon circulating B cell populations and therefore previously published 'signatures' of operational tolerance.

Methods

117 stable RTR with a median duration of immunosuppression of over 20 years were recruited. Circulating immune phenotype was assessed by flow cytometry and RT-PCR. The presence of anti-HLA antibodies was identified using Luminex assays. The effect of immunosuppression upon variables was assessed using multivariate regression.

Results

Azathioprine therapy was independently associated with a reduction in the number of circulating naïve and transitional B cells, whilst calcineurin inhibition was associated with an increase in the number of isotype switched memory B cells and plasmablasts. Azathioprine and corticosteroid therapy were linked to changes in multiple aspects of the European signature of operational tolerance, whilst calcineurin inhibition was associated with alterations in aspects of the American signature.

22/117 RTR (19%) exhibited donor-specific antibodies (DSA). Surprisingly, given the effect upon circulating plasmablasts, calcineurin inhibition was not associated with the presence of DSA. However, upon correction for clinical risk factors, azathioprine therapy remained independently associated with the presence of DSA (OR [95%CI]: 4.5[1.0–20.2], p=0.048).

Discussion

Immunosuppression has a marked effect upon the circulating B cell phenotype, which independently impacts upon both the previously published European and American signatures of operational tolerance and may limit their use in their current form for future clinical studies. The point prevalence of DSA in a very long-term transplant cohort, reported here for the first time, is similar to that described in RTR in the first decade post-transplant and suggests that prevalence remains stable with time. Azathioprine therapy is independently associated with DSA and may provide a rationale for a switch to MMF. Longitudinal follow-up will confirm the pathogenicity of these DSA.

O004

Activated cytoprotective mechanisms in DBD donor kidneys correlate with kidney function in transplant recipients: A study using clinical samples from the UK QUOD Biobank

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Introduction

Brain dead organ donors are the main source of deceased donor kidneys for transplantation. The onset of complex and abnormal pathophysiological changes following brain death adversely impact on the short and long term function of kidneys following transplantation. Understanding and delineating the biological mechanisms that affect kidney quality will allow better allocation of donated kidneys, minimising discard and promoting the development of novel interventions that will improve allograft outcomes.

Methods

Deceased donor clinical samples and associated donor and recipient clinical and demographic data were received from the QUOD biobank. Kidney biopsies obtained at kidney retrieval from 40 DBD donors were matched for donor and recipient age, cold ischemic time and grouped according to kidney function following transplantation. The combination of delayed graft function (DGF) in the recipient and a median eGFR of 28ml/min (range 16 to 39 ml/min) at 3 month post transplantation was defined as suboptimal kidney function while immediate kidney function and median eGFR of 64ml/min (range 50 to 79 ml/min) at 3 months follow up as good function. Initially, using label free quantitative proteomics we compared 5 individual samples per group using tandem mass spectrometry (LC-MS/MS, Q Exactive). Proteins of interest were validated by immunoblotting on a separate cohort of 15 samples per group. Kidney biopsies from living donors were analysed in parallel as control group.

Results

Without “*a priori*” assumptions and based only on kidney proteomic signatures in the donor we could differentiate the donors with kidneys that developed suboptimal function after transplantation (Fig1). An increased regulation of the apoptosis mediator signal transducer and activator of transcription factor-1 (STAT-1) was found in addition to enhanced degradation of cytoskeletal proteins and extracellular matrix integrin proteins of kidneys with suboptimal function. This indicated, that prior to retrieval, donor kidneys had suffered from injury associated with acute kidney injury. An increased abundance of antioxidant proteins such as thioredoxin and peroxiredoxins in good outcome-associated kidneys demonstrated the parallel activation of repair mechanisms.

Discussion

The fingerprint of brain death on donor kidneys conveys biological information to the tissue proteome that can discriminate the kidneys with suboptimal function from those with good function in the recipient. Donor kidney quality depends on the balance of ischemia and repair and interventions in the donor should aim to reduce injury and enhance repair mechanisms.

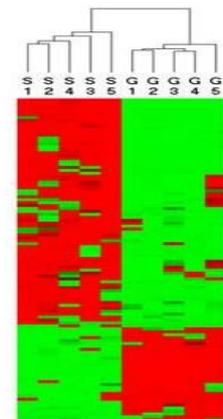


Fig1. Proteomic signature of donor kidneys clusters groups separately. S: suboptimal G: Good outcomes

O005

The role of the transcription factor Nrf2 as a potential enhancer of hepatic regeneration

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Introduction

The liver has a remarkable capacity for regeneration following hepatectomy; however, acute hepatic failure remains a significant and often fatal complication following major hepatectomy. The transcription factor Nrf2 plays a pivotal role as a master regulator of cyto-protection against oxidative stress, nevertheless, its role in hepatic regeneration is still ill-defined. We sought to investigate the prospect of Nrf2 as a potential enhancer of hepatic regeneration, which could pave the way for promising translational outcomes.

Methods

A murine model was used utilising C57BL/6J mice and two thirds partial hepatectomy was performed, followed by culling the mice at different time points. The liver tissue was collected at both the time of surgery and the time of cull. Pharmacological induction of Nrf2 was implemented by intra-peritoneal administration of CDDO-Me both pre and post op. Nrf2 knockout mice were used as negative controls. Western blots for the proliferation marker PCNA were performed, and correlated to Nrf2 and Nrf2 downstream protein NQO1. Gene expression of the Nrf2 dependent proteins was investigated using qPCR.

Results

A significant correlation between the increase of proliferation and Nrf2 activity was observed at 48 hours post-hepatectomy especially in the CDDO-Me treated mice as compared to the non-treated and knockout mice. The Nrf2 knockout mice showed decrease in proliferation at 24 hours post-hepatectomy as compared to the other 2 groups.

Conclusion

The transcription factor Nrf2 has a potential major role at the early stages of liver regeneration. Pharmacological or dietary induction of Nrf2 pre and post major hepatectomy could be a simple and effective way of decreasing the incidence of the devastating occurrence of post-hepatectomy liver failure.

O006

Diagnosis and treatment of acute antibody mediated rejection in the UK: results of a multicentre survey

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On behalf of the renal transplant units in the UK, NA, UK

Introduction

Acute AMR (aAMR) is strongly associated with the development of chronic AMR (cAMR), which is the leading cause of allograft failure in the modern immunosuppressive era. Despite this, the treatment of aAMR is diverse and there are no published clinical trials either in the UK or abroad to guide its management. The aim of this study was to perform a scoping questionnaire to establish how aAMR is diagnosed and treated in the UK with a view to potential collaboration and development of appropriate multicentre clinical trials.

Methods

An electronic questionnaire was sent to all 23 adult renal transplant units in the UK. Respondents were asked questions as to how aAMR was diagnosed and treated. All 23 units responded and the results are summarised below.

Diagnosis of aAMR:

Respondents were asked if they would apply their aAMR treatment protocol in the following clinical settings if a patient had allograft dysfunction.

| Criterion | Units affirming [N=23] | % |
|----------------------|------------------------|-------|
| Histology+/C4d+/DSA- | 17 | 73.91 |
| Histology+/C4d-/DSA+ | 21 | 91.30 |
| Histology+/C4d-/DSA- | 11 | 47.83 |
| Histology-/C4d+/DSA+ | 15 | 65.22 |

(*histology+ = classical aAMR changes including capillaritis, glomerulitis etc)

Treatment for aAMR:

Respondents were asked which treatment protocols they have used for patients meeting full aAMR criteria: Histology+, C4d+, DSA+ and graft dysfunction.

| Agents Used | Units affirming [N=23] | % |
|--------------------------|------------------------|--------|
| Plasma exchange (PEX)/IA | 23 | 100.00 |
| Iv Ig | 21 | 91.30 |
| Rituximab | 14 | 60.87 |
| Bortezomib | 3 | 13.04 |
| ATG | 15 | 65.22 |

In addition the number of PEX's and the dose of iv Ig varied significantly between each unit. Furthermore, 4/23(17.39%) units had performed splenectomies for aAMR and 8/23 (34.78%) had used eculizumab.

Discussion

The clinical criteria used to treat aAMR and the corresponding therapeutic agents employed varies amongst the transplant units in the UK. Given the impact of aAMR on allograft survival, priority should be given to establish appropriate guidelines which could be developed by focused collaborative working in the form of a multicentre trial amongst the UK transplant units.

O007

An effective strategy for kidney transplantation in highly sensitised individuals

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Introduction

Kidney transplantation in highly sensitised individuals is a major challenge. The limited access to transplantation for this group has prompted modifications to allocation schemes worldwide. Highly sensitised patients have a prolonged waiting time prior to transplantation resulting in the accumulation of comorbidities on dialysis which are detrimental to graft and recipient survival. In January 2013, our centre had the third longest waiting time for kidney transplantation in the UK (median 1631 days) with 30 individuals (18% of active list) who had waited more than five years for a kidney transplant. Nineteen of these patients had a calculated reactive frequency (cRF) > 85%.

Methods

The unacceptable antigens listed with ODT for each patient were reviewed by the Histocompatibility and Immunogenetics laboratory in conjunction with the transplant nephrologist. For each patient, their source of sensitisation, antibody profile over time, HLA type and clinical status were considered. Additional testing including C1q assays, IgM assays and exploratory complement dependent cytotoxicity (CDC) cross matching was undertaken on a case by case basis. Unacceptable antigens were removed which maximised each individual's chance of receiving a compatible offer (with preferential removal of antigens in linkage disequilibrium with the patient's own HLA type) while ensuring that the clinical risk of transplantation remained acceptable. Unacceptable antigens were not removed if the patient currently demonstrated a complimentary antibody which would be anticipated to cause a CDC positive cross match.

The course of action was discussed with each patient with the increased risks of transplantation explained. In addition, patients were encouraged to explore potential living donor options.

Results

29/30 patients have been transplanted since 2013. Living donors were the transplant source in 5/29 recipients while 24 received kidneys donated after brain death. Two recipients underwent desensitisation for HLA incompatible transplantation. In addition, six individuals had historically positive CDC cross matches and three patients had historically positive isolated flow cross matches. Lymphocyte depleting induction was administered in these cases. All recipients received tacrolimus, mycophenolate mofetil and prednisolone.

25/29 recipients currently have functioning grafts. Two kidneys from extended criteria donors had primary non-function; the paired kidneys also failed to function in these cases. One individual who underwent desensitisation for an HLA incompatible transplant lost his graft from recurrent disease at 10 months. There was no acute rejection. One recipient died six months after transplantation from a myocardial infarction.

There are currently two patients on the active transplant list at our centre whose waiting time exceeds five years. The median waiting time is now 315 days.

Discussion

Timely transplantation of highly sensitised recipients is possible with detailed review of the sensitisation history and acceptance of an associated increased risk by both the patient and transplant professionals. Judicious removal of unacceptable antigens did not result in an increased incidence of acute rejection or early graft loss in this cohort. This strategy is now applied to all highly sensitised patients and has allowed the pre-emptive transplantation of two individuals whose cRF exceeded 90%.

O008

Renal and haematological outcomes with Eculizumab in native kidney and transplanted patients with atypical Haemolytic Uraemic Syndrome (aHUS): analysis of 100 patients

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Introduction

Patients (pts) with aHUS often progress to end-stage renal disease. In pts with aHUS there is a high risk of early graft loss after transplantation. Eculizumab inhibits thrombotic microangiopathy (TMA), irrespective of renal transplant status. We evaluate the outcome of pts with native and transplanted kidneys who were enrolled in four prospective studies of eculizumab.

Methods

Data were pooled from 4 prospective phase II eculizumab trials with long-term extensions (N=100). Median (range) eculizumab treatment duration was 71 (0–186) weeks. Primary efficacy outcomes include: haematological normalisation (platelet count and lactate dehydrogenase [LDH]) and complete TMA response (haematological normalisation and $\geq 25\%$ decrease in serum creatinine from baseline, both for >2 measurements ≥ 4 weeks apart). We compare results for native kidney (n=74) and transplanted pts (n=26).

Results

Baseline characteristics between the groups were comparable in terms of gender, mutation status, platelet count, LDH and estimated glomerular filtration rate (eGFR). However transplanted pts were significantly older and had longer time to treatment. Prior to eculizumab use, grafts had been lost in pts with aHUS (38 transplants in 26 pts). Treatment with eculizumab led to complete TMA response in 74% (55/74) of native kidney and 65% (17/26) of transplanted pts. Similarly, haematological normalisation occurred in 96% (71/74) and 85% (22/26), respectively. The mean (standard error [SE]) increase in platelet count at 18 months was $135.6 (15.4) \times 10^9/L$ for native kidney pts and $83.1 (29.8) \times 10^9/L$ for transplanted pts. The mean (SE) eGFR at start of treatment was 24.2 (2.5) and 25 (3.3) mL/min/1.73m² for native kidney and transplanted pts, respectively. eGFR significantly increased from baseline in both groups over time. At 18 months, mean (SE) eGFR was 65.7 (5.3) and 41.5 (6.0) mL/min/1.73m², respectively. No pts lost their graft after initiation of eculizumab. No unexpected safety concerns were reported: most adverse events were mild or moderate. Two pts (one per group) had a meningococcal infection. Both pts had been vaccinated and were not on prophylactic antibiotics at the time of infection. Infection resolved with antibiotic treatment and the native kidney pt continued receiving eculizumab.

Discussion

In pts with aHUS, eculizumab is well tolerated and improves renal function irrespective of renal transplant status. Early recognition and treatment of aHUS is important to minimise irreversible organ damage and should reduce the need for transplantation in pts with aHUS.

O009

Deceased donor ABO-incompatible kidney transplantation: a feasibility study

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Introduction

Blood group incompatible transplantation is widely accepted and practised worldwide. In some centres, tailored desensitisation treatment is based on baseline anti-A or anti-B antibody titre and, in cases of low titre ABO-antibody ($\leq 1:8$), pre-treatment prior to transplantation may not be necessary. Although ABO-incompatible deceased donor cardiac and liver transplantation is utilised, deliberate ABO-incompatible transplantation for kidney recipients is not a feature of the modern era of transplantation. We studied the distribution of baseline ABO-antibody titres of adults on the kidney transplant waiting list, as a first step to estimate the numbers of patients suitable for low-titre deceased donor ABO-incompatible transplantation.

Methods

A prospective study of adult patients on the waiting list for a transplant in 2 London transplant centres. A total of 237 patients have been recruited to the study. Anti-A and Anti-B titres and CRF were measured at baseline. ABO-antibody measurements (anti-A and anti-B) were measured by indirect antiglobulin test (IAT) using gel card agglutination (DiaMed) in a single laboratory. Antibody levels are expressed as dilutions.

Results

Of the 237 patients, blood groups are as follows: Blood Group A n= 68 (28.7%), AB n = 6 (2.5%), B = 41 (17.3%), O = 122 (51.5%); AB patients and those (n=4) with atypical ABO antibodies did not have titre analysis. Ethnicities were: Asian = 23 (9.7%); Black = 110 (46.4%); White = 90 (38.0%); other = 14 (5.9%). 74.2% of patients were on haemodialysis, 10.8 on peritoneal dialysis and 15% were not currently dialysing. For blood group O patients, mean waiting time was 885d (± 710 d); blood group B 899d (± 581); group A 767d (± 552) and AB 634d (± 590). Median dilution of anti-A titre was 7 (titre 1:128 ,IQR 6-9,); mean dilution of anti-B titre was 5 (3-7). Patient of blood group O generally had higher anti-A or anti-B titre measurements than patients with anti-A or anti-B antibody alone: of blood group O, median anti-A titre dilutions were 8 (titre 1:256 ,IQR 6-9) compared to anti-A titre dilutions of 4 (titre 1:16, IQR 3-5) in blood group B patients ($p < 0.05$). Similarly, anti-B titres of Blood Group O patients were 6 (titre 1:64, IQR 5-8) compared to 3 (titre 1:8, IQR 2-4) in blood group A patients (median dilution (3, IQR 2-4, $p < 0.05$). There was no correlation between CRF and anti-A titre dilution ($r=0.095$, $p = 0.37$); or anti-B dilution ($r = -0.04$, $p=0.66$). Of patients with anti-A antibody, 7% had a titre of 1:8 or less; while for patients with anti-B antibody, 27% had a titre of 1:8 or less.

Discussion

Blood group O patients generally have higher antibody titres than Groups A or B. There does not appear to be any correlation between patients with high CRF and those with a high ABO antibody titre. While the blood group distribution within our sample reflects a diverse London population, over a quarter of this sample might be suitable for low-titre ABO-incompatible transplantation from a deceased donor with no additional treatment. For patients with a baseline titre of 1:64 or less, a single session of double column IA or DFPP would bring ABO-antibody level down sufficiently to allow for transplantation to proceed, thus increasing the scope of this deceased donor transplant strategy. Deceased donor ABO-incompatible transplantation is feasible, and further work to model the difference in UK transplantation rates, by blood group, if low-titre ABO-incompatible graft allocation were permissible, is planned.

O010

Proteasome inhibitor-based therapy for antibody mediated rejection in renal transplant recipients

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Introduction

Antibody-mediated rejection (AMR) in renal transplantation is less responsive to conventional therapies and is associated with reduced allograft survival. The proteasome inhibitor, bortezomib, is a promising new therapy for the treatment of AMR. We report our experience of bortezomib in the treatment of early and late AMR.

Methods

We undertook a retrospective review of renal transplant recipients who received bortezomib as rescue therapy in the management of AMR from 1st Jan 2013 until 1st Nov 2015. AMR was diagnosed by supportive histology (microvascular inflammation, intimal arteritis), the presence of circulating donor specific antibodies (DSA) with or without evidence of C4d staining. We collected data on serial creatinine, DSA levels (expressed as cumulative median fluorescence intensity ,cMFI), allograft biopsies, adverse events and graft survival.

Results

Ten patients received bortezomib for AMR. Five were diagnosed with acute active (early) AMR (median 7 days (5-11) post transplant, all had pre-formed DSA). Five were diagnosed chronic active (late) AMR (median 1641 days (213 -2766) post transplant, all had de novo DSA). All patients also received plasma exchange (PEX) and intravenous immunoglobulin (IVIG, 100mg/kg post PEX). Median follow up from time of transplant was 636 days (144 – 3164), from first dose of Bortezomib was 421 days (131 – 778). In patients with early AMR, mean percentage reduction in cMFI was 82% (+/- 10) following treatment. Complete resolution of microvascular inflammation with improved allograft function was reported in four out of five patients. Four patients had a functioning graft at latest follow-up with mean eGFR of 48ml/min/1.73m² (+/-7) with one graft failure due to transplant glomerulopathy. In patients with late AMR, treatment resulted in 50% (+/- 19) mean reduction in cMFI. However four of five patients demonstrated on-going chronic active AMR with moderate to severe transplant glomerulopathy on repeat biopsy. At end of follow up, three patients had a functioning graft with a mean eGFR 64ml/min/1.73m² (+/- 27) and two grafts failed. No serious adverse effects were reported during the study period.

Discussion

Our results, in a small cohort of patients, suggest that bortezomib, with PEX and IVIG, is effective at lowering DSA cMFI, reversing microvascular inflammation and improving renal allograft function in selected patients with early acute AMR. Its efficacy and role in late AMR remains to be defined. Larger studies with longer follow up are needed to examine these findings.

O011

Is it possible to identify patients at an increased risk for early graft loss and mortality in HLA-antibody incompatible renal transplantation?

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Introduction

Waiting times on the deceased donor list are adversely affected by preformed antibody, and therefore sensitised patients may choose to undertake an HLA-antibody incompatible transplant from a living donor (HLAiLD). However, in some patients, HLAiLD is complicated by aggressive early rejection and/or death. The aim of this study is to determine which patients are at increased risk of this poor outcome.

Methods

We performed a retrospective study of patients receiving desensitisation (antibody removal +IVIG) for a FCXM positive HLA-antibody incompatible LD kidney transplant in a single centre from 2005 – 2015. 50 eligible patients (31 female, 19 male, aged 14 – 66) were divided into those who had 'poor outcome' (PO HLAiLD) defined as either graft loss or death within 6 months of transplantation and those who were alive with a functioning graft at 6 months follow-up ('good outcome'; GO HLAiLD). We considered demographic and immunological features characterising each group of patients. Pearson Chi-Square test was used to compare proportions. T-test was used for testing of equality of means.

Results

| Characteristics | POHLAiLD N=8 | GOHLAiLD N=42 | Stat significance P value | Pos predictive value | Neg predictive value |
|-----------------------------------|-----------------|------------------|------------------------------|-------------------------|-------------------------|
| Female | 87.5% | 57% | P = 0.134 | 25% | 95% |
| Age more than 40 | 100% | 50% | P = 0.009 | 28% | 100% |
| Repeat mismatch from pregnancy | 100% | 64% | P = 0.043 | 23% | 100% |
| from previous tx | 87.5% | 40% | P = 0.001 | 41% | 97% |
| | 12.5% | 24% | P = 0.131 | 6% | 78% |
| DSA | | | | | |
| Class I alone | 12.5% | 33% | P = 0.239 | 7.7% | 78.8% |
| Class II alone | 0% | 14% | P = 0.254 | 0% | 57% |
| Class I+II | 87.5% | 48% | P = 0.065 | 21% | 95% |
| Baseline MFI (mean) | 28346 | 18980 | P = 0.71 | | |
| Pre-tx MFI (mean) | 10914 | 9289 | P = 0.51 | | |
| Baseline FCXM (mean) | | | | | |
| Allo T cell | 4.938 | 3.322 | P = 0.258 | | |
| Allo B cell | 8.803 | 5.511 | P = 0.044 | | |
| Pre Tx FCXM (mean) | | | | | |
| Allo T cell | 1.84 | 1.3135 | P = 0.042 | | |
| Allo B cell | 3.045 | 2.024 | P = 0.051 | | |

A combination of age more than 40 with, repeated mismatch to pregnancy antigens and presence of both class I and II was predictive of a poor outcome (p,0.001) with a predictive value of 100% and negative predictive value of 93%.

Discussion

In our HLAiLD cohort patients with poor outcome were mostly females aged more than 40 with repeated mismatch to pregnancy antigens and class I and II DSA. Baseline MFI was not associated with a poor outcome. This phenomenon is most likely related to factors shaping immunological memory, and provides useful initial data in risk stratification of HLAi recipients.

O012

A health economic analysis of induction therapy with rabbit antithymocyte globulin (rATG, Thymoglobulin®) versus basiliximab after kidney transplantation: a German perspective

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Introduction

A major cost of transplantation is the induction regimen but robust comparisons of the economic implications of different induction agents are rare. We undertook a health economic analysis to quantify the economic consequences of acute rejection and serious adverse events in patients receiving induction with rATG (Thymoglobulin®) vs the monoclonal antibody basiliximab (Simulect®) during the first year after kidney transplantation from a German perspective.

Methods

Current costs at 3 German centers during the first year after kidney transplantation were obtained and applied to the database from a randomized trial of rATG versus basiliximab in 278 kidney transplant patients (Brennan DC et al. N Engl J Med 2006; 355: 1967-77). A 4-state Markov model was applied to analyze transitions between health states (never transplanted, alive/functioning graft, alive/graft failure and dead), and quality-adjusted life years (QALYs) were calculated.

Results

During year 1, the mean treatment cost of induction therapy was €5,378 more per patient for rATG than basiliximab (€7,792 vs €2,414). The mean cost for managing rejection was lower under rATG vs basiliximab (€471 vs €1,515, $p=0.02$) due to a lower rate of acute rejection (15.6% vs 25.5%, $p=0.02$) and rejection requiring antibody therapy (1.4% vs 8.0%, $p=0.005$). The costs associated with managing delayed graft function, graft failure, and dialysis after graft failure were numerically lower in the rATG group. Costs related to treatment of infection were virtually identical with either agent. At 1 year post-transplant, 91% vs 88% of grafts were functioning in the rATG and basiliximab groups, respectively ($p=0.40$), incurring higher routine graft maintenance costs in the rATG cohort (€8,905 vs €8,539, $p=0.34$). In total, the estimated treatment cost to year 1 post-transplant was €85,306 with rATG vs €83,144 with basiliximab ($p<0.01$). Due to improved graft survival under rATG, costs per patient were projected to be €514 lower at 2 years, and €4,405 lower at 10 years, using rATG vs basiliximab. The initial utility difference of 0.007 QALYs per patient for rATG versus basiliximab increased to 0.096 QALYs by year 10 post-transplant.

Discussion

The higher treatment cost for rATG vs basiliximab is partly offset during the first year after kidney tx by lower costs for managing rejection and other adverse events. After the first post-transplant year, a lower rate of return to dialysis in rATG-treated patients results in a QALY advantage and a substantial cost reduction versus basiliximab, which increases over the first 10 years post-transplant.

Best Practice Kidney
14:30 Wednesday 24 February
Alsh Suite

O013

Donor smoking increases kidney allograft recipient mortality in a national population cohort analysis

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Introduction

Current evidence from single-centre analyses suggest cigarette smoking in living donors is associated with worse patient but not graft survival in kidney allograft recipients. The effect of donor smoking status on recipient outcomes has not been clearly documented in a UK population. The aim of this nationwide analysis was to explore whether a kidney from a donor with a history of smoking had any impact upon hard recipient outcomes like mortality or allograft loss.

Methods

This study analysed the NHS Blood and Transplant dataset for all kidney transplants performed in the UK from April 2001 to April 2013. The effects on transplant outcome (graft and recipient survival) were examined with respect to the donors smoking history. Kaplan-Meier survival analysis and Cox proportional hazard modelling was used with covariates including donor variables, recipient variables and transplant variables included in the model.

Results

We analysed data on 21,805 kidney allograft recipients, with average follow up of 1,961 days. The cohort comprised on the following; first kidney transplant (n=18,922, 86.8%), incompatible kidney allograft (n=933, 4.3%), deceased donors (14,042, 64.4%), male (11,021, 50.5%) and Caucasian ethnicity (20,132, 92.4%). From the cohort, 7068 (32.4%) of the donors had a documented history of smoking. Donors after brain death or cardiac death were more likely to have smoking history compared to living donors (47.1% versus 43.7% versus 31.5% respectively, $p < 0.001$). Donors who were smokers were more likely to be younger than the median age of 48, male and Caucasian. Recipients of kidneys from smoking donors were slightly older than those receiving kidneys from non-smokers (45.5 versus 45.0 respectively, $p = 0.029$). Our main finding was that donor history of smoking versus non-smoking significantly decreased patient survival (88.3% versus 89.8% respectively, $p = 0.003$) but did not affect graft survival (84.1% versus 84.5% respectively, $p = 0.252$).

Conclusion

Donor smoking is not associated with adverse kidney allograft survival but is associated with decreased recipient patient survival. This data corroborates some single-centre analyses and requires further investigation, with data linkage across registries to minimise risk of confounding from unappreciated variables.

O014

Donation after circulatory death kidney transplantation for paediatric recipients

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Introduction

Donation after circulatory death (DCD) is an important source of organs for kidney transplantation and evidence in adults suggests that similar graft outcomes are achieved to donation after brain death (DBD) kidney transplantation. There is very little evidence reporting the use of DCD kidneys in children. The aim of this study was to determine graft outcomes for children in the UK who have received a DCD kidney and compare these to outcomes for all kidney transplants.

Methods

Data was collected on all kidney transplants performed for paediatric recipients (age <18 years) in the UK from the NHS Blood and Transplant registry from 2000-2014 and separated into DCD, DBD and living donor (LD) kidney transplants. Kaplan-Meier analysis was used to estimate 3-year renal allograft and patient survival. The univariate log-rank test was used to compare renal allograft survival across the three donor groups. All data were fully anonymised and ethical principles adhered to.

Results

1,773 kidney transplants were performed in children in the UK from 2000-2014. 22 (1.2%) of these were from DCD donors, 955 (53.9%) were from DBD donors and 796 (44.9%) were from LD donors. 3-year renal allograft survival was 95.5% in the DCD group, 87.1% in the DBD group and 92.9% in the LD group. Overall patient survival is 100% in the DCD group, 98.7% in the DBD group and 98.8% in the LD group. In the DCD group the median time to asystole was 12.5 minutes and the median functional warm ischaemia time was 25 minutes. In the DCD group there was 1 case of primary non-function and 5 cases of delayed graft function.

Discussion

This is one of the largest studies reporting outcomes in children who receive DCD kidney transplants. Children receiving a DCD kidney transplant have good graft survival at 3-year follow up, comparable to those receiving a kidney from a DBD donor or a living donor. This limited evidence encourages the use of selected DCD kidneys in paediatric transplantation as favourable graft outcomes can be achieved, and DCD allocation algorithms may need to be amended in view of this.

O015

5 years of 1-Days: Outcomes of potential living kidney donors undergoing a 1-day assessment pathway

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Introduction

Renal transplantation is the optimal treatment for end stage renal disease with improved patient survival and quality of life. Living versus deceased kidney donation affords an increased benefit to both recipient and graft survival in addition to facilitating earlier transplantation. Prior to 2010, our region had a low rate of living donor renal transplantation with few of these performed pre-emptively. A major contributing factor was a lengthy donor work-up process with multiple assessment stages, often leading to donor fatigue and drop-out.

From March 2010, suitable donors selected after a screening questionnaire attended a 'one-day' assessment with all appropriate assessments organised for a single day. This required a transformative process with collaboration between multiple specialties. Investigations included HLA typing and crossmatch, EDTA GFR estimation, urine screening, virology testing, electrocardiogram, chest X-ray, ultrasound scanning, contrast enhanced computed tomography and a medical evaluation by a consultant nephrologist. We assessed the outcomes of potential living kidney donors who had been through this process and explored reasons why some potential donors did not proceed to donation. The impact on the living donor transplant rate was evaluated.

Methods

A prospectively kept database of all potential live donors from March 2010 to March 2015 in our region was interrogated. Donor demographics, donation rates and reasons for donor exit from the programme were determined.

Results

Following a simple screening questionnaire, 431 were considered potentially suitable to donate and proceeded to one-day assessment. 190 (44%) were male with mean age 48 years (range 22-78yr.). 23 were assessed for non-directed altruistic donation. 269 (62%) ultimately donated while 34 (8%) remain active as potential donors in the programme.

128 (30%) potential donors exited from the programme. Of these, 44 (34%) were unsuitable to donate due to concerns with donor anatomy or renal function, 17 (13%) withdrew, and 3 donors became unsuitable. For 36 donors (28%), of whom 29 were incompatible and 7 were compatible but not ideal, recipients found an alternative living donor or received a deceased donor transplant. For 23 donors (18%) the recipient had issues that made transplantation inappropriate and 5 recipients withdrew for other reasons.

There has been a significant and sustained increase in the living donor kidney transplant rate in our region from a mean of 4.3 pmp per annum in 2000-2010 to 32.6 pmp per annum in 2011-2015.

Discussion

A 1-day assessment process for potential living kidney donors is safe and efficient. It has contributed to a sustained increase in the number of living donor kidney transplants in our region. A philosophy of making it as easy as possible to donate should be adopted to increase the number of living donor kidney transplants and enhance the donor experience.

Pregnancy outcomes in renal transplant recipients in England over 15 years

Nadia Sarween¹, Sian Hughes², Felicity Evison², Irena Begaj², Clara Day¹, Ellen Knox³, Graham Lipkin¹

¹University Hospitals Birmingham NHS Foundation Trust, Department of Renal Medicine, West Midlands, UK, ²University Hospitals Birmingham NHS Foundation Trust, Department of Health Informatics, West Midlands, UK, ³Birmingham Women's Hospital NHS Foundation Trust, West Midlands, UK

Introduction

Pregnancy outcomes in renal transplant recipients are usually favourable but are frequently complicated for both mother and baby. Current pre-pregnancy advice is largely based on outcomes reported by international (non-UK) registries with voluntary submissions and single centre case series which may suffer reporting bias. Furthermore, early pregnancy losses and data on long term renal graft outcome is limited. We report, for the first time pregnancy outcomes in renal transplant recipients using Hospital Episode Statistics (HES) data which is used in England.

Methods

Using HES data we identified all women under the age of 45 years who had received a new renal transplant between January 2001 and April 2015. Pregnancy was confirmed by a pregnancy outcome, identified through loss, abortive and delivery codes. Non singleton pregnancies were excluded. We imposed a 3 month restriction between early pregnancy losses and a 9 month restriction between deliveries to prevent the same pregnancy outcome being identified multiple times. Mortality data was obtained from the Office of National Statistics. Statistical analysis was performed using Stata[®] version 13.

Results

A total of 5108 women were identified as having received a new renal transplant. 569 pregnancy outcomes were identified in 387 of these women since transplantation (mean age at time of pregnancy was 29 (range 17-49) years. Most pregnancies (92%) occurred after first transplant. The mean time interval from date of transplant to pregnancy outcome was 48 months. Compared to the general population, 68.5% of pregnancy outcomes in the transplant cohort had a live delivery vs 79.6%, 13.4% had an abortive loss compared to 11.2% and 18.1% who had a pregnancy loss from another cause (both pre and post 24 weeks) compared to 9.2% in the general population ($P<0.001$), illustrated in table 1. Of these losses, < 5 still births were noted in the transplants compared to general population figure of 0.5%. In those women who had a live delivery, 63.1% were by caesarean section and 34.6% had a vaginal delivery. No cases of ectopic pregnancies were identified. In the transplant group vs the background pregnant population, the rate of intrauterine growth restriction (9.3% versus 2.4% $p<0.001$), gestational diabetes (12.9% versus 2.8% $p<0.001$) and hospital admission with UTI (10.3% versus 1.9% $p<0.001$) were higher. Puerperal infections following delivery were also higher (5.2 % versus 1.3% $P<0.001$) in the renal transplant than in the general population cohort. Just over 4% of the transplant recipients had an episode of graft dysfunction identified with the code of renal failure during or within 3 months of pregnancy outcome. Since pregnancy outcome, 6.2% of the transplant group have received a new transplant and 2.3% have died.

Discussion

We systematically report, for the first time contemporary pregnancy outcomes in almost 600 renal transplant recipients using HES data. In keeping with previous studies, we report that most pregnancies in renal transplant recipients which progress beyond the first trimester result in a successful outcome. However, our results raise the possibility of increased early pregnancy losses which needs to be further investigated. As compared with the general population, the rate of delivery by caesarean section and pregnancy complications including fetal growth restriction, gestational diabetes and post-partum infections are considerably increased. The impact of pregnancy on short and long term graft function will be discernible for the UK population by future data-linkage of HES to NHSBT and the UK Renal registries.

| Outcome | Transplant Cohort | General Population | P value |
|--------------------------|-----------------------------|----------------------------|---------|
| Live Delivery | 68.5% | 79.6% | |
| Pregnancy Loss | 13.4% abortive, 18.1% other | 11.2% abortive, 9.2% other | <0.001 |
| Fetal growth restriction | 9.3% | 2.4% | <0.001 |
| Puerperal Infection | 5.2% | 1.3% | <0.001 |

Table 1: Comparison of pregnancy outcomes between transplant cohort and general population.

O017

Comparison of baseline GFR levels with 1 year, 5 year and 10 year outcomes and analysing the rate of decline of GFR in living kidney donors: UK cohort study

Nithya Krishnan¹, Lisa Bradbury², Graham Lipkin³, Neil Raymond¹

¹University Hospitals Coventry & Warwickshire NHS Trust, Coventry, UK, ²National Health Service Blood & Transplant, Bristol, UK,

³University Hospitals Birmingham, Birmingham, UK

Introduction

Living kidney donation has significantly improved recipient and graft survival world wide. With a move to increase these numbers further, it becomes mandatory to have a better understanding of the long term outcomes and risks of kidney donation.

Aim

Comparison of baseline GFR levels by age bands as recommended by the current BTS guidelines with 1 year, 5 year and 10 year outcomes and the rate of decline of GFR.

Methods

National Health Service and Blood and Transplant, U.K (NHSBT), obtains informed consent from all patients undergoing a transplant in the UK for continuing data collection and subsequent analyses. The study protocol was reviewed and passed by the Renal Registry (RR) projects advisory group, UK. From January 1, 2001 until December 31, 2013 inclusive, all live kidney donors were included in the study. No formal sample size estimate was produced for the study; all eligible patients records were used. December 31, 2014 was considered the study end, meaning that all patients had at least one year of follow-up. Datasets, based on regular returns from individual transplant centres across the UK, were obtained from NHSBT.

Results

A total of 9750 live donor records were available; out of which 9229 had GFR measured at baseline. Nine donors were excluded as they were above 80 years of age and there are no current recommendations for that age group. The baseline GFR was divided into 3 groups – 1. Meeting the recommended levels (n= 9047). 2. Up to 5 mls/min/m² less than the recommended levels (n=121) and 3. More than 5 mls/min/m² less than the recommended levels (n=52). The difference in 1, 5 and 10 year outcomes in these 3 groups were compared.

None of the 173 donors in groups 2 & 3 had died during the 10 year follow-up period in comparison to 48 in Group 1. In group 2, two had UTI and one had renal mention; and one in group 3 had operation related condition. There were no significant differences in the comorbid conditions at 1 year between those in group 1 (422/ 9047) versus those in group 2 (3/121) or 3 (1/52). Similarly, at years 5 and 10, no donors (72 in 5 years and 18 in 10 years) in groups 2 and 3 reported any medical conditions in comparison to 140 (3%) in 5 years and 35 (2%) in 10 years in group 1. For group 1, the mean (M) and standard deviation (SD) of the rate of decline in GFR (mls/min/m²) in year 1 is 35.37 (15.21). In 5 years it is 7.65 (3.6) and in 10 years it is 4.34(2.02). For group 2, M and SD of the rate of decline in GFR in year 1 is 19.80 (11.36). In 5 years it is 3.03 (1.8) and in 10 years it is 1.46 (0.63). For group 3, M and SD of the rate of decline in GFR in year 1 is 6.41(22.58). In 5 years it is 0.46 (5.62) and in 10 years it is 0.75 (0.21). Further analyses by dividing group 1 to different age bands from <30 to 70+, showed a decline in GFR of 34.4(17.9) to 25(13.4) at 1, 7.1(3.7) to 6.4(2.5) in 5 and 4.1(2) to 3.9 (0.8) in 10 years. However using GFR at year 1 as baseline, showed an increase of 0.9(3) to 0.8 (2.2) in 5 and a very minimal decline in year 10.

Conclusions

No significant difference in 1,5 and 10 year outcomes including ESRD in live donors with lower GFRs at baseline. Though there was a significant difference with a slower rate of decline in GFRs in lower baseline groups the numbers are too small to draw definitive conclusions. Using 1 year GFR as baseline, there is very little change in the follow up period.

O018

Recurrent IgA nephropathy in kidney transplantation: the effect of immunosuppression regimen

Konstantinos Koutrotsos¹, Andreas Kousios¹, Laura Leighton¹, Rawya Charif¹, Dawn Goodall¹, Jack Galliford¹, Terence Cook², David Taube¹, Marina Loucaidou¹

¹Imperial College Kidney and Transplant Centre, London, UK, ²Department of Histopathology, Imperial Healthcare NHS Trust, London, UK

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 effect of maintenance immunosuppression on the recurrence of IGAN.

Methods

We reviewed prospectively collected data on 133 (102 male, mean age 44.2 +/-11.5 years) kidney transplant recipients with biopsy proven IGAN as their primary diagnosis, transplanted in our centre between September 2002 and January 2014. 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 indication and/or protocol renal biopsies staining positive for IgA Immunoglobulin.

Results

52 (39.1%) (40 male, mean age 45.2 +/-10.7 years) out of 133 patients developed biopsy proven recurrent IGAN. Mean follow up was similar between the patients with (57.5±34.7) and without recurrence (51,8±32.3) 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.(43.5±15.1 vs 49.9±11.9 years, p=0,008) Mean time from transplantation to recurrence was 39.1 (±29.6) months). Kaplan Meier analysis showed that initiation of maintenance immunosuppression with MMF and / or Prednisolone within the 1st year post transplant reduces the risk for IGAN recurrence. (log rank p=0.04) A multivariate Cox regression model, adjusted for donor and recipient age, recipient race and gender, type of transplant, and induction immunosuppressant medications, revealed older donor age (HR: 1.03, p=0.01) as a significant risk factor for recurrence, while both MMF exposure (HR: 0.63, p<0.001) and IL2 induction (HR: 0.21, p=0,008) had a protective effect. During the follow up period, 10 grafts were lost. Recurrence of IGAN did not have an effect on graft survival on multivariate analysis (p=0.29).

Conclusion

Our results indicate that induction therapy, as well as maintenance immunosuppression choice can potentially affect post-transplant IgAN recurrence. In this medium term data series recurrent IGAN and the immunosuppression regimen did not appear to affect graft outcomes.

Chapter of Surgeons
14:30 Wednesday 24 February
Boisdale Suite

O019

Establishing a learning curve for laparoscopic living donor nephrectomy

Zubir Ahmed, Pankaj Chandak, Nikolaos Karydis, Nicos Kessarlis, Francis Calder, Nizam Mamode
Guy's Hospital, London, UK

Introduction

Despite over 5000 hand assisted laparoscopic donor nephrectomies (HALDNs) having been performed in the UK a paucity of data still exists in establishing how many procedures are required in order to safely ascend the learning curve. The production of such parameters is essential to the development of appraisal, safety and training programmes in this expanding surgical programme within transplantation. Recent data from other equivalent surgical procedures suggests both intraoperative and postoperative outcome data parameters can be used to establish the learning curve.

Methods

The caseload of two surgeons who had individually performed over 180 HALDNs was interrogated. Using cumulative sum analysis (CUSUM), operating time, hospital stay, the occurrence of major and minor complications and the need for readmission or reoperation were assessed. The learning curve was analysed using graphical representations to detect an inflexion point which would represent a stability of process. The number of procedures required to arrive at this point was assumed to represent successful ascent of the learning curve. Statistical analysis using the $Pr > zL$ statistic was also used to quantify whether such a stability of process had been achieved.

Results

Surgeons 1 and 2 performed 189 and 183 cases over an 8 year period. All were intraperitoneal HALDNs using a standardised technique. Patient demographics between the 2 surgical caseloads were similar (% female: 51 v 52%, mean age 44.1 v 44.7 yrs, mean BMI 26.5 v 27.2, % left sided cases 80 v 85%). CUSUM analysis revealed no discernible inflexion points for hospital stay ($zL = 0.3$ $p=0.07$), occurrence of Clavien 2 and above complications ($zL = 0.84$, $p=0.337$), readmission ($zL=0.696$ $p=0.243$) or reoperation ($zL= -0.366$ $p=0.643$). Operating time however demonstrated a visible stability of process initially at case 25 but this was more sustained by case 40 to 45 for both surgeons.

Discussion

A learning curve can be reproducibly established for HALDN using operating time as a surrogate marker. Contrary to popular belief true ascent of the learning curve may mean the performance of up to 50 procedures rather than 20 – 25. In our series the occurrence of initial stability in operating times at case 25 was likely biased by careful patient selection. Hence the stability achieved by case 45 is likely more representative of a normal surgical HALDN casemix. We anticipate this data will better inform the development of an efficient and effective surgical training programme for HALDN.

O020

Effect of baseline co-morbidity on all cause mortality in living kidney donors – 10 year UK cohort study

Nithya Krishnan¹, Lisa Bradbury², Neil Raymond¹

¹University Hospitals Coventry & Warwickshire NHS Trust, Coventry, UK, ²National Health Service, Blood & Transplant, Bristol, UK

Introduction

Living kidney donation has significantly improved recipient and graft survival world wide. With a move to increase these numbers further, it becomes mandatory to have a better understanding of the long term outcomes and risks of kidney donation. Aim: To investigate the effect of baseline co-morbidity on all-cause mortality in kidney transplant living donors – 10 year follow up.

Methods

National Health Service and Blood and Transplant, U.K (NHSBT), obtains informed consent from all patients undergoing a transplant in the UK for continuing data collection and subsequent analyses. The study protocol was reviewed and passed by the Renal Registry (RR) projects advisory group, UK. From January 1, 2001 until December 31, 2013 inclusive, all live kidney donors were included in the study. No formal sample size estimate was produced for the study; all eligible patients records were used. December 31, 2014 was considered the study end, meaning that all patients had at least one year of follow-up. Datasets, based on regular returns from individual transplant centres across the UK, were obtained from NHSBT.

Results

There were 9750 live donor records available. All cause mortality and baseline comorbidity was analysed. 9043 donors had no baseline co morbid condition. The baseline comorbidities analysed were kidney stones (9), microscopic haematuria (9), angina/ischemic heart disease (6), CABG (4), CVA/TIA (5), hypertension (HT) (220), HT on more than 3 medications (1), HT with left ventricular hypertrophy (12). diabetes (2), depression (33), asthma (130), hypercholesterolemia (22) and different BMI bands, BMI <18.5 (82), 18.5 -<25 (3208), 25-<30 (4270), 30-<35 (1449), 35-<40 (158), 40+ (28). There were 48 deaths in total; out of which 2 had baseline HT (2/220), 3 had unspecified comorbidities (3/258) ; and 43 deaths had occurred in the group which had no baseline co-morbidities in the 10 year follow up period. Cox proportional hazards regression modelling, showed no individual baseline comorbidity or "any" combined baseline comorbidity to be a significant predictor of mortality over the follow-up period.

Conclusion

There is no significant association between baseline co-morbidities and mortality in living donors in the 10 year follow up UK cohort study.

O021

Initial experience of en-bloc kidney transplantation from donors under two months of age in the UK

Imeshi Wijetunga¹, Sonsoles Martinez-Lopez¹, Rupaly Pande¹, Shahid Farid¹, Muhammed Jameel¹, Vivek Upasani¹, Lutz Hostert¹, Matthew Wellberry-Smith², Chas Newstead², Andrew Lewington², Clare Ecuyer¹, Richard Baker², Niaz Ahmad¹

¹Department of Hepatobiliary and Transplant Surgery, St. James's University Hospital, Leeds, UK, ²Department of Renal Medicine, St James's University Hospital, Leeds, UK

Introduction

Kidney transplantation from donors under two years of age is rare in the UK (1-2 transplant per year over the last two decades). Kidney transplantation from a donor less than two-months of age was first performed in the UK in 2013. Until recently (2015), UK legislation did not permit the diagnosis of brain-stem death (BSD) in infants under two months of age and only DCD donation has been possible. We describe our initial experience of kidney transplantation from this donor category including neonatal donors.

Methods

Kidney transplants performed at our centre from donors under two months of age were identified from a prospective database. All kidneys were retrieved and transplanted en bloc with abdominal aorta and inferior vena cava. Hypothermic machine perfusion was used in some cases where in-situ flush was deemed inadequate. Recipients were young/middle-age adults with BMI<30 and no cardiovascular risk factors. Donor & recipient characteristics as well as short-term graft & recipient outcomes were examined.

Results

Seven en bloc kidney transplants (EKT) were performed from donors less than two months of age from March 2013 to October 2015, six from DCD (86%) and one from DBD donor. Median follow up was 231days (range 15-964). Median donor age and weight were 23days (range 0-58) & 3.4kg (range 1.9-5kg), respectively. Median recipient age and weight were 33yrs & 49.5kg, respectively. One primary non-function was observed and the recipient was excluded from subsequent analysis of graft function. This graft was from a 0d old 1.9kg DCD donor. Primary function was observed in 6 (86%) recipients with no early post-operative complications. Median GFR (Cockcroft-Gault, in ml/min/1.73m²) at 1-month and 6-months post-transplant was 25 and 54 respectively. Graft function continues to improve over the first year with those grafts reaching one year achieving a GFR>60.

Discussion

This is the first reported series of kidney transplant from donors less than two months of age including neonatal donors in the UK. The recipient and graft outcomes are encouraging. Our study identifies small infants and neonates as a potential 'new' donor pool for kidney transplant. We suggest further consolidation of experience in this area in a designated transplant centre in the first instance.

O022

Double adult kidney transplantation in the UK: short-term outcomes

Lisa Bradbury¹, Elinor Curnow¹, Adam McLean², Paul Gibbs³, Richard Baker⁴, Niaz Ahmad⁴, [Chris Callaghan](#)^{5,1}

¹NHS Blood and Transplant, Bristol, UK, ²Hammersmith Hospital, London, UK, ³Queen Alexandra Hospital, Portsmouth, UK, ⁴St James's Hospital, Leeds, UK, ⁵Guy's Hospital, London, UK

Introduction

Deceased donor kidney transplantation is expanding in the UK, but average donor age and co-morbidity burden are also increasing. In an attempt to utilise kidneys from highly marginal donors that might previously have been discarded, many surgeons are implanting both kidneys into a single recipient. We performed an analysis of the UK Transplant Registry to examine the short-term outcomes of double adult kidney transplantation (DAKT).

Methods

Data on deceased donor adult-to-adult (18 years or older) kidney transplants from 1.4.03 to 31.3.13 were obtained from the Registry, recorded at 7.12.14. En bloc transplants were excluded. UK Kidney Donor Risk Index (UKKDRI) was used to quantify donor kidney 'quality'. Outcomes included one-year death-censored graft survival, and one-year eGFR (4-variable MDRD) stratified into CKD stages 1-5. Risk-adjusted Cox regression analysis was used to investigate the relationship between graft survival and whether the recipient received a single kidney transplant (SKT) or DAKT. Risk-adjusted multinomial linear regression analysis was used to investigate the relationship between eGFR and SKT/DKT. Kidneys from younger donors are transplanted as DAKT for varied reasons and younger and older DAKT donors do not form a homogeneous group. Hence, regression analyses were restricted to donors aged 60 years or more.

Results

Within the study period, 12,356 SKTs and 175 DAKTs were performed. The majority of DAKTs were implanted in the last three years of the study (120/175, 69%). The majority of DAKT donors were aged 60 years or older (122/175, 70%) and came mainly from DCD donors (138/175, 79%). DAKTs were predominantly implanted into recipients aged 50 years or older (145/175, 83%). Mean (SD) UKKDRI was higher for DAKT than SKT (1.7 (0.4) versus 1.2 (0.4), respectively). Mean (SD) one-year eGFR was similar between DAKT and SKT groups (47 (21) versus 50 (18) mL/min/1.73 m², respectively). When analysis was restricted to transplants from donors aged 60 years or over, one-year graft survival was no different between the SKT and DAKT groups (90% versus 88%, p=0.40). After risk-adjustment for donor and recipient factors, there was no difference in one-year graft survival when comparing SKT and DAKT (p=0.32, hazard ratio 1.36 (95% CI 0.76-2.45)). Risk-adjusted analysis of one-year recipient eGFR (CKD stage) suggested that kidney function after DAKT was significantly better than after SKT (p=0.01). The odds of being at a better (lower) CKD stage were nearly twice as great (odds ratio 1.81 (95% CI 1.16-2.82) after DAKT compared to SKT.

Discussion

DAKT is uncommon in the UK, but is rapidly increasing in frequency. Because the majority of DAKTs were performed in recent eras, only short-term outcome analyses could be performed. These suggest that one-year graft survival and eGFR are acceptable, and that DAKT is a valid strategy to expand the donor pool. Further analyses of long-term outcomes are awaited. Future UK deceased donor kidney allocation strategies may have to take into account the expansion of DAKT to facilitate this approach to marginal organs.

O023

Periodical peer review of a pancreas transplant programme: can it enhance performance?

Zia Moinuddin, Aneeza Arif, Hemant Sharma, Omar Masood, Afshin Tavakoli, Ravi Pararajasingam, Kay Poulton, Judith Worthington, Bence Forgacs, Titus Augustine, Raman Dhanda
Department of Kidney and Pancreas Transplantation, Manchester Royal Infirmary, Manchester, UK

Introduction

In the UK, NHS Blood and Transplant (NHSBT), the national transplant regulatory body, monitors centre specific performance in terms of 30-day graft loss and patient mortality by CUMulative SUMMation statistical methodology (CUSUM). A CUSUM trigger is generated each time the observed rate of graft loss and/or mortality exceeds the expected rate (1.2% for patient mortality and 10% for graft loss). Between September 2010 and June 2013, 4 triggers were identified in Manchester related to 15 graft losses. This initiated a centre generated invited external review (IER) followed by a formal NHSBT review (NHSBTR). All pancreas graft losses (n=18) and the major surgical complications (portal vein thrombosis, arterial thrombosis, enteric leaks and graft pancreatitis) between 2011-2013 were peer reviewed. The underlying reasons were deemed to be technical failure and prolonged cold ischaemia time (CIT) (Range: 12-17 hrs). The recommendations of IER and NH SBTR were to develop the following:

- Uniform agreed protocols for recipient assessment, selection and information
- Standardized donor selection criteria
- Clinics for assessment and monitoring of patients on waiting list
- Pancreas transplant specific listing multi-disciplinary team (MDT) meetings
- Standardized, uniform surgical technique for pancreas transplantation
- Logistical pathway to reduce cold ischaemia time
- Consensus-based management of post-operative complications.

This study explores the process of restructuring the programme in the wake of the review and its subsequent impact on outcomes after pancreas transplantation.

Methods

In line with the peer review recommendations, a new restructured uniform unit protocol was developed along with agreed guidelines. Dedicated clinics, MDT meetings and standardised patient information booklets, assessment, anaesthetic management, post-operative and follow-up care plans and documentation were developed. Education of multidisciplinary staff was undertaken to ensure strict adherence to a time-efficient logistic pathway and the use of virtual crossmatching to enable a reduction in CIT was expanded. Surgical technique across the entire team was standardised. The use of separate teams for back-benching and implantation was made mandatory.

The key clinical outcomes were compared between 2 periods:

Period 1 (before change in practice): January 2012 – June 2013

Period 2 (after change in practice): July 2013 – September 2015

Results

48 transplants were performed in period 1 and 67 in period 2. There was a significant increase in the number of virtual crossmatches reported in period 2 (24/48, 50% v/s 63/67, 94%; $p < 0.0001$, Chi-square test). In period 2, there was a significant reduction in CIT (median 760 min v/s 562 min) ($p < 0.0001$, unpaired t-test), re-exploration rate (39.5% v/s 25.0%) and major surgical complications rate (37.5 % v/s 11.9%) ($p = 0.0236$, Chi-Square test) (period 1 v/s period 2). Pancreatic graft loss was also significantly reduced from 29% in period 1 to 6% in period 2 [$p = 0.0062$, Chi-square test], as was the mean hospital stay (28 days in period 1 to 19 days in period 2) [$p = 0.028$, t-test].

Discussion

Restructuring the pancreas transplant programme following an external peer review has led to significantly reduced CIT (now the lowest in the UK) and resultant improved graft and patient outcomes. This illustrates the positive impact a peer review can have on improving the overall quality and outcomes of a national service. Therefore, periodical external review of practice may help in sustained improvement in practice.

O024

Urgent multi-visceral or modified multi-visceral transplantation following widespread splanchnic ischaemia has good outcomes and should be considered in patients presenting with abdominal catastrophes

Irum Amin¹, Charlotte Rutter², Neil Russell¹, Andrew Butler¹

¹University of Cambridge, Department of Surgery, Addenbrooke's Hospital, Cambridge, UK, ²Cambridge University Hospitals NHS Foundation Trust, Department of Gastroenterology, Cambridge, UK

Introduction

Patients may present with life threatening loss of small bowel at all ages and anecdotally, a proportion of those undergoing laparotomy for bowel ischaemia are not actively treated. It is essential that all management options are explored and modified (MMVT) or multi-visceral transplantation (MVT) is a potential option for these abdominal catastrophes. Our unit has received an increasing number of referrals for this indication since 2013. All patients referred for intestinal and multi-visceral transplant undergo a period of assessment before being discussed at the National Adult Small Intestinal Transplant (NASIT) forum, which is held six times a year and attended by representatives from the two intestinal failure and two intestinal transplant centres. Agreement at NASIT is mandatory for listing. When patients need to be listed urgently a virtual forum is held and listing is agreed by email. The aim of this study was to analyse referral patterns, the assessment and listing process, surgical variables and the outcomes of these critically ill patients to determine whether organs are being used appropriately.

Methods

Retrospective analysis of all patients who underwent transplantation in our unit between 1st January 2007 and 31st October 2015. All patients who were referred following an abdominal catastrophe and transplanted urgently were included in the study. Time to transfer, listing and transplant was recorded as was age, operative blood loss, length of stay and survival.

Results

61 transplants were performed between 1st January 2007 and 31st October 2015 (36 MVT, 9 MMVT, 16 SBT). 6 patients underwent re-transplant and their second surgery was excluded from the analysis; all patients remain alive. 7/55 (12.7%) patients were transplanted urgently (6 MVT; 1MMVT). Five were female and two male with a median age 27 years (range 19-50). This was significantly younger than the patient's transplanted non-urgently, median age 47 years (range 18-64), $p < 0.01$. 6/7 patients required intra-operative haemofiltration, but none required intra-operative bypass. Operative blood loss was 9.75L, comparable to the non-urgent transplants 11L. Length of stay however was significantly longer in the urgent group, median 122 days (range 75-165), when compared to the non-urgent group, median 72 days (range 0-193), $p = 0.02$. This likely reflects the urgent group being inpatients at time of transplant.

The patients that were transplanted acutely have a 59 month of 80%, compared to 53.3% at 5 years for the non –urgent transplant.

Discussion

Patients who are transplanted urgently for widespread splanchnic ischaemia are younger and subsequently have better outcomes.

The whole process of assessment and listing is a testament to the flexibility of NHSBT in a timely fashion.

Basic Science: ischemia reperfusion injury
08:00 Thursday 25 February
Alsh Suite

O025

Ex-vivo normothermic with the addition of argon reduces the effects of renal ischaemic injury

Sarah Hosgood, Mazin Hamed, Tom Adams, Michael Nicholson
University of Cambridge, Cambridge, UK

Introduction

Noble gases can exert biological actions that may help to reduce transplant related ischaemic injury. The aim of this study was assess the effects of argon administered directly to the kidney during *ex-vivo* normothermic perfusion (EVNP).

Methods

Under Home Office Animals (Scientific Procedures) Act 1986 porcine kidneys were retrieved after 10 minutes of warm ischaemia. After 17h static cold storage, kidneys underwent 1h of EVNP with a leukocyte depleted blood based solution with either argon (n = 6) [70% argon/25% O₂/5% CO₂], oxygen (n = 6) [95% O₂/5% CO₂] or nitrogen (n = 6) [70% nitrogen/ O₂/5% CO₂]. After EVNP kidneys were reperfused *ex-vivo* for 3h with oxygenated whole blood to assess renal function and injury.

Results

The argon treated kidneys produced significantly more urine during EVNP compared to the oxygen treated kidneys (argon 278 ± 88 vs oxygen 180 ± 42ml vs nitrogen 199 ± 88ml; P = 0.049).

During reperfusion levels of oxygen consumption at 1h were significantly higher in the argon kidneys (argon 31.4 ± 8.8 vs oxygen 16.3 ± 11.0 vs nitrogen 32.0 ± 14.8ml/min/g; P=0.027). Creatinine clearance (CrCL) was also significantly higher [(Area under the curve (AUC) argon 4.5 ± 3.5 vs oxygen 1.8 ± 1.0 vs nitrogen 3.4 ± 1.9ml/min/100g.h; P=0.030). The renal blood flow was also significantly higher in the argon treated kidneys (AUC argon 318 ±123 vs oxygen 166 ± 118 vs nitrogen 316 ± 158ml/min/100g.h; P = 0.054). There was no significant difference in levels of IL-6 or TNFα after reperfusion between the groups; P = 0.657, 0.328).

Discussion

Kidneys treated with argon during EVNP had improved renal function and oxygen consumption during reperfusion compared to kidneys treated with oxygen. Pre-treatment of kidneys with argon may enhance EVNP conditions to improve early graft function. Furthermore, this technology can be translated into clinical practice with relative ease.

Ethics and psycho-social care
09:30 Thursday 25 February
Lomond Auditorium

O026

Integrating mental and physical healthcare in kidney transplant patients: a comparison of psychological morbidity in three patient groups

Amy Carroll¹, Sharon Frame¹, Carleen Kerr¹, Adora Beleno-Harriott¹, Erwin Desendario¹, Joesph Taylor², Faith Matcham², Anna Simpson², Matthew Hotopf², Antonia Cronin^{1,2}

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Background

There is an increased prevalence of depression and anxiety in kidney transplant patients, and this is associated with increased mortality and co-morbidity. Integrating physical and mental health care is a key national priority in the UK. IMPARTS (Integrating Mental and Physical Health Care in Research Training and Services) is a screening package that has been developed to facilitate this through the electronic collection of patient reported data. To investigate the prevalence of psychological morbidity in kidney patients we incorporated IMPARTS into three clinical areas: (i) The Annual Transplant Review Clinic (ATRC), for long-term kidney transplant patients (KTR); (ii) The Transplant Support Clinic (TSC), for KTR with declining graft function (GFR<20mL/min); and (iii) A satellite dialysis centre.

Methods

Between July 2013 and January 2015 we screened n=577 patients using an electronic tablet. Screening measures for depression and anxiety included: (i) Patient Health Questionnaire (PHQ-9); and (ii) Generalised Anxiety Disorder Questionnaire (GAD-7). The results were uploaded in 'real-time' to the Electronic Patient Record.

Results

There were a total of n=577 screening encounters (ATRC n=380, TSC n=35, Dialysis n=162). The mean age of patients screened was 50.4 years (ATRC 53.4 years, TSC 43.6 years, Dialysis 54.2 years). On average 39% screened were female (ATRC 38%, TSC 48%, Dialysis 41%). The prevalence of depression and anxiety across each clinical group is shown in table one. All patients who reported psychological difficulties were offered follow up with a clinical psychologist. Referrals were also made to liaison psychiatry and community mental health teams.

Table One: Prevalence of Depression and Anxiety across ATRC, TSC and Dialysis

| | | ATRC (%) | TSC (%) | Dialysis (%) |
|--------------------|---------------------------|------------|-----------|--------------|
| Depression: | No symptoms | 290 (90.9) | 22 (62.9) | 82 (70.1) |
| | Some Symptoms | 17 (5.3) | 6 (17.1) | 23 (19.7) |
| | Probable Major depression | 12 (3.8) | 7 (20) | 12 (10.3) |
| Anxiety: | No symptoms | 287 (90) | 27 (77.1) | 92 (78.6) |
| | Mild anxiety | 14 (4.4) | 3 (8.6) | 10 (8.5) |
| | Probable GAD | 18 (5.6) | 5 (14.3) | 15 (12.8) |

Discussion

We have successfully embedded IMPARTS into 3 distinct clinical areas and identified significant psychological morbidity across all kidney patient groups screened. This has resulted in patients being offered increased psychological support and prompted a more holistic approach to patient care. It has also identified important areas for further evaluation and service development. For example providing psychological support for patients attending TSC, who have a particularly high prevalence of probable major depression and GAD, has been identified as a priority. 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.

O027

Socio-demographic and comorbidity differences between dialysis, waitlisted and transplant patients in the UK and impact on 1-year survival: findings from the ATTOM Study

Diana Wu¹, Matthew Robb², Christopher Watson³, Rommel Ramanan⁴, John Forsythe¹, Wendy Metcalfe¹, Christopher Dudley⁴, Clare Bradley⁵, Heather Draper⁶, Andrew Bradley³, Gabriel Oniscu⁰

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Introduction

Access to Transplantation and Transplant Outcome Measures (ATTOM) is a prospective cohort study involving all 72 UK renal units, investigating factors affecting equity of access, survival, quality of life and cost effectiveness of renal transplantation.

Methods

6842 patients aged 18-75 years were recruited between 2011-2013, including 2621 incident dialysis, 2262 incident transplant and 1959 waitlisted patients (matched to transplant patients for centre, age, time on waiting list, pre-emptive status and diabetes). Socio-demographic and comorbidity data were collected at recruitment. Differences between groups were analysed by Chi-square and Kruskal-Wallis tests. Factors affecting the likelihood of being in the transplant versus waitlisted group were analysed by multivariate logistic regression. 1-year patient survival was calculated using the Kaplan-Meier method and a step-wise Cox proportional hazards model was built to analyse predictors of 1-year mortality on dialysis. P-values<0.05 were considered significant. All data were analysed using SAS®9.4.

Results

Compared to waitlisted and transplant patients, dialysis patients were significantly older (58.4 vs 50.7yrs), had a higher prevalence of renal vascular disease and diabetes as primary renal disease, lower levels of education, greater social deprivation and higher prevalence of all comorbidities. 58.2% dialysis patients had a Charlson Comorbidity Index (CCI) score ≥ 1 , compared with 32.1% waitlisted and 31.6% transplant patients.

The likelihood of being transplanted versus remaining on the waiting-list was significantly reduced by female gender, previous transplantation, O blood group, non-white ethnicity, greater social deprivation, lower education level, smoking and comorbidity (CCI score ≥ 1). Gender and previous transplantation were no longer significant after including calculated reaction frequency in the model. Further modelling by type of transplant showed that social deprivation, education and comorbidity had no effect on the likelihood of receiving a donor after brain death kidney transplant.

There was significant inter-centre variation in the mean CCI scores as well as the prevalence of diabetes, coronary heart disease, heart failure, atrial fibrillation, chronic respiratory disease, malignancy and smoking amongst dialysis, waitlisted and transplant populations. However, these did not lead to significant centre differences in 1-year survival for any of the 3 cohorts.

Survival at 1 year for incident dialysis patients was 93.0% (95% CI: 91.8 - 94.0). The most common causes of death were cardiac disease (20.2%), infection (19.2%) and malignancy (18.2%). Significant predictors of mortality at 1 year included increasing age (per year, hazard ratio (HR) 1.02, p=0.013), congestive heart failure (HR 2.34, p<0.0001), chronic respiratory disease (HR 2.08, p=0.0001), liver disease (HR 3.37, p<0.0001), malignancy (HR 1.82, p=0.0018) and unemployment (HR 3.01, p=0.0016).

There were no significant differences in survival between matched waitlisted and transplant patients at 1 year, for both deceased donor transplantation (Waiting list 96.6% [95% CI: 94.1-98.0] vs Transplant 97.3% [95.5-98.3], p=0.61) and LD transplantation (Waiting list 98.5% [96.2-99.5] vs Transplant 98.9% [97.1-99.6], p=0.69).

Discussion

Patients selected for transplantation have less comorbidity, are younger, more highly educated and less socially deprived than those on dialysis. Once listed, ethnicity, blood group, sensitisation, comorbidity, education level and social deprivation predict the likelihood of receiving a transplant. The comorbidity profile of listed as well as transplanted patients varies significantly between centres in the UK, suggesting different selection criteria. Several comorbid conditions affect 1-year survival on dialysis and could assist the selection process for transplantation.

O028

Pre-emptive transplantation in the UK: an unfair advantage?

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Introduction

Equity of access to the cadaveric waiting list underpins the UK transplant allocation process. UK renal registry data on modality 90 days after commencing renal replacement therapy indicate increased transplantation rates for patients who have been registered with the regional transplant centre, as opposed to a peripheral unit. These figures raise genuine concerns about equitable access to this process, if indeed pre-emptive transplantation is advantageous. Historical data from the United States suggests that pre-emptive transplantation is beneficial with improved patient and graft outcomes but contemporary data for the UK has not been available. With the assistance of NHSBT we have investigated the outcomes of pre-emptive transplant recipients between 2000 and 2014 in the UK.

Methods

A retrospective study was performed using records obtained from the UK Transplant Registry held by NHSBT. A total of 21,782 patients receiving their first kidney only transplant between 2000 and 2014 were included, and analysed according to donor type (DCD, DBD, LD). Patients were then stratified according to time spent on dialysis (pre-emptive, and 0-6, 6-12, 12-24, 24-36, 36-48, >48 months respectively), and outcomes were compared using the Kaplan-Meier method.

Results

A detrimental 'dose dependent' effect of dialysis was noted on patient survival. The five-year patient survival for DBD recipients was 94% in the pre-emptive group (95% CI 92.8-95.0), 93.9% (95%CI 91.1-95.9) after 6-12 months of dialysis, and 83.1% (95% CI 81.2-84.7) after 48 months. In DCD recipients, the five-year survival was 90% in preemptive transplants (95% CI 87.4-92.0), 88.9% after 6-12 months (95% CI 82.4-93.1), and 80.9% after 48 months of dialysis (95% CI 77.8-83.9). Similar findings were noted in the LD group. Graft survival was also affected by time on dialysis. Time on dialysis remained a significant factor on patient and graft survival when added to a risk-adjusted Cox Proportional Hazards model.

Discussion

Time spent on dialysis negatively impacts both patient and graft survival following renal transplantation. This data highlights the importance of timely transplant listing. Efforts should be made to streamline and standardise listing practices across the United Kingdom.

O029

Non-directed altruistic kidney donation: an 8-year single centre experience

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Background

Non-directed altruistic donation is permitted under the Human Tissue Act 2004. This audit analyses an eight-year experience in a large kidney transplant centre.

Methods

Data was analysed from all NDADs who made contact with our centre and underwent assessment between 1st April 2007 and 31st March 2015.

Results

131 people made initial contact for advice and/or information. 40% (n=53) made no further contact and 60% (n=78) requested preliminary assessment. 44% (n=57) proceeded to investigative testing, nephrological review and mental health assessment. An equal proportion of potential donors (n=6) left the pathway due to an absolute medical contra-indication, a relative medical contra-indication or withdrew due to family or donor preference. 5/57 were excluded on mental health grounds alone. 24% (n=32) proceeded to surgical review and independent assessment for Human Tissue Authority (HTA) approval. All were accepted at surgical review; 2 did not achieve HTA approval. Overall, 22% (n=29) of donors proceeded to donation (22%); 86% (n=25) chose to donate directly to the national waiting list rather than into an altruistic donor chain. 97% were Caucasian, median age 50 (range 21-75), 48% blood group O. The number of NDAD kidneys donated from and received by our centre is equivalent. Lengths of stay and complication rates were comparable with all living donors but donor assessments exceeded the 18 week standard in all cases. Key rate-limiting steps include donor preference, access to mental health and specialist opinions and delays between identifying a matched recipient and surgery.

Discussion

Our centre is a leading contributor to the UK NDAD programme, reflecting national trends in donor characterisation, activity and outcomes. Whilst, donor triage is effective, duration of donor assessment is below standard and is under review.

O030

Do kidney transplant recipients care where their organs come from?

Stephen Bond, Christopher Watson

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Introduction

In 2013 the BTS/NHSBT published guidance recommending that recipients should be counselled on donor organ-associated risk factors such as age, whether DCD or DBD and risk of transmissible disease. In response to this guidance we adapted our consenting process to ensure patients were able to make an informed choice as to whether they were willing to accept kidneys from donors with the following characteristics: donation after circulatory death, donors over 60 years old, donors who exhibit high risk behaviour and donors who either have a current brain cancer or a past history of cancer.

Methods

195 patients being considered for kidney transplantation were counselled on the potential types of deceased donor kidneys that might be offered to them and the risks involved with either accepting or refusing them. The recipients' choices were analysed with respect to factors such as their gender, age and duration of dialysis.

Results

- 98% of all patients consented were happy to receive a kidney from a donor after circulatory death.
- 58% of all patients were happy to receive a kidney from a donor whose behaviour put them at higher risk of viral infections, this number dropped in females (50%) and 18 to 34 year olds (39%).
- Although 92% of all patients were happy to accept a kidney from a donor over 60, perhaps unsurprisingly only 83% of 18 to 34 year olds were willing to take this risk.
- 81% of all patients were happy to receive a kidney from a patient with an active brain cancer, this number dropped in females (76%), 18 to 34 year olds (72%), patients with over 3 years on dialysis (71%) and in patients who had a history of cancer (71%).
- 77% of all patients were happy to receive a kidney from a donor who had a history of cancer, this number dropped in 18 to 34 year olds (72%), females (70%), patients with over 3 years on dialysis (66%) and in patients with a previous history of cancer (50%).
- 88% of all patients were happy to receive a dual kidney transplant, this number only dropped in patients who'd had a previous kidney transplant (79%) and in 18 to 34 year olds (72%).

Discussion

Potential kidney transplant recipients are willing to make decisions on the types of donor organs they wish to receive. It appears that age, sex, time on dialysis, previous transplants and a previous history of cancer can all have a bearing on the risks patients are willing to take when consenting to deceased donor kidney transplantation.

O031

Quality of life and decision modelling in donation after circulatory death (DCD) liver transplantation

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Introduction

Donated after circulatory death (DCD) liver transplantations are increasingly used to meet waiting list demands, yet provide inferior clinical and quality of life (QoL) outcomes compared to donated after brain death (DBD) allografts. This study aimed to determine the optimal decision for patients offered a DCD allograft based on their current Model for End-Stage Live Disease (MELD) score – to accept or remain on the waiting list for DBD transplantation.

Methods

A Markov decision process model was constructed to predict the 5 year clinical course of patients on the liver transplant waiting list. Clinical outcomes (transition probabilities) were determined from the UK Transplant registry or appropriate literature. Utility values, in quality-adjusted life years (QALYs), were determined using the condition-specific “Short form of liver disease quality of life” (SF-LDQOL) questionnaire. This was administered to pre- and post-transplant patients attending a UK liver transplant unit between 16th July and 13th Aug 2015. Sensitivity analyses were conducted to assess the impact of parameter uncertainties on conclusions.

Results

211 / 245 (86.1%) eligible patients completed the questionnaire. 50 respondents (24%) were pre-transplant, and 161 were post-transplant - either DBD (57%) or DCD-recipients (9%); re-transplanted (8%); or with ischaemic cholangiopathy (3%). The mean score for post-transplant groups [144.1, 95% CI (140.5-147.7), n=161] was significantly higher ($p < 0.001$) than pre-transplant patients [122.7, 95% CI (114.5-131.0), n=50]. Quality-adjusted life years (QALYs) accumulated after 5 years were significantly higher in DCD-recipients (3.78, 95% CI=3.63-3.93) than those remaining on the waiting list with MELD scores of 15-20 (3.33, 95% CI=3.29-3.74), or >20 (3.03, 95% CI=3.05-3.58). There was no significant difference for MELD scores <15 (3.52, 95% CI=2.71-3.33).

Discussion

This model predicts that patients on the UK liver transplant waiting list with MELD scores >15 should accept any DCD allograft offered. However, the optimal decision for patients with MELD scores <15 still remains unclear.

BTS/BASL/BTLG Liver Forum
09:30 Thursday 25 February
Alsh Suite

O032

Surgical experience of normothermic machine perfusion in human liver transplantation

David Nasralla¹, Hynek Mergental², Wael Jassem³, Annemarie Weissenbacher¹, Chris Morris⁴, Les Russell⁴, Peter Friend¹
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Introduction

Normothermic machine perfusion (NMP) offers a potential solution to the organ shortage crisis affecting liver transplantation. It involves perfusing an organ with oxygenated blood, nutrients and medications at 37°C to preserve it in a functioning, physiological state. It requires the liver backtable to be performed at the donor hospital followed by cannulation of the vessels before commencing the perfusion. NMP continues during transport and storage until transplantation. We report the logistical impact and surgical expertise that has emerged during our first 100 transplanted NMP livers using the OrganOx *metra*.

Methods

100 livers were successfully preserved using NMP until transplantation. For all livers the following details were recorded – cold ischaemic time (CIT; cross clamp to start NMP), backtable and cannulation time (liver explant to start NMP), cannulation technique, liver anatomy, ability to commence and complete NMP.

Results

Back-table preparation and cannulation has been identified as the critical step in achieving a successful liver NMP. DBD and DCD livers (71:29) were perfused. Average CIT was 2hrs 3min with no significant difference between DBD and DCD livers (1hr 59min vs 2hr 12min; p=0.09) and similar cannulation times in both groups (1hr 30min DBD vs 1hr 36min DCD; p=0.39). This did not seem to prolong the retrieval process unless abnormal anatomy was encountered (1hr 49min abnormal vs 1hr 24min normal; p=0.00002).

IVC cannulation problems were rare. The only challenge related to PV cannulation was the risk of twisting of the vein. This was identified by absent PV flow measured by the device and corrected by untwisting the vessel.

HA cannulation has posed the greatest challenge to NMP technique due to common aberrant anatomy. One liver was not perfused due to aberrant left hepatic artery (aLHA) arising directly from the aorta (not included in analysis). Aberrant arterial anatomy was encountered in 31/100 cases (10xaRHA, 16xaLHA, 5xaLHA+aRHA) requiring either arterial reconstruction to be performed at the time of retrieval (n=10), or for the aortic tube to be excised intact with coeliac and SMA, enabling cannulation and perfusion directly through the aorta (n=3). More recently a bifurcated cannula has been used to perform dual perfusion of aberrant vessels (n=2). In 2 cases the distance between aortic patch and the origin of LHA was too short for cannulation, requiring the use of an extension graft. All livers were successfully transplanted.

Discussion

NMP can be employed with all types of commonly encountered aberrant liver anatomy. With normal liver anatomy NMP should not significantly prolong the retrieval process but abnormal anatomy can cause a delay before commencing NMP. A reasonable level of surgical expertise and meticulous cannulation technique are required for successful perfusion.

O033

Back-scatter of red light predicts early liver allograft dysfunction following transplantation

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Introduction

Back-scatter of red and near infrared light from immediately beneath the liver surface has been shown previously to correlate with steatosis (McLaughlin et al, Phys Med Biol 2010). Steatotic livers are associated with a higher incidence of early allograft dysfunction (EAD) and primary non-function (PNF) following transplantation. The surgeon's subjective assessment of steatosis, and hence his/her ability to predict outcomes following transplantation, is poor hence the need for a rapid near-patient objective test to predict PNF/EAD. We developed a hand held device which, when placed against the liver surface, measured back-scatter of red and near infrared light from just below the liver surface. We correlated the device's readings to liver transplant outcomes.

Methods

Patients awaiting liver transplantation were enrolled. Back-scatter measurements were taken from each donor liver at bench work and following reperfusion. Outcome data were collected and factors that might predict EAD/PNF such as donor type, donor age, ischaemic time, surgeon's and histopathologist's grades of steatosis, and back-scatter measurements were analysed by logistic regression. EAD was defined using the Olthoff criteria (Liver transplantation 2010).

Results

102 patients who underwent liver transplantation were studied, including 82 DBD and 20 DCD donor livers. Median donor age was 54y (range 14-80), and median cold ischaemic time was 7h59m (range 3h20m to 16h52m). Following transplantation 2 patients (1.9%) suffered PNF and 24 (23.5%) patients developed EAD. Of the variables considered to possibly predict the occurrence of EAD/PNF, only the back-scatter reading was found to actually predict EAD/PNF in the study cohort. The odds ratio for EAD/PNF was 1.04 (95% CI 1.015, 1.065) for every unit increase in red light back-scatter. The range of red light back-scatter readings was 42 to 230 units.

Discussion

Measurements of red and infrared light back-scatter may be a valuable tool in assessing livers to determine suitability for transplantation or the requirement for manipulation/resuscitation during extra-corporeal storage.

O034

Urgent multivisceral or modified multivisceral transplantation has good outcomes and should be considered in patients with abdominal catastrophes

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Introduction

Patients who present with abdominal catastrophes not amenable to conventional treatments are anecdotally treated palliatively with uniformly fatal outcomes. With increasing experience of bowel transplantation novel salvage procedures are becoming available including modified (MMVT) or multivisceral transplantation (MVT). Our unit has received a number of referrals for this indication since 2013. Usually the assessment and listing process for bowel containing grafts is prolonged and involves discussion at the National Adult Small Intestinal Transplant (NASIT) forum held six times a year; agreement at NASIT is mandatory for listing. When patients need to be transplanted urgently a 'virtual' forum is held. We describe the referral patterns, assessment and listing processes, surgical variables and outcomes of these critically ill patients.

Methods

A retrospective analysis was undertaken of all patients who underwent bowel transplantation in our unit between 1st January 2007 and 31st October 2015. All patients referred following an abdominal catastrophe and transplanted urgently were included in the study. Time to transfer, listing and transplant was recorded as was age, operative blood loss, length of stay and survival.

Results

Sixty one transplants were performed between 1st January 2007 and 31st October 2015 (36 MVT, 9 MMVT, 16 small bowel transplant). Six patients underwent re-transplantation (their second transplant was excluded from the analysis). Seven of the fifty-five (12.7%) patients were transplanted urgently (6 MVT; 1 MMVT). Indications for transplantation were arterial ischaemia (5), venous ischaemia (1) and one uncontrollable gastrointestinal bleed (1). Five were female and two male with a median age of 27 years (range 19-50). This was significantly younger than those patients transplanted non-urgently, median age 47 years (range 18-64), $p < 0.01$. Median time from presentation to referral was 7 days, referral to transfer was 2 days, assessment time was 4 days and listing to transplantation was 3 days. Median time from referral to transplantation was 9 days. Four patients were transplanted from intensive care, 3 were ventilated prior to transplant. Three patients were transplanted from high dependency. Five patients had abdominal sepsis; in 3 patients this was due to multi-resistant organisms. Six patients required intra-operative haemofiltration but none required intra-operative bypass. Length of stay was significantly longer in the urgent group, median 122 days (range 71-193), when compared to the non-urgent group, median 78.5 days (range 35-159), $p = 0.03$. This may reflect the urgent group being inpatients at the time of transplant. Patients transplanted acutely have an 80% 5-year survival compared to 53.3% in those transplanted non-urgently.

Discussion

Although a small group this data suggests that patients referred following abdominal catastrophes can undergo successful urgent multivisceral transplantation and this should be considered as a potential treatment option. These patients are younger which may contribute to better outcomes. The successful transplantation of these patients depends on a flexible approach by both NASIT and NHSBT to ensure that assessment and listing of these patients is achieved as rapidly as possible.

O035

Molecular characterization of acute cellular rejection occurring during intentional immunosuppression withdrawal in liver transplantation

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Introduction

The molecular characteristics of acute rejection in human liver transplantation have not been adequately defined. To simultaneously assess the blood and liver tissue molecular profile of liver recipients undergoing acute rejection, we analysed sequential biological specimens collected from liver transplant patients enrolled in two prospective multicentre European immunosuppression (IS) withdrawal trials, in which IS drugs were gradually discontinued over a 6-9 month period.

Methods

Out of the 136 enrolled patients, 58 were successfully weaned while 72 underwent acute cellular rejection. For the current study we analysed samples from 55 rejecting patients (9 HCV-pos and 46 HCV-neg). Liver tissue and blood samples were available before the initiation of IS withdrawal and at the time of rejection. In addition, at least 6 sequential blood samples were collected before the diagnosis of rejection. Gene expression profiling was conducted employing a combination of Illumina whole-genome microarrays and Fluidigm real-time PCR. Microarray differential gene expression was assessed employing LIMMA ($p < 0.05$ and $FC > 1.2$).

Results

Acute cellular Rejection resulted in distinct blood and liver tissue transcriptional changes in patients who were either positive or negative for hepatitis C virus (HCV). Gene expression changes were mostly independent from pharmacological immunosuppression, and their magnitude correlated with severity of histological damage. Differential expression of a subset of genes overlapped across all conditions. These were used to define a blood predictive model that accurately identified rejection in HCV-negative, but not HCV-positive, patients. Changes were detectable 1-2 months before rejection was clinically diagnosed.

Discussion

Our results provide insight into the molecular processes underlying acute cellular rejection in liver transplantation and help to clarify the potential utility and limitations of transcriptional biomarkers in this setting.

O036

A Scottish study of the impact of HLA donor specific antibodies in liver transplantation

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Introduction

Historically, preformed HLA donor specific antibodies (HLA DSA) have been considered to have limited impact after liver transplantation. This has been attributed to the liver's unique ability to neutralise DSA by mechanisms such as phagocytosis of antigen-antibody complexes and secretion of class I HLA molecules. Recently, however, large studies have found an association between HLA DSA detectable by Luminex technology and recipient survival. We have therefore investigated the impact of HLA DSA in the Scottish liver transplant population.

Methods

Recipients of all liver transplants performed at the Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh from 1st January 2007 to 31st December 2014 were included. Clinical demographics and data on transplant outcomes were collected prospectively. Day of transplant serum samples were tested using Luminex single antigen beads and reactivity >1000 MFI against individual HLA class I and II donor antigens summed to give a cumulative MFI value. Data analysis was performed using SPSS v 22.

Results

644 liver transplants were performed in the study period; 368 (57%) recipients were male. The median recipient age at transplantation was 56 years. A first transplant was performed in 603 recipients, a second in 36, a third in four and a fourth in one. The most common cause of hepatic failure was alcoholic liver disease (22%) while 10% of recipients had hepatitis C as their primary pathology. There were 38 cases of death-censored graft loss and 107 deaths in the follow up period. Pre-transplant serum samples were available for 459 (71%) of recipients. DSA were detected (MFI >1000) in 88 (19%) recipients. DSA were stratified as low level (MFI <5000) or high level (MFI >5000). In univariate analysis, there was no statistically significant association between the presence of DSA, HLA DSA class or DSA MFI and either graft or recipient survival. In a multivariate Cox regression analysis only age was associated with recipient survival (HR 1.03 per annum, p = 0.006).

Discussion

In the Scottish liver transplant population, the presence of HLA DSA is not associated with reduced recipient survival. This may reflect the small proportion of recipients in this cohort whose primary liver pathology was hepatitis C. The studies which have reported an association between HLA DSA and recipient mortality after liver transplantation have been performed in cohorts with a high incidence of hepatitis C infection. For populations with an alternative disease demographic, this study does not support a role for HLA DSA in graft or recipient survival following liver transplantation.

O037

Identifying factors associated with de-listing and mortality on the liver transplant waiting list

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Introduction

Once patients are listed for liver transplantation, waiting time for cadaveric transplantation is dependent on blood group and severity of liver disease. Severity of liver disease, blood group and time to transplant all contribute to mortality on the liver transplant waiting list. Minimisation of waiting list mortality by timely transplantation of patients remains a major challenge in an era of organ paucity. We sought to identify factors that contributed to mortality and removal from the transplant waiting list, to ascertain whether these could be identified at the time of assessment.

Methods

Retrospective analysis of all liver transplantation assessments in 2014. Information was collected from clinical notes and electronic liver database. Data was analysed using t-test and Chi-squared, comparing those who were transplanted with those who were de-listed or died.

Results

Of the 222 patients assessed and listed for transplant in 2014, 139 (62.6%) have been transplanted, 13 died (5.9%) and 23 were de-listed (10.4%). There was no significant difference between age ($p=0.45$), UKELD ($p=0.3$), MELD ($p=0.1$) or Child-Pugh ($p=0.51$) at assessment between those that did and did not achieve transplantation. There was no significant difference between blood groups ($p=0.11$), hepatocellular carcinoma as an indication ($p=0.15$), aetiology of liver disease ($p=0.96$) or those assessed urgently or electively ($p=0.41$). The mean time from assessment to death or de-listing was 185 days. There was no difference between rates of prioritisation on the transplant waiting list, 5 (13.9%) of those who died or were de-listed had been prioritised compared to 26 (18.7%) who have been transplanted ($p=0.78$). Of those de-listed, 8 were due to HCC progression beyond criteria, 5 were in multi-organ failure, 4 had significant co-morbidities, 4 improved clinically and 2 were drinking alcohol or using recreational drugs.

Discussion

Despite previously recognised risk factors for mortality on the transplant waiting list, we were unable to identify any factors which were present at the time of assessment for liver transplant, which impacted on mortality or de-listing on the waiting list. A number of patients were prioritised on the waiting list in order to facilitate earlier transplantation, but despite this they either died or were de-listed. This reinforces the fact that the clinical trajectory of patients requires close monitoring on the waiting list, and that they should be informed of the significant risk of not surviving to transplantation.

O038

Impact of donation on long term cardiovascular morbidity risk in elderly living kidney donors using the QRISK equation as a risk assessment tool

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Introduction

Living donor renal transplantation (LDRTx) is the gold standard treatment for ESRD. Elderly living donation (ELD) is becoming a common norm. Impact of this donation on their long-term cardiovascular morbidity (CVM) is not very well studied. In this retrospective study we aimed to answer this question by looking into CVM in ELD by using simple QRISK equation at the time of donation and thereafter.

Methods

This retrospective study included 221 LDRTx performed at our centre from 2008 to 2012. The study population was divided into two cohorts according to their age into cohort A ≤ 59 years (n=176) and cohort B ≥ 60 years (n=45). We calculated their QRISK at pre-donation and at 6, 12 and 24 months post donation. We then compared inter and intra group QRISK scores for any significance.

Results

General demographics are shown in table 1.

| Demographics | Cohort A (≤ 59 yrs; n=176) | Cohort B (≥ 60 yrs; n=45) | Significance |
|------------------------------------|----------------------------|---------------------------|--------------|
| Age (years) | 45.3 | 64.1 | < 0.0001 |
| BMI (Kg/m ²) | 26 | 26 | 0.509 |
| Systolic BP (mmHg) | 127 | 130 | 0.0926 |
| Treated hypertension (%) | 3 | 13 | < 0.0001 |
| eGFR (mL/min/1.73 m ²) | 95.4 | 88.8 | 0.0061 |

We observed that donors ≥ 60yrs are at increase risk of cardiovascular morbidity irrespective of time when compared to ≤ 59yrs donors (Fig 1). Also within each group after two years there is significant increase in CVM (Fig 2).

Figure 1: QRISK inter group comparison

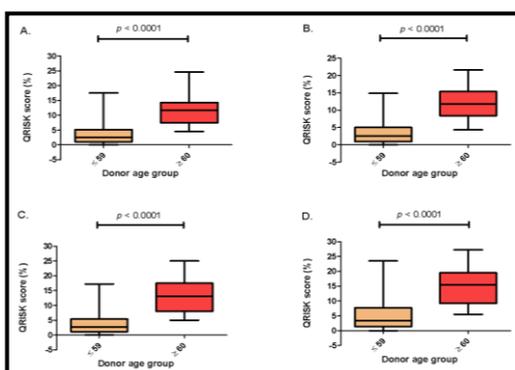
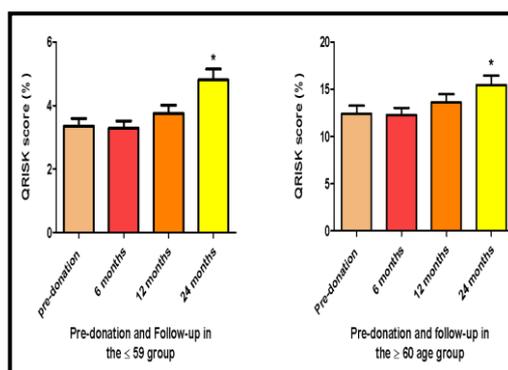


Figure 2: QRISK intra group comparison



Discussion

These results show that risk of CVM event in 10 years following donation is higher in ELD. This does not rule them out as a donor but demands vigorous pre donation cardiac investigations and long term postoperative care in addition to specific counselling for lifestyle modification to reduce modifiable CVM risk factors.

O039

Should we accept organs from donors with Meningitis and/or Encephalitis?

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Introduction

Many patients who die from meningitis/ encephalitis (M/E) may be able to donate organs. This study aimed to quantify the risk of infection from such donors along with the risk of discarding these organs.

Methods

UK Transplant Registry data on recipients of transplants from donors who died from M/E in the UK between 2003 and 2015 were reviewed. Kaplan-Meier tables and Cox proportional hazards were used to compare graft and patient recipient survival compared with all other deceased organ recipients.

Results

70 donors were identified who died of an unknown/unspecified cause of M/E (UKME) and 188 donors who died of known cause M/E (KME). This resulted in 894 solid organ transplants. The UKME donors were younger than those who died of other causes (median 29.5y IQR [23.0] vs. median 50y IQR [23.0], $p < 0.0001$) and the organs were more likely to be transplanted into younger recipients. Livers from UKME donors and hearts from KME donors were more likely to be transplanted into super-urgent recipients ($p = 0.06$) and urgent recipients ($p = 0.0002$) respectively. The unadjusted 10-year patient survival from transplantation for KME kidney recipients was 88% compared to 76% for kidney recipients from donors who died from other causes, ($p = 0.002$). Graft and Patient survival was similar for all other types of organ transplant. Of the 121 kidney transplants from UKME donors, 2 died as a result of infection from the same donor. Unadjusted 5-year survival for patients listed for liver transplantation was 85% for those receiving a liver from a KME or UKME donor vs. 39% for those who remained on the transplant waiting list ($p < 0.0001$).

Discussion

Recipients of organs from KME and UKME donors have similar patient and graft survival to all other deceased donor transplants, and have improved survival compared to patients who remained on the waiting list. These organs should however be used with caution and with informed consent from the recipient.

O040

Patients selected for kidney transplantation have higher health literacy: results from the ATTOM study

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Introduction

'Health literacy' defines the ability to access, understand and use health-related information to improve health. Limited health literacy (HL) is a risk factor for poor outcomes in patients with chronic diseases, including chronic kidney disease (CKD).

The capacity of renal replacement therapy (RRT) patients to cope with their disease and treatment and negotiate the process of transplant work-up is likely to be influenced by their level of health literacy. Limited HL has been associated with socioeconomic status (SES), comorbidity and outcomes in small studies of RRT patients in the USA. We report results from a large, UK-wide study.

Methods

This cross-sectional study uses baseline data from the 'Access to Transplantation and Transplant Outcome Measures'(ATTOM) cohort. ATTOM recruited incident dialysis and transplant patients aged 18-75 years in the UK during 2011-2013 and also wait-listed patients similar to those transplanted (matched controls). HL was measured by the question 'How often do you need someone's help to read instructions, leaflets, or other written material from your doctor or pharmacy?' answered on a scale from 1-Never to 5-Always. Limited HL was defined as a score greater than 2. The three groups were analysed for associations between Limited HL and demographics, SES factors and comorbidity, using univariate and multivariate analysis, $p < 0.05$.

Results

6842 patients were recruited: 2621 incident dialysis (ID), 2262 incident transplant (IT) and 1959 wait-listed (WL). 6373/6842(93%) completed the health literacy assessment. Prevalence of Limited HL was 20% in the ID, 12% in the IT and 15% in the WL group.

In all groups, in adjusted models, Limited HL was associated with markers of lower SES and comorbidity. Black patients in the WL and IT groups were far less likely to have Limited HL (OR 0.2 compared to white patients).

Significant differences in Limited HL between the WL and IT groups were not present after adjustment for Ethnicity. Differences in Limited HL between the ID and IT groups persisted until adjustment for comorbidity and SES.

Discussion

In this large, UK-wide study, patients selected for kidney transplantation are more health literate than patients starting dialysis. Socioeconomic status and comorbidity are associated with Limited HL. Black patients who reach the point of transplantation are more health literate than their white counterparts. Differences in HL related to SES may influence dialysis patients' likelihood of achieving kidney transplantation.

**Moderated Poster Session
Wednesday 24 February
18:30 – Hall 1 and 2**

Category Summary

| | |
|--------------------|--|
| P001 – P024 | Immunosuppression |
| P025 – P067 | Kidney Transplantation |
| P068 – P086 | Liver Transplantation |
| P087 – P109 | Organ Donation |
| P110 – P132 | Outcomes |
| P133 – P152 | Pancreas and islets |
| P153 – P169 | Basic and Translational Science |
| P170 – P204 | Renal Surgery |

P001

Do clinical trials reflect reality? A systematic review of inclusion and exclusion criteria of immunosuppression trials in renal transplantation

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Introduction

Renal transplant recipient and donor populations are becoming increasingly more marginal, with more expanded criteria (ECD) and donation after circulatory death (DCD) donors and older recipients. Despite this, high risk donors and recipients are often excluded from clinical trials, leading to uncertainty about the generalisability of findings to the current recipient population.

Methods

We searched the Transplant Library database for all full text reports from randomised controlled trials comparing immunosuppressive interventions in adult renal transplant recipients published over a 5-year period between January 2010 and December 2014. Data regarding demographics and inclusion/exclusion criteria were extracted and analysed.

Results

Literature search identified 213 reports from 182 trials. 130 (71.8%) trials recruited living (LD) and deceased donor (DD) recipients, with 28 (15.4%) recruiting only DD recipients and 24 (13.2%) recruiting only LD recipients. 128 (70.3%) studies recruited *de novo* recipients with 54 (29.7%) recruiting stable patients post-transplant. The most common exclusion criteria was age, with 71 studies (39.0%) specifying an upper age limit for inclusion. The proportion of studies excluding patients over 60, 65 and 70 years was 2.7%, 17.6% and 28.0% respectively. 69 studies (37.9%) excluded patients by number of previous transplants, with 38 (20.9%) limiting inclusion to recipients of a first transplant only. 76 (41.8%) studies excluded patients based upon current PRA, with a median cut-off of 30% (range 20-50%). 52 (28.6%) studies excluded ABO or HLA incompatible recipients. Exclusion criteria relating to donor characteristics were also common, with 27.2% and 7.0% excluding DCD and ECD donors respectively. Other common exclusion criteria included donor age (15.9%), maximum cold-ischaemic time (21.4%), haematological parameters (21.4%), maximum body mass index (BMI) (4.9%), current infection (21.4%), positive viral serology (21.4%), previous malignancy (26.9%) and glomerulonephritis with the potential for recurrence in the graft (5.5%).

Discussion

Many recent immunosuppression trials have restrictive inclusion criteria which do not reflect the changing nature of current donor and recipient populations. Caution is advised when applying the results of these trials to older, higher risk recipients and recipients of more marginal organs. There is a need to consider these populations for inclusion in future trials.

P002

Earlier repletion of lymphocytes after alemtuzumab induction is associated with a lower incidence of infection following renal transplantation

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Introduction

Alemtuzumab has been increasingly used as an induction agent in renal transplantation, although the optimal dose is unknown. We have previously reported that alemtuzumab dose adjusted for weight (AD) resulted in a reduction of microbiologically proven infection episodes compared with a historic control group who received a standard dose of 30mg (SD), without an apparent increase in rejection rates.

Methods

In this study we have examined the rate of leucocyte repletion in 366 patients receiving AD (0.4mg/kg) and 590 patients receiving SD alemtuzumab induction. All received tacrolimus monotherapy.

Results

There was no difference in gender, ethnicity, type of graft, regrafts, diabetes and HLA mismatch between the groups. The AD group were older [52.3±12.9 versus 48.9±13.3, p=0.001] and were more likely to be sensitised [139/366(38.0%) versus 129/590(21.9%), p<0.001]. There was no difference in weight at the time of transplant [75.4±17.9 versus 76.1±17.5kg, p=0.58], with the range of doses given in the AD group of 13.6-50mg. On multivariate analysis, factors associated with infection were older age (p=0.0048), diabetes (p=0.002) and female gender (<0.001). Receiving a live donor transplant (p=0.0017) and AD alemtuzumab (p=0.019) were protective against infection. The table below shows the mean total WCC, lymphocytes and monocytes in the SD and AD groups during the first year after transplantation. In the AD group there was a significantly earlier time to repletion of lymphocytes and monocytes.

| Mth | Total WCC | | | Lymphocytes | | | Monocytes | | |
|-----|-----------|---------|-------|-------------|---------|---------|-----------|---------|--------|
| | SD | AD | p | SD | AD | p | SD | AD | p |
| 1 | 4.8±1.6 | 5.0±1.8 | 0.30 | 0.3±0.2 | 0.4±0.4 | <0.0001 | 0.3±0.2 | 0.4±0.2 | 0.008 |
| 2 | 4.9±1.8 | 5.0±1.9 | 0.46 | 0.5±0.3 | 0.6±0.4 | <0.0001 | 0.4±0.2 | 0.4±0.2 | 0.02 |
| 3 | 5.3±1.8 | 5.7±1.9 | 0.002 | 0.7±0.4 | 0.9±0.5 | <0.0001 | 0.5±0.2 | 0.5±0.2 | 0.0005 |
| 6 | 5.9±1.9 | 6.3±1.9 | 0.002 | 1.0±0.5 | 1.2±0.6 | <0.0001 | 0.5±0.2 | 0.5±0.2 | 0.013 |
| 9 | 6.3±2.0 | 6.6±2.2 | 0.06 | 1.1±0.5 | 1.3±0.5 | <0.0001 | 0.5±0.2 | 0.6±0.2 | 0.08 |
| 12 | 6.3±2.2 | 6.7±2.2 | 0.06 | 1.2±0.6 | 1.3±0.5 | 0.0002 | 0.5±0.2 | 0.6±0.2 | 0.33 |

Discussion

Alemtuzumab dose adjusted for weight at the time of transplantation is associated with a reduction in infection episodes. Repletion of total WCC, lymphocytes and monocytes occurs significantly earlier in the AD group, which may explain the reduction in infective episodes.

P003

The effect of donor age on acute rejection age: The clinical impact of donor immuno-senescence in the modern immunosuppressive era

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Introduction

Experimental work of Tullius et al. has shown that donor age may not only affect intrinsic function but also alter the immune response of the recipient so that older donor grafts elicit a stronger immune response in the early period after transplantation. Clinical data supporting this notion was so far lacking.

Aim of the study was to see the impact of donor age to the frequency of rejection in both DBD and DCD kidneys.

Material and methods

All recipients of deceased kidney transplants in a single centre over 4 years were analysed for the presence of biopsy proven acute rejection. The rejection was correlated with donor and recipient age, matching, presence of DGF and, given the differing immunosuppression in age groups and types of donor, the induction used.

Results

During a 4-year period 338 deceased transplants took place in a single centre (142 DBD, 196 DCD) with a median donor age of 58 years. 44.7% of the donors and 47% of the recipients were over 60 years old. 75% of DBD kidney recipients received Basiliximab induction as opposed to 66% of DCD recipients receiving either ATG or Campath induction and 34% Basiliximab.

There was no difference between the rejection rates of younger vs. older recipients ($p=0.47$) but this might have been affected by the mal-distribution of the induction used in those 2 subpopulations. There was a 15.2% vs. 7.5% rejection rate in the *older donor kidney recipients* (Fisher exact test $p=0.03$, OR 1.1-4.8).

In order to check for all the factors affecting the rejection rate and avoid potential confounders, we performed binary logistic regression. The older donor age was the only significant factor for rejection ($p=0.008$) whereas the recipient age, DGF, overall mismatch and DR mismatch were not.

In subgroup regression analysis in DBD donors again only donor age was significant factor for rejection ($p=0.009$) whereas in DCD kidneys, only the induction regime was significant for rejection ($p=0.017$) (whereas donor age was not) with significantly less patients on Campath or ATG having rejections compared to basiliximab (7.9 vs. 13.8%).

Discussion

This is the largest clinical study showing that senescence of the donor kidney affects the rejection rate in the modern immunosuppressive era particularly in brain dead donor kidneys. This is not mediated via DGF. We do not know whether it is that aggressive induction in DCD donor kidneys in our centre is blocking this effect or the phenomenon is altogether absent in the absence of the brain storm that follows the brain death.

P004

Biopsies for DGF after Alemtuzumab induction in kidney transplantation: The incidence of early rejection after Alemtuzumab is very low but not negligible

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Introduction

Standard UK practice advocates performing transplant biopsy around day 7, and weekly thereafter in the presence of delayed graft function (DGF) because, if missed in this context, early rejection is known to adversely affect long term graft survival. Due to profound depletion of lymphocytes and monocytes, Alemtuzumab induction regimens are associated with very low early rejection rates and this may alter the risk/benefit balance for biopsies during periods of DGF. We analysed the findings of biopsies done within 30 days of transplantation in a large cohort of patients, most of whom received Alemtuzumab induction with short (7 day) steroid exposure and Tacrolimus maintenance monotherapy.

Methods

Biopsies done within 30 days of transplantation were identified from histology and renal unit data sources. Biopsies for delayed graft function were broadly defined as patients requiring dialysis after transplant, or whose creatinine levels failed to fall fast enough, or far enough during the initial post-transplant period. Histology findings were reviewed in the context of clinical outcomes comparing these with biopsies undertaken for rising Creatinine. The rejection rate, and other biopsy findings were compared between Alemtuzumab-treated recipients and the smaller group of patients (who did not fulfil local criteria for the Alemtuzumab/Tacrolimus regimen) who were transplanted under anti-IL2-R monoclonal antibody blockade induction (IL2RMoAb)/Tacrolimus/MMF.

Results

909 patients underwent renal transplantation between 23/12/2009 and 16/10/2015, including recipients of simultaneous kidney and pancreas transplants. 804 (88.4%) were treated with Alemtuzumab induction, and 105 (11.6%) received IL2RMoAb induction. 258 patients had renal allograft biopsies within the first 30 post-operative days; 226 Alemtuzumab treated (of which 112 were for broadly defined DGF) and 32 after IL2RMoAb (18 for DGF). Cellular rejection during DGF after Alemtuzumab induction was found in only 2 patients (1 of whom failed to deplete after Alemtuzumab and had ACR at day 8). Overall rejection during DGF occurred in 3.6% of Alemtuzumab treated vs.12.5% after IL2RMoAb. Rejection during DGF after Alemtuzumab occurred at 8, 22, 24, and 28 days post-transplant.

| | ATI | CNI | Focal Infarct | Graft Pyelo. | Sub-ACR Infiltrate | ACR | Mixed/ AbMR | TMA/GN |
|--------------------|-----|-----|---------------|--------------|--------------------|-----|-------------|--------|
| Alemtuzumab | | | | | | | | |
| DGF | 99 | 2 | 2 | 3 | 1 | 2 | 2 | 1 |
| Rise | 80 | 6 | 3 | 3 | 7 | 5 | 8 | 2 |
| IL2RMoAb | | | | | | | | |
| DGF | 10 | 0 | 0 | 1 | 1 | 2 | 2 | 2 |
| Rise | 5 | 1 | 0 | 0 | 3 | 5 | 0 | 0 |

Discussion

Rejection during dialysis-requiring, or “failure to fall” DGF after Alemtuzumab induction is very rare, but does occur, as do other conditions (notably graft pyelonephritis, and recurrent glomerular disease) whose detection on transplant biopsy will alter management and lead to improved graft outcomes. Delayed graft function remains an indication for kidney transplant biopsy after Alemtuzumab induction.

P005

Insights into the treatment of Post-Transplant Focal Glomerulosclerosis: Experience gained from a concise diagnostic and management protocol

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Background

Recurrence of Focal Glomerulosclerosis (FSGS) after kidney transplantation is associated with poor graft survival and currently optimal treatment remains controversial. We present results from a concise diagnostic and management protocol that was introduced in our institution in 2011 and proposed treatment of post transplant FSGS with Plasma Exchange (PEX) and Rituximab (RTX).

Methods

We compare the outcomes between 10 consecutive kidney transplant recipients (KTR) with post-transplant FSGS that were treated with a protocol based on histology for diagnosis and that consisted of RTX (total of 2gr over 2 infusions, 2 weeks apart) and monthly cycles of 5 PEX over 7 days for 6 months to a historic control group of 9 KTR's with post-transplant FSGS. We retrospectively selected the historic group, based on the same histopathology criteria that were applied to the patients under our current protocol. Patients with a primary diagnosis of FSGS as well as transplant recipients with non-biopsy proven primary diagnosis that developed post transplantation proteinuria with evidence of segmental or focal glomerulosclerosis on light microscopy or diffuse effacement of podocyte foot processes on electron microscopy (EM) were included.

Results

10 consecutive patients (8 male, mean age 51 years, range 23-67) were treated with the new protocol (group A) while the historic control group consisted of 9 KTR's (6 male, mean age 54 years, range 34-71) (group B). The mean time to diagnosis was 6.8 (0.1 – 34.6) for group A and 13.5(1.5-40.3) months for group B. All group A patients received treatment with at least 2gr of RTX in total and PEX, while group B received a variety of treatments; IVIG+PEX (n=4), PEX (n=4) or no treatment (n=1). 9 out of 10 patients in group A achieved remission after the conclusion of treatment (4 complete and 5 partial), while in Group B 5 out of 9 patients achieved remission (2 complete and 3 partial). During the follow up period, 1 patient from each group relapsed, and ended up requiring dialysis at 11 and 24 months post diagnosis, respectively. In relapse free responders there was a significant reduction in mean uPCR between diagnosis (645+/-667 mg/mmol) and 1 year (126+/-130 mg/mmol) in group A (p=0.026), but not in group B. (777+/-867 mg/mmol vs 152+/-158 mg/mmol, p=0.17)

Conclusion

The present study demonstrates the significant benefits in the treatment of post transplant FSGS with a uniform diagnostic and treatment protocol with PEX and RTX. These promising preliminary results will have to be confirmed on a larger population and over a longer follow up.

P006

Age adapted immunosuppression for elderly kidney allograft recipients: Balancing risks for cancer versus rejection

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Introduction

Cancer is a growing cause of morbidity and mortality after kidney transplantation, driven by the milieu of immunosuppression. Age is one of the strongest risk factors for developing cancer after transplantation and, with immunosenescence in the elderly well documented, age-adapted immunosuppression may be warranted for older adults to reduce overall immunosuppression burden but this requires further investigation.

Methods

Data was extracted by the hospital informatics team for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up 4.4 years post-transplantation. Median age for the study cohort was 47 and we classified older at this dichotomised age of 47 and over compared to younger recipients aged under 47. Older versus younger recipients had increased risk for death post-transplantation (10.6% versus 3.3% respectively, $p < 0.001$) but not death-censored graft losses (9.1% versus 11.3% respectively, $p = 0.130$). Cancer-related mortality for older versus younger recipients was 12.9% versus 5.9% respectively. Cancer was more common in older versus younger recipients (9.0% versus 3.1% respectively, $p < 0.001$), with increased risk among older versus younger adults for both skin cancer (3.0% versus 0.9%) and non-skin cancers (6.1% versus 2.2%). Cancer-related mortality occurred in 12.9% of patients who developed cancer post-transplant (all non-skin cancer related). Older versus younger recipients were more likely to have cardiac events (9.6% versus 2.2% respectively, $p < 0.001$) and cerebrovascular events (3.2% versus 1.5% respectively, $p = 0.039$) post-transplant. However, older versus younger recipients had the same risk for cellular rejection (13.7% versus 12.6% respectively, $p = 0.324$) but reduced risk for either antibody-mediated rejection (2.7% versus 4.7% respectively, $p = 0.047$) or mixed rejection (1.4% versus 3.5% respectively, $p = 0.015$). Of note, older recipients were more likely to be receiving their first kidney allograft versus younger recipients (94.6% versus 85.6% respectively, $P < 0.001$), which confounds the risk for rejection among this cohort.

Conclusion

Older kidney allograft recipients have increased risk for death and immunosuppression-related complications including cancer, cardiac and cerebrovascular events but reduced risk for rejection. Our data supports the rationale of older recipients may benefit from tailored immunosuppression to reduce risk from immunosuppression-related complications but targeted clinical trials in the older adult population are warranted.

P007

Late renal allograft rejection is predicted by high inpatient variability of Tacrolimus levels

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Introduction

Nonadherence (NA) to immunosuppressive medication is associated with rejection and graft loss. We have previously shown that inpatient variability (IPV) of tacrolimus trough levels between 6-12 months post-transplant can be used as a surrogate marker for adherence and that a high IPV can predict rejection and graft loss. In this study we assess the variability of tacrolimus levels preceding an episode of late first episode rejection (after one year).

Methods

We retrospectively analysed 668 patients who received a low risk kidney only transplant between 01/11/2005 and 01/09/2013. Patients who developed rejection in the first year post transplant were excluded. All patients received alemtuzumab induction and tacrolimus monotherapy with a steroid sparing protocol with a target pre-trough tacrolimus level of 5-8ng/ml. Controls were chosen as patients transplanted immediately before and after each rejection case from the overall cohort (N=124). Tacrolimus levels at matched time intervals to the rejection cases were used for analysis.

Results

62 cases of late first rejection episodes were identified. The mean time to rejection was 2.28 ± 1.16 years. Mean follow up 5.65 ± 2.12 years

| | Rejection | Non-rejection | p value |
|---------------------------|-------------------|-------------------|---------|
| IPV pre-rejection** | 25.88 \pm 12.17 | 22.38 \pm 9.18 | 0.0298 |
| Mean tacrolimus level | 6.81 \pm 1.25 | 6.89 \pm 1.21 | 0.68 |
| Mean Max tacrolimus Level | 11.49 \pm 4.47 | 10.62 \pm 3.52 | 0.15 |
| Mean Min tacrolimus Level | 3.96 \pm 1.23 | 4.44 \pm 1.27 | 0.015 |
| Mean tacrolimus count | 24.71 \pm 13.84 | 20.31 \pm 14.95 | 0.078 |

**Tacrolimus levels were taken from 6 months up until rejection in the rejection cases or matched time points in the controls.

Discussion

This study shows that high IPV and lower minimum tacrolimus levels predict late first episode rejection. This analysis supports the need for a prospective study to assess strategies which minimise nonadherence, reduce the variability of tacrolimus levels, maintain patients within the therapeutic range of tacrolimus and reduce the risk of development of late rejection and graft loss.

P008

Immunosuppression tapering for BK virus allograft nephropathy is not associated with increased risk for rejection or death-censored allograft failure

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Introduction

BK polyomavirus-associated nephropathy (BKVAN) affects 1-15% of kidney allograft recipients and has been associated with premature kidney allograft failure in the transplantation literature. However, the impact of BKVAN on kidney allograft outcomes in the contemporary setting remains unclear. The aim of this single-centre study was to review the risk factors for BKVAN in a contemporary transplant cohort, review the clinical management of such patients and analyse the effect of BKVAN on both patient and kidney allograft outcomes.

Methods

Data was extracted from hospital informatics systems for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events. Immunosuppression utilised during this time for patients included basiliximab induction and standard maintenance immunosuppression of tacrolimus, mycophenolate mofetil and low-dose corticosteroids. Screening for polyoma virus replication was by indication in the context of kidney allograft dysfunction.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up to 4.4 years post-transplantation. The median age for the cohort was 47, males (n=681, 59.7%), Caucasian ethnicity (n=822, 72.1%), deceased-donor recipients (n=633, 56.4%), repeat transplants (n=111, 9.7%), diabetes as cause of end-stage kidney disease (n=117, 10.3%) and previous/active smoking exposure (n=274, 24.0%). In total, 29 patients had evidence of polyomavirus in viraemia and nephropathy (3.4%), 25 had evidence of viraemia alone (2.2%) and 1,070 patients had no polyoma virus. Receiving an ABO-incompatible kidney transplant was the only independent risk factor for development of BKVAN. Management of BKVAN was heterogeneous with the five commonest strategies including; mycophenolate cessation (56.4%), tacrolimus reduction (25.6%), tacrolimus conversion to ciclosporin (10.3%), tacrolimus conversion to sirolimus (12.8%), or mycophenolate conversion to leflunomide (17.9%). There were only a handful of cases utilising cidofovir (n=1), IVIG (n=1) and corticosteroid boluses (n=2). BKVAN was associated with risk for rejection (10 cases, p=0.043), but the majority of BKVAN occurred *after* rejection (n=3, 60.0%) versus *before* rejection (n=3, 30.0%) and there was only one case of simultaneous BKVAN and rejection (10.0%). BKVAN versus no BKVAN was not associated with any significant difference in patient survival (92.3% versus 92.9% respectively, p=0.534), death-censored graft survival (94.9% versus 89.6% respectively, p=0.222) or overall graft survival (87.2% versus 83.9% respectively, p=0.390).

Discussion

Immunosuppression tapering appears to be heterogeneous and varied among clinicians. Despite this, in a contemporary setting, immunosuppression tapering for patients with BKVAN is associated with low risk for rejection and there is no observed difference in short-to-medium term patient and kidney allograft outcomes post-transplantation.

P009

Low level immunosuppression in the ReMIND Study: Achieving trough level targets up to one year post renal transplant

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Introduction

The ReMIND study is a phase IV open label, controlled trial testing the hypothesis that Rituximab induction allows minimisation of maintenance immunosuppression using low level Tacrolimus (Symphony protocol) and early steroid withdrawal following renal transplantation. The ReMIND study protocol requires Tacrolimus trough levels of 3-7ng/ml, and in our institution Advagraf once daily is used for these patients. For non study patients, the standard care Tacrolimus trough level target is 10-12ng/ml in the first 2 months following transplantation, and 8-10ng/ml thereafter, in the standard risk group (Adoport, twice daily).

Tacrolimus for ReMIND study participants at the host site is routinely prescribed by outpatient clinicians who are not directly associated with the study, but aware of the protocol trough target levels.

Methods

Tacrolimus trough levels were taken >24 hours post dose from 43 ReMIND study patients and >12 hours post dose for 40 non ReMIND patients at 6 time points between the day of transplant and one year post transplant. These values were grouped as either within or out of range, and converted to a percentage of the total number of results for each time point. An independent t test was also used to compare Tacrolimus trough levels in the two groups.

Results

As expected, Tacrolimus trough levels were significantly different in the ReMIND study patients when compared with the non ReMIND study patients at days *7, **30 and ***90. *p<0.05, **p<0.01, ***p<0.001 (independent t-tests).

On average 58% of Tacrolimus trough levels for the ReMIND study were within protocol range across the six time points, compared to an average of 31% of non ReMIND study Tacrolimus trough levels.

Using a Chi-square test, the number of trough levels (%) within range were compared in the ReMIND and non-ReMIND groups. Advagraf recipients achieved the given target more often than Adoport patients. Day 0 (65% vs 17% p<0.001), Day +7 (60% vs 16% p<0.001), Day +30 (54% vs 31% p=0.001), Day +90 (48% vs 48% p=1), Day +180 (65% vs 36% p<0.001), Day +365 (57% vs 35% p=0.001) (Chi-square test).

Discussion

The data demonstrates that there is better compliance with the protocol target range for the Advagraf group when compared to the Adoport group. Influencing factors may include increased compliance with a once a day regimen in comparison to twice daily regimens, past medical history and clinical preference. This also illustrates that the low levels of Tacrolimus described in the Symphony study may not be accurately reproduced in clinical practice. These findings could inform future studies where the required drug level range is lower than that of standard care.

A systematic review of the quality of outcome reporting in immunosuppression trials in renal transplantation

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Introduction

Interpretation, comparison and combination of the results of clinical trials is reliant on accurate and complete reporting of outcomes. Studies in other disciplines have demonstrated significant variability in the quality of outcome reporting. This review aims to assess the quality of outcome reporting in clinical immunosuppression trials following renal transplantation.

Methods

We searched the Transplant Library database for all full text reported from randomised controlled trials comparing immunosuppressive interventions in renal transplant recipients published over a 5-year period between January 2010 and December 2014. All outcomes reported in the studies were extracted, along with data regarding completeness of reporting and whether a clear definition of the method (consensus definition, score, test or equation) used to assess the outcome measure was provided.

Results

213 reports from 182 studies were identified. In total, 4,760 outcomes were reported. Overall, 90.3% outcomes were completely reported; 2.1% had missing measures of variance, 4.5% were only reported as significant/non-significant, 0.7% had a graphical representation only and 2.3% were mentioned as assessed in the methods but not reported. 45% of outcomes did not have a clear definition provided. Primary outcomes were more likely to be clearly defined than secondary (OR 4.27, $p=0.002$). The most commonly reported efficacy outcomes were acute rejection (81.7%), measures of graft function (81.7%), graft survival (68.5%) and patient survival (68.1%). Efficacy outcomes were clearly defined in 90.9% of cases, and were more likely to be clearly defined than safety outcomes (OR 0.022, $p<0.001$) or patient reported outcomes (OR 0.014, $p<0.001$). The most commonly reported safety outcomes related to infections (58.2%), malignancies (42.3%), new onset diabetes (43.7%), hyperlipidaemia (48.4%) and hypertension (44.1%). Overall, only 39.3% safety outcomes had a clear definition. Patient reported outcomes (PROMs) were reported in less than half of studies (46.5%) and only 5 studies (2.3%) reported quality of life data using a validated tool. Only 12.8% PROMs had a clear definition. The greater the number of outcomes a study reported, the less likely that outcomes would be clearly defined.

Discussion

Whilst completeness of outcome reporting is good, the outcomes reported in trials in renal transplantation are often poorly defined making interpretation difficult. In particular, safety and patient reported outcomes are less often measured and are poorly reported. There is also a great deal of variation in the definitions used for individual outcomes, making comparison and combination of studies difficult. Very few studies report validated measures of quality of life.

P011

A retrospective, tertiary centre analysis of variability in immunosuppression levels and allograft rejection in young adult patients after transition to adult services

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Introduction

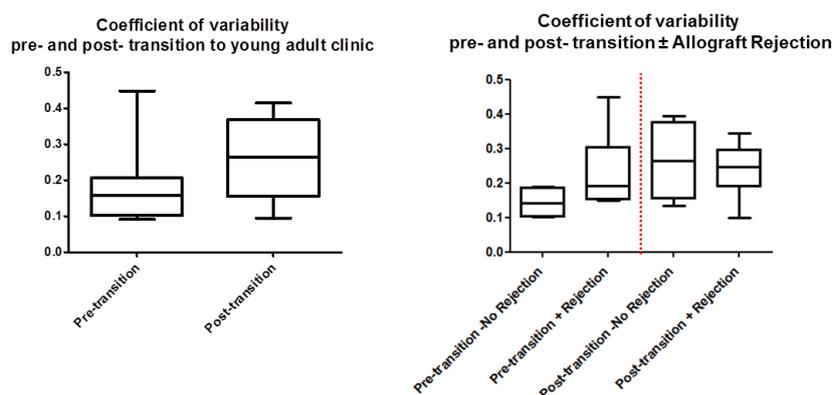
Transition from paediatric to adult services is well recognised as a perilous period for adverse outcomes in a broad range of chronic conditions including renal transplantation. Medication non-adherence has previously been implicated as an important factor in allograft rejection and failure in this cohort of patients. Here we test the hypothesis that high intra-patient variability in immunosuppressant levels is a predictor of allograft rejection.

Methods

This single centre retrospective study reviewed variation in immunosuppressant levels in 17 young adult patients over a four year period around the time of transition from paediatric to adult services. The data were collected from the renal and pathology department databases. Wilcoxon Signed Rank and Mann-Whitney U Tests were used for statistical analysis.

Results

There was no difference in age at transition ($p=0.534$), age at transplantation ($p=0.445$), gender ($p=1$), type of donor ($p=0.559$), use of steroids ($p=0.1$) or type of calcineurin inhibitor (CNI) ($p=0.462$) between the sub-group of patients, who had rejection versus that who did not. The coefficient of variability of CNI levels was greater after transition to adult services, although this was not statistically significant ($p=0.214$). Similarly, comparison of the coefficient of variability of CNI levels prior to transition between patients, who went on to develop allograft rejection and those who did not, revealed greater variability in the cohort who developed rejection ($p=0.257$).



Discussion

The cohort of patient with higher variability in immunosuppressant drug levels in the year prior to transition to adult services went on to have allograft rejection and although there was no statistically significant difference, this trend may be an early indication for clinicians in determining those at greatest risk of non-adherence and worse outcomes in the post-transition period. By individualising care for these patients (with patient education, adherence tools and greater clinician awareness of variability in drug levels), early intervention and prevention of allograft loss is possible.

P012

Variability in the reporting of renal function endpoints in immunosuppression trials in renal transplantation: time for consensus?

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Introduction

Gold standard for the assessment of renal function is a formal measurement of glomerular filtration rate (GFR), but this is often impractical for use in clinical trials. Recent publications suggest that estimated GFR (eGFR) using the MDRD or CKD-EPI equations offer the best estimates of true GFR in renal transplant recipients. This study aimed to assess the variability of reporting of graft function endpoints in contemporary clinical trials of immunosuppression.

Methods

We searched the Transplant Library database for all full text publications from randomised controlled trials comparing immunosuppressive interventions in renal transplant recipients published over a 5-year period between January 2010 and December 2014. Data regarding renal function endpoints (serum creatinine, measured GFR, creatinine clearance (CrCl) and eGFR) were extracted and analysed.

Results

213 reports from 182 trials met the inclusion criteria. 174 (81.7%) reports included a measure of renal function; in 44 (20.7%) this was the primary endpoint. 103 manuscripts (48.4%) reported serum creatinine, 142 (66.6%) reported eGFR and 26 (12.2%) reported measured GFR. Formulas used for GFR estimation were MDRD (42.3%), Cockcroft Gault (23.5%), Nankivell (15.0%) and CKD-EPI (0.9%). 6 studies (2.8%) did not report the formula used to estimate GFR. In the papers reporting formal renal function measurements, 14 (6.6%) reported creatinine clearance and 14 (6.6%) reported radioisotope measured GFR (EDTA 2, iothalamate 7 and iohexol 5). 2 studies did not report the method used. Renal function was completely reported in 86.1% of these studies; 3.2% had missing measures of variance, 3.5% were only reported as significant/non-significant, 1.4% had a graphical representation of results only, and in 6% renal function endpoints were mentioned in the methods but not reported.

Discussion

There is a great deal of variability in the reporting of renal function endpoints in clinical trials of kidney transplantation, with a significant proportion of studies using under-performing estimates that are not recommended for use in transplant recipients. Measured GFR is rarely used in clinical trials due to cost and complexity. Variability in reported renal endpoints makes comparison of trials and combination in meta-analysis difficult. There is a need for consensus as to the best tool for monitoring and reporting renal function post-transplant, and in particular for use in clinical trials and registries.

P013

Management of recurrent aHUS after adult kidney transplantation despite Eculizumab Prophylaxis

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Background

Eculizumab (EZB) is authorised to prevent and treat recurrent aHUS after kidney transplantation.

Purpose

We report aggressive recurrence of aHUS post transplant in a patient despite eculizumab and a multi-disciplinary and collaborative approach to manage the disease.

Report

A 58 year old female was called for deceased donor transplantation. She had presented 3 years earlier with aHUS and heterozygous Factor H mutation. Plasma exchange (PLEX) restored haematological parameters but the patient was left dialysis dependent. She received a kidney from a young donor, HLA mismatch 111. EZB 900mg was given preimplantation with basiliximab, tacrolimus, mmf and prednisolone. Delayed graft function occurred and platelets and haemoglobin fell to $91 \times 10^9/l$ and 95g/l with blood film fragmentation and LDH 1715 (day 3). Further EZB 900mg was given and biopsy performed which showed florid thrombotic microangiopathy with C3 deposition and negative C4d. HLA antibody screen was negative. Serum C3 was reduced but CH100/AP100 showed no lysis/activity suggesting effective blockade of the terminal complement pathway. Platelets fell further with rising LDH and oligo-anuria. Daily PLEX was commenced (day 6) using Octaplas then FFP alongside haemodialysis. ADAMTS13 was 32% and C5 polymorphism (EZB resistance) excluded. EZB was administered after every PEX. Haematological parameters improved over the first week with subsequent increase in urine output. PEX was discontinued after 15 daily sessions and dialysis discontinued on post-transplant day 23. Increased EZB dosing, 1200mg weekly then 1500mg two weekly from week 8 was administered. Repeat biopsy (2 months) showed healthy glomeruli but fibromyxoid change in 2 vessels with current creatinine 342umol/l (GFR 12).

Discussion

Early recurrence of aHUS may occur despite eculizumab and apparent terminal complement pathway blockade (AP100/CH100). Improved understanding of possible recurrence related factors such as ischaemia-reperfusion injury and non-complement pathway driven TMA is needed to identify individuals who may benefit from therapies such as intensive PLEX.

P014

Post- renal transplantation weight gain: No difference with early steroid withdrawal

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Introduction

Weight gain after renal transplantation is common with increased risk of hypertension, hyperglycaemia and hyperlipidaemia which increases cardiovascular risk. Factors implicated in this weight gain include steroid treatment and relaxation of dietary restrictions required when on dialysis. The objective of this study was to analyse the effects of early steroid withdrawal on weight gain in post-renal transplant patients.

Methods

We have evaluated all patients who had kidney transplantation undergoing renal followed up at St. George's Hospital, Tooting, London between April 2009 and April 2014 who were older than 18 years of age and who had at least 12 months of follow-up after renal transplantation. We have examined the changes in weight after renal transplantation over 12 months in patients treated with either early steroid withdrawal (ESW) (<1 month) or continuous steroid treatment.

Results

The study population included 154 recipients; 37% female and 63% males, their mean age was 51 years. Fifty- four patients were withdrawn from steroids within 1 month and one hundred patients were on maintenance steroids after 12 months post-transplantation. Mean post-transplant body weight gain was 0.50 ± 4.37 kg and 0.38 ± 4.29 kg after 3 months, 1.26 ± 4.81 kg and 0.89 ± 7.09 after 6 months, 3.44 ± 6.21 kg and 2.72 ± 8.66 kg after 12 months in ESW and CS respectively.

Discussion

Weight gain in the first 12 months after kidney transplant was independent of the steroid regimen. This emphasises the importance of dietary advice to avoid weight gain after transplantation.

P015

Alemtuzumab induction allows better rejection free graft survival in comparison to Basiliximab although with increased post transplant viral infections

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Introduction

3C study concluded that in comparison to basiliximab, alemtuzumab induction reduces the risk of biopsy proven acute rejection (BPAR) in renal transplant recipients. In our experience at Liverpool, Alemtuzumab and Basiliximab induction safely provided steroid-free maintenance immunosuppressive regimen but the rejection and infection incidence were not established. We compared alemtuzumab and basiliximab induction followed by standard two drug maintenance immunosuppression to assess rejection & infection rate.

Methods

Data was collected retrospectively from patients transplanted between 1/08/2009 to 31/12/2013. 436 patients were analysed, 235 received basiliximab, 198 received alemtuzumab and data was not available for 3 patients. Tacrolimus and MMF were used as maintenance immunosuppression in both groups. Demographics, BPAR episodes, viral infections, and creatinine levels were analyzed using Medcalc 13.0 statistical software.

Results

Review of the data showed no significant differences for demographic details, graft survival, patient survival.

Basiliximab group had increased incidence of BPAR, 52/235, 22.1% as compared to Alemtuzumab 15/198, 7.5% (Yates correction <0.001, Fischers Exact test one tailed p<.0001). Median creatinine level at 6 weeks was 128± 21 µmol/L (Basiliximab) & 115± 16 µmol/L (Alemtuzumab).

On the contrary, incidence of Viral infections was higher in the Alemtuzumab group vs Basiliximab [CMV (77/198 vs 57/235, Fischer Exact test one tailed p<0.0002, Pearson Test p< 0.0004), BK (34/198 vs 17/235, Fischers Exact test one tailed p<0.0006)].

Discussion

Alemtuzumab induction significantly reduces the incidence of rejection but at the cost of increased viral infections. Our Study corroborates the 3C Trial findings. Further review of data over time will assess long term graft outcomes.

P016

Description of the method to embed a variability calculator into the renal CV5 IT system

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Introduction

Reports suggest that high inpatient variability in tacrolimus trough levels may predict poorer transplant graft outcomes. Using an off-the-shelf variability calculator within the UK NHS is challenging with strict criteria for technology in relation to security of patient identifiable data. The aim was to use a calculator embedded in the hospital IT system to calculate the patient's coefficient of variability (CV) using trough tacrolimus levels. This would offer an objective measure of variability in tacrolimus levels and would be available for review during a patient's clinic visit, in a similar way that the clinician would review the renal function. This would help to determine appropriate management steps to improve graft survival outcomes.

Methods

The renal IT database system uses CV5, plus Crystal, to generate reports of interest, e.g. usage of a specific drug. This can be used to generate a report on the last five tacrolimus levels from a patient and subsequently give you a read out of the coefficient of variability in these five tacrolimus levels.

Results

A database search for all transplant patients taking all formulations of tacrolimus yielded drug levels. Five values per patient generated each patient's CV. This CV data could be displayed as a report generated for all transplant patients or could be included in an electronic annual review document generated in CV5. It took around two days to write and test this for use in the renal CV5 database system. It can be run for all 500 transplant patients in a matter of seconds each time it is needed. The results will be used for adherence support and can be shared with all renal transplant unit staff.

Discussion

The range of CV results in the cohort was 'startling' and the clinical team will look into the reasons for this. It may be that patients are not taking their drugs at the correct times or in the prescribed manner. Careful interpretation is important. Nevertheless, this tool which was simple and cheap to embed into the renal CV5 IT system offers objective evaluation and identifies where an intervention may be required.

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Introduction

Tacrolimus (Tac) is a critical component of immunosuppressive therapy after kidney transplantation. Achieving a balance between therapeutic and nephrotoxic levels is a challenge for each patient. Furthermore, Tac levels have been previously reported to be affected by key factors like Age, Gender, Ethnicity and Body Mass Index (BMI) of the recipient. In this study, we investigated the effect of inpatient Tac variability on the development of Donor Specific Antibodies (DSA), rejection episodes and long term outcome, taking into consideration above mentioned contributing factors in a single high volume centre.

Methods

The study included 209 kidney transplant recipients aged between 17 and 79 (mean 47) years, between 1 January 2013 and 31 December 2013. Of them, 138 were cadaveric and 71 Living donation kidney grafts. Kidney transplants that failed within the first 3 months post transplantation, were excluded. We calculated the Mean, Standard Deviation (SD) and Coefficient Variability (CV%) of inpatient Tac variability for five consecutive Tac trough measurements after completion of the first three months post transplantation. A Tac variability calculator was utilized to calculate the CV using the formula “Coefficient of Variability = (Standard Deviation/Mean) x100”. CV greater than 20% was considered significant. Primary end points of rejection episodes at the end of evaluation period as long as graft outcome at 1 year, were recorded.

Results

Of the whole cohort, 25.4% (n=53) achieved the desired, as per protocol, average Tac levels (4-7ng/ml) at the end of three months post transplantation. Only 62% (n= 130) achieved Tac CV ≤ 20% (Fig. 1) of which 2.3% (n = 3) developed a rejection episode at the end of Tac record period. 38% (n=79) of the recipients had a Tac CV >20% of which 5.13% (n = 4) developed a rejection episode at the same period (Fig.2) (p = 0.43). DSA development followed the same pattern, with 3.4% developing DSA for the Tac CV>20% group and only 2. 4% DSA for the Tac ≤20% group. There were no significant correlations of Tac CV with age, and BMI (Pearson’s correlation). Gender and ethnicity as categorical variables did not associate with Tac CV (Chi-square). Nevertheless, when comparing ethnicity, mean Tac levels were highest in the White recipient group (8.7ng/ml) and lowest on the Black group (4.4ng/ml) (p=0.006 student t test). Overall, at one year post transplantation, 98% (n=205) of the recipients had a functioning renal graft. Of the failed ones, all of them had Tac CV>20% in our study period, with one death (no rejection episodes), and two graft failures due to rejection episodes. When comparing the mean Tac levels during the study period with rejection episodes, there was 2.6% rejections in the group with mean Tac levels higher that the desired, while in the group with mean Tac levels within the desired range the rejection rate was 4%. Similarly, development of DSA was only 2.6% in the high mean Tac group and 4% in the normal range mean Tac group.

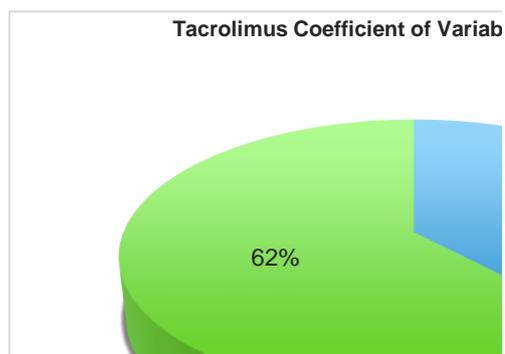


Fig. 1

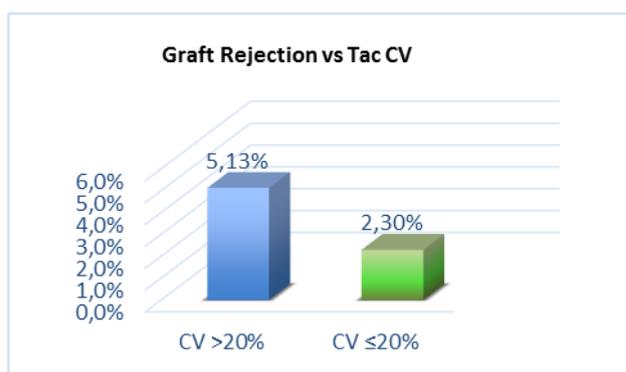


Fig. 2

Discussion

38% of our cohort presented with high Tac variability during the study period. As the positive episodes for rejection and DSA development were low in our cohort, we found no statistically significant correlation between Tac CV, rejection episodes and DSA, even though there was a trend for higher rejection episodes and DSA in the Tac CV >20% group. We had two graft losses due to rejection, both from the high Tac CV group. Interestingly, there was no association between Tac CV and age, gender BMI or ethnicity. However, the mean Tac levels were highest in the White group and lowest in the Black group, as expected. Further studies are required to investigate the impact of Tac variability on outcomes.

P018

Tacrolimus level in first 2 weeks post-kidney transplant and the impact on rejection rates.

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Introduction

It takes 2-3 weeks for tacrolimus level to be optimised after kidney transplant and results during this time period often show quite a lot of fluctuation. We wanted to see if there is a correlation between 0-2 week post-transplant tacrolimus level and rejection. Other aims were to see if our transplant unit has a high incidence of rejection and whether we need to increase our current starting dose of tacrolimus of 0.1 mg/Kg/ day.

Methods

1-year retrospective data of all kidney transplants carried out at our centre in 2013-14 was collected using hospital electronic records and transplant databases. We looked at delayed graft function (DGF), GFR at 3, 6, and 12 month, incidence of rejection at 0-6 months, type of rejection. Analysis of rejection risk was done with lowest & average tacrolimus levels during first two weeks post-transplant, induction agent administered, and cold ischemia times. Data was analysed using SPSS.

Results

There were 67 transplants, M:F ratio of 3.7:1, age range 20-80 years. 13.4% were pre-emptive transplants. Induction agent was basiliximab in 89.6%, alemtuzumab in 8.9%, and rituximab in 1.5% recipients. 25.4 % had DGF. 11 patients had rejection; vascular (n=6), cellular (n=3), mixed (n=1), and AMR (n=1). There was no statistical significance in 0-2 week average tacrolimus levels for no rejection vs rejection (8.2ug/L;SD=2.9 and 8.3ug/L;SD=4.2 respectively; p=0.99) and for lowest tacrolimus levels 5.7 and 5.4 respectively (p=0.75). Rates of rejection were lowest in live donors (9.5%) and highest in DBD (22.2%) and 14.8% in DCDs. Cold ischaemic times in DBD was 16.9 hours in the no rejection group vs 14.3 hours in rejection group (p=0.28). CIT in DCD in no rejection vs rejection group was 23 hours vs 4 hours respectively (p=0.69).

Discussion

Although our tacrolimus level were on the low side, there was no statistical difference between the average level for 0-2 weeks post-transplant and rates of rejection at the starting dose of 0.1mg/Kg/day. It would be beneficial to compare our study with rejection rates at other transplant units across the UK to assess whether low tacrolimus level in the early post-op period predispose to rejection.

P019

Intra-patient variability in trough tacrolimus level. Can this predict graft outcomes for renal transplant recipients?

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Introduction

Tacrolimus remains the backbone of the maintenance immunosuppressive regimen for renal transplant recipients. Its narrow therapeutic index and wide inter-patient variations in pharmacokinetics necessitates close monitoring and frequent dose adjustments to achieve adequate immunosuppression and avoid calcineurin toxicity. It has been suggested that wide intra-patient variability in trough tacrolimus level is associated with poor graft outcomes.

Methods

Retrospective analysis was performed to calculate the coefficient of variation (CV) for trough tacrolimus levels for all renal transplant recipients taking twice daily tacrolimus (Adoport) from 1st January to 31st December 2011. Transplants less than 6 months old were excluded. Target tacrolimus trough level was 5-8µg/L. High variability (HV) was defined as CV>median and low variability (LV) defined as CV<median. Primary outcomes were episodes of acute rejection (AR), graft loss and change in MDRD estimated GFR (eGFR) at 1, 2, 3 and 4 years.

Results

A total of 117 patients were included in the study with 95.7% completing the 4 year follow up period. The median coefficient of variation was 21.4%. 58 patients were allocated to LV and 59 to HV. There was no significant difference in gender, age of patient, co-morbidities, age of transplant or adjuvant immunosuppression between the 2 groups. The HV group had higher rate of acute rejection (4 vs 0, p=0.04), but no difference in graft failure (2 vs 0, p=0.15) compared to the LV group. There was no significant change in eGFR between the 2 groups at 1, 2, 3 or 4 years.

Discussion

Close monitoring of trough tacrolimus levels is of great importance in the management of renal transplant recipients. Many patients display a high variability in trough level despite a stable dosage. Factors such as variable tacrolimus pharmacokinetics and poor compliance can result in high variability in trough tacrolimus level. We have demonstrated higher rates of acute rejection in patients with high variability in trough tacrolimus level, however these patients did not experience inferior graft outcomes at 4 year follow up. A similar study in the published literature performed comparable analysis on 314 patients and demonstrated poorer outcomes for AR as well as graft survival and eGFR at 4 years in the HV group. These differences may be a result of the smaller sample size in our study, or differences in inter-departmental immunosuppressive regimens. Nevertheless, the finding of higher AR rates in our study is significant as episodes of acute rejection has been associated with poorer graft outcomes and increased mortality. The results from this study support the routine testing for trough tacrolimus variability in renal transplant recipients after the initial 6 month post-transplant period. HV patients may benefit from education to improve compliance, heightened surveillance or possibly a switch a longer acting once daily tacrolimus preparation.

P020

Successful renal transplantation in Atypical Haemolytic Uraemic Syndrome: A report of two cases

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Introduction

The relatively rare atypical variant of haemolytic uraemic syndrome (aHUS) continues to pose significant clinical challenges due to the widespread and devastating effects of thrombotic microangiopathy (TMA). These patients have a notoriously poor prognosis despite plasma exchange with 33-40% developing end-stage renal disease. Renal transplantation has historically been associated with poor outcomes due to recurrent TMA leading to graft dysfunction and loss in 90% of cases. In addition, TMA may be attributed to the high incidence of cardio/cerebro-vascular complications leading to sudden, unexplained death in these patients. Eculizumab (EZ), a humanized monoclonal antibody that is a terminal complement inhibitor was approved by NICE in 2011. The number of patients having been successfully transplanted is low and the long term data is scarce. Our report of 2 cases includes UK's first successful cadaveric kidney transplantation in aHUS patients with EZ as part of the immunosuppression strategy.

Methods

Both patients reported are female: ages 41 years (A) and 34 years (B). Patient A was diagnosed with ESRD due to Factor H mutation aHUS in 1997 with strong genetic association in the family. Her first live related kidney transplant in 1999 failed in 2002 following recurrence of TMA in the renal allograft despite plasma therapy. She underwent cadaveric kidney transplantation in December 2013 from 1:1:1 mismatched brainstem dead donor. Patient B was similarly diagnosed with ESRD in 2011 secondary to factor H mutation aHUS with a positive family history. She underwent cadaveric kidney transplantation in March 2015 from a 2:2:0 mismatched donor. Both transplants were uneventful with standard extraperitoneal placement of graft in the right iliac fossa. Both patients received 900 mg of Eculizumab at induction of surgery and then 3 further weekly doses followed by 1200mg fortnightly thereafter. Both patients had serial complement monitoring in the early post operative period. Standard immunosuppression regimen included Basiliximab induction and Tacrolimus + Mycophenolate mofetil + prednisolone as maintenance therapy.

Results

Both patients had prompt primary function with creatinine of 154 mmol/L (A) and 89mmol/L (B) at day 5. Both patients were discharged home within 10 days with no reported complications and are currently under active follow-up (Patient A: 23 months; Patient B: 8 months). Latest serum creatinine is 82mmol/L (GFR 67) and 71 mmol/L (GFR >90), respectively. There are no reported surgical or medical complications at present. **Discussion:** This case reports good initial and early outcomes of Eculizumab therapy as an adjunct to standard immunosuppression protocols for successful renal transplantation in patients with atypical HUS.

P021

Immunosuppression-induced de novo Haemolytic Uraemic Syndrome in paediatric renal transplant recipients

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Introduction

Recurrence or de novo haemolytic uraemic syndrome with haemolysis, thrombocytosis and graft failure can occur after renal transplantation. Ischaemia/reperfusion injuries, viral infections, complement gene abnormalities and immunosuppressive drugs have all been implicated. Thrombotic microangiopathy has been reported in 0.8-14% of all kidney transplants in adults. In the case of calcineurin inhibitors, plasma exchange and change of drug is an accepted method of treatment. No particular immunosuppressive drug has been shown to have an advantage in preventing de novo HUS.

Cases

We report a 5 year old boy, recipient of a living related renal transplant, who developed de novo HUS. He has a background of CKD due to posterior urethral valves. He had previously had a bladder augmentation, Mitrofanoff procedure and had undergone bilateral native nephrectomies. His transplantation was uneventful. By day 3 post transplantation, however, he developed thrombocytopenia and anaemia. This haematological profile was accompanied by low haptoglobin, raised lactate dehydrogenase, hypertension and graft dysfunction. He was negative for CMV and EBV. On day 4, his calcineurin inhibitor (tacrolimus) was changed to sirolimus. He also received 7 days of plasma exchange with octaplas from day 5. This successfully treated the HUS and he was discharged home 3 weeks after his transplantation date.

A 9 year old girl with Feingold syndrome, who had CKD due to renal dysplasia and reflux nephropathy developed de novo HUS post renal transplant. She was the recipient of a second deceased donor kidney, after her first failed due to thrombosis. Her initial immunosuppression was ciclosporin. She developed a haemolytic anaemia by day 2, with evidence of fragmented red blood cells, low haptoglobin and thrombocytopenia. She was treated by conversion of her ciclosporin to tacrolimus. Her haemolysis resolved and she was discharged 3 weeks after transplantation.

Summary

We present two paediatric cases of de novo HUS after renal transplantation. Both had evidence of haemolysis and thrombocytopenia within the first week of transplantation. They were treated with change of immunosuppressive drug or change of drug and plasma exchange. In both cases, it was successful in terminating the microangiopathic process. This is consistent with experience in adult renal allograft recipients. Early recognition and appropriate intervention is needed to prevent graft loss.

P022

Excellent outcome following discontinuation of Sirolimus in two patients with Sirolimus induced Pneumonitis

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Introduction

Sirolimus (mTOR inhibitor) was introduced into clinical transplantation in 1999 and has led to an increase of unexplained interstitial pneumonitis. Drug withdrawal is the usual treatment, although regression of pneumonitis is also described after dose reduction. We report 2 recent cases of suspected sirolimus induced pneumonitis in the Wessex Kidney Centre with successful outcomes after complete cessation of sirolimus.

Case Reports

A 68 year old gentleman presented to clinic with a 3 month history of dry cough and worsening dyspnoea on minimal exertion. His cadaveric kidney transplant was 25 months old and although initially on tacrolimus for the first 7 months post-transplant, he was then entered into the 3C Study and switched to maintenance sirolimus. His mean sirolimus level was 8.0ng/ml (SD 3.2ng/ml) with a level 11.0ng/ml on the day of presentation. HRCT revealed patchy bibasal consolidation and early fibrotic changes, raising the possibility of sirolimus related lung toxicity. Therefore, sirolimus was promptly stopped. Tacrolimus was commenced, with prednisolone to cover the change and reduce inflammation and fibrosis. Symptoms improved 3 days after this. All cultures that had been sent on presentation were reported as negative or insignificant. He reported complete resolution of respiratory symptoms 13 days after cessation of sirolimus and CXRs in the following months showed steady improvement in the appearances of basal atelectasis.

The second patient, a 52 year old gentleman was admitted to our renal unit with fever, cough and dyspnoea. His second living kidney transplant was 32 months old and he had been switched to maintenance sirolimus from tacrolimus 3 months post-transplant, with the hope to reduce the propensity of skin malignancies. His mean sirolimus level was 10.5ng/ml (SD 2.8ng/ml). CT chest revealed a patchy mid and bibasal lung parenchymal process with architectural distortion. Initially he was treated with tazocin and azithromycin. However, all cultures including BAL were negative so his sirolimus dose was reduced. This did not lead to improvement in his hypoxia so sirolimus was discontinued and tacrolimus was initiated with prednisolone cover. There was a rapid improvement in his oxygenation and he declared complete resolution of respiratory symptoms in clinic 4 months later.

Conclusion

Sirolimus induced pneumonitis is a difficult diagnosis of exclusion that can present long after patients have been established on maintenance sirolimus that was seemingly well-tolerated. These two case reports demonstrate rapid response to sirolimus cessation. Conversely, reduction of sirolimus dose may not necessarily result in resolution of symptoms in some patients.

P023

Is Tacrolimus level and variability at 1 year associated with long-term kidney graft function?

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Introduction

Tac immunosuppression was introduced in our unit in late 2010. The aim of this study was to review kidney graft outcome of our 2011 cohort of live donor recipients and check for association with Tac level and Tac variability at 1year.

Methods

Data were collected from hospital electronic patient records and NHSBT. Local patients with complete data transplanted in 2011 were included in the study. This was to give us the longest follow up. All transplants were from live donors. Patients were divided according to immunological risk (low, standard & high). The first 5 trough Tac levels were recorded after the first year of transplantation and the average was calculated as well as variability. Demographic data were analysed. Mann-Whitney U Test was used for non-parametric data analysis.

Results

| | Low risk (2-7 ug/L Tac level) | Standard risk (8-10 ug/L Tac level) | High risk (8-10 ug/L Tac level) |
|--------------------------|----------------------------------|--|------------------------------------|
| Number of patients | 19 | 20 | 10 |
| Age at Tx (IQR) | 43 (13) | 44 (20) | 37 (12) |
| Sex | 5F, 14M | 7F, 13M | 3F, 7M |
| Mean Tac level ug/L (SD) | 7.14 (1.8) | 8.15 (1.6) | 8.23 (2.78) |
| Variability % (IQR) | 19 (14) | 15 (14) | 21 (11) |
| Graft or patient loss | 1 | 1 | 1 |

Discussion

Tac level and Tac variability at 1 year post kidney transplant was not associated with long-term graft outcome. We will expand our study to include deceased donors and subsequent years.

P024

Conversion of transplant patients from twice daily Prograf to once daily Advagraf: results of a pilot therapeutic review

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Introduction

Ensuring that the post-transplant patient adheres optimally to immunosuppressive therapy is essential to maximise clinical benefit and minimise the risk of graft rejection. Tacrolimus, twice daily (Prograf), has been the standard of care for renal transplantation (RT) patients in the UK since the NICE guidelines were published in 2004. A prolonged release formulation of tacrolimus, Advagraf, has been available since 2009. It provides a once daily tacrolimus regimen, which patients find simple to adhere to; reduced intra-patient variability (IPV) in drug levels; and increased graft survival rates compared to Prograf.

We conducted a pilot therapeutic review to identify patients who might benefit from converting from Prograf to Advagraf, and also explored what practical difficulties needed to be overcome in the conversion process.

Methods

RT patients taking Prograf with IPV >15% were eligible to take part in the pilot study; each case was discussed with the transplant consultant and the multidisciplinary team. During a routine clinic visit, the renal specialist nurse explained the rationale for converting to Advagraf and provided a leaflet about the proposed conversion to each eligible patient. Patients were encouraged to discuss the change with their families. The nurse specialist contacted patients 48 hours after the clinic visit to establish if they wished to convert to Advagraf. Education and adherence support were provided. Tacrolimus levels were measured 10-14 days post-conversion and 14-21 days after the first measurement, and regularly thereafter. Dose adjustments were implemented where necessary. IPV values will be calculated once the patient is on a relatively stable dose and 5 consecutive tacrolimus levels had been obtained.

Results:

37 Prograf-treated RT patients with IPV >15% were identified and all except one agreed to convert to Advagraf. Tacrolimus levels were monitored regularly post-conversion and dose adjustments were made as necessary.

Logistic issues about Advagraf stocks in Lanarkshire pharmacies were overcome via communication with local pharmacists.

Discussion

After converting to Advagraf, patients reported that it was easy to adhere to the once daily regimen. Shift workers found the conversion particularly beneficial. In this pilot study, conducting a therapeutic review and converting eligible patients to Advagraf appears achievable and tolerable. A longer-term review of the effect on Advagraf of reducing IPV is currently under evaluation.

P025

Co-trimoxazole desensitisation in a deceased renal allograft recipient with *Stenotrophomonas* infection

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Introduction

We present a case report of a 29 year old female deceased renal transplant recipient with a previously known cutaneous allergic reaction to co-trimoxazole. *Stenotrophomonas maltophilia* and *Pantoea agglomerans* were isolated from her transport perfusion fluid. The *Stenotrophomonas* was sensitive only to co-trimoxazole and Timentin (Ticarcillin and Clavulanate). At the time of treatment, Timentin was unavailable due to a national shortage, and so the authors were obliged to successfully utilise an oral desensitisation regime for co-trimoxazole. This has not been described previously in transplant patients.

Methods

The Information was collected prospectively from the hospital electronic patient record and clinical examination. A Medline and Embase search were undertaken via Ovid to locate relevant literature.

Results

An 11-step drug-specific oral desensitisation regime with ascending doses of co-trimoxazole was successfully utilised for the first time in our department, with escalation to a full dose co-trimoxazole treatment regime. There was no indication for the use of anti-histamines during the procedure. The effectiveness of this method was likely enhanced by concomitant use of high dose corticosteroids post-transplant. The patient developed no sequelae of *Stenotrophomonas* infection and was discharged day eight post-operatively.

Discussion

Co-trimoxazole is widely used for prophylaxis against *Pneumocystis* infection in immunocompromised patients. When cutaneous reactions to this drug occur alternative antibiotics are usually used. We wish to highlight to the transplant community the possibility of using a desensitisation protocol in the case of very limited pharmacotherapeutic options. Our patient's previous drug reaction manifested as angioedema. Previous evidence of Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) to the implicated drug are contraindications to desensitisation.

P026

Case report: Liver abscess; uncommon complication following renal transplantation

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Introduction

Infection is the major reason for morbidity and mortality in transplant recipients. Intra-abdominal and biliary infections remain the commonest in transplant population. Contrary to liver transplant; renal transplant recipients showed no increase in the risk of pyogenic liver abscess compared to overall public. Similarly; Therapeutic approach is similar in transplant recipients as in other general population.

We are presenting a renal transplant recipient who presented as a fever of unknown origin; clinical and laboratory test did not show any clue to the diagnosis, isotope leukoscan followed with USS had revealed unexpectedly large size liver abscess. He responded well to a course of antibiotics together with Metronidazole therapy beside abscess drainage.

Methods

29 years old renal transplant recipient presented to emergency department with high grade fever and rigors. There was no history suggestive of infection elsewhere and there was no history of contact with sick patients; however, 2 months back he escorted his father in a trip to India.

Clinical examinations apart of fever 39.9c were unremarkable. Laboratory tests showed only leukocytosis 18.4×10^3 with mildly elevated SGPT. He showed poor response to an empirical antibiotic course.

To identify the focus of infection he underwent an isotope leukoscan, which showed a large cold area at the posterior aspect of the right Liver lobe suggestive of cystic lesion. Simultaneous USS-KUB revealed an incidental finding of focal lesion in the right liver lobe suggesting a large hepatic abscess, confirmed on CT.

Results

Antibiotic was changed to Meropenem and Metronidazole was added. Considering the abscess size, aspiration was done and culture was negative. He showed marked clinical recovery thereafter and was discharged with an aim to continue antibiotics for the total of 4 weeks.

Discussion

Infectious complications are common in transplant population, especially in the early post-operative period reflecting the magnitude of surgery augmented by immunosuppression. In contrary to liver transplant; renal transplant recipients showed no increase in the risk of pyogenic liver abscess compared to general population.

Diagnosis of hepatic abscess in transplant patient can be challenging since signs and symptoms could be insidious and mortality rate can reach up to 100% if left untreated; hence early diagnosis with institution of right therapy is mandatory. Ultrasonography is the primary imaging modality for investigation and evaluation of liver abscess; it is safe, accurate and sensitive in 80-100%.

Therapeutic management of hepatic abscess is similar to non-transplant patients. Antimicrobial agent should provide adequate coverage against gram-negative bacilli, microaerophilic streptococci, and anaerobic organisms. Usually, a combination of two or more antibiotics is given. Therapy should continue for 3 to 4 weeks.

Amoebic liver abscess should be considered in travellers to endemic areas or tropics, clinical signs, symptoms, laboratory tests and imaging cannot distinguish amoebic from pyogenic liver abscesses. If amoebic liver abscess is suspected, then treatment with Metronidazole for 10 days is necessary. Diagnostic aspiration of abscess fluid and subsequent culture can guide antibiotic choice.

P027

Avoidance of enhanced immunosuppression in highly sensitised kidney transplant recipients without donor specific HLA antibodies is not detrimental to outcome

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Introduction

Highly sensitised patients (calculated reaction frequency (cRF) >85%) are considered to be at increased risk of immunological injury after kidney transplantation and routinely receive lymphocyte depleting induction in many transplant centres. Many of these individuals have had previous transplants and have already had prolonged exposure to immunosuppression. While there is evidence that transplantation in the presence of an HLA donor specific antibody (DSA) is detrimental to graft survival, the association with pre-existing non-DSA HLA antibodies is less clear.

Methods

1. All highly sensitised patients transplanted in our centre from January 2010 - August 2015 were reviewed.
2. Recipients with current HLA DSA or those with historic DSA associated with a positive cross match were excluded because they received lymphocyte depleting induction.
3. The demographics, immunosuppression and outcomes for the remaining recipients were recorded.

Results

67 highly sensitised patients were transplanted; 19 were excluded from analysis as there was a current (3) or historic (16) positive cross match due to HLA DSA. In the remaining 48 recipients, the median age was 47 years and 31% were male. 14/15 male and 12/33 female recipients had had previous transplants. The median cumulative HLA mismatch at A, B, DR was 2; 16 recipients received kidneys matched at A, B and DR. The median cRF was 97%. Basiliximab was administered to 15 patients; the remainder did not receive induction therapy.

Five (10%) recipients had acute cellular rejection; two required treatment with anti-thymocyte globulin while the remaining three responded to intravenous corticosteroid. There was one case of acute accelerated antibody mediated rejection in a recipient who had been sensitised in pregnancy. No grafts were lost secondary to immunological injury. The median creatinine 12 months after transplantation was 107 µmol/L.

Discussion

In highly sensitised patients without HLA DSA, early immunological outcomes are comparable to other recipients at our centre without the administration of lymphocyte depleting induction therapy. The majority of these individuals have had prolonged exposure to immunosuppression because of previous transplantation and already have a significantly increased risk of malignancy. Avoidance of further enhanced immunosuppression in this group is possible without compromising graft outcomes provided that an accurate HLA antibody history is available.

P028

Random forests classification model for risk stratification of antibody mediated rejection following HLAi Kidney transplantation

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Introduction

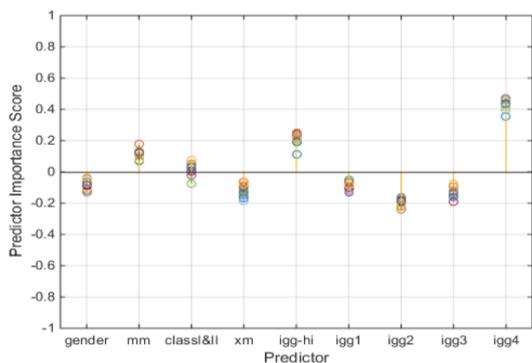
A few published studies in kidney transplantation domain employ machine learning; we have previously demonstrated use of Decision Tree (DT) analysis for prediction of antibody mediated rejections. In this work, we have explored use of Random Forest (RF) classification models in application to HLA-incompatible kidney transplantation.

Methods

RF is a powerful machine learning technique based on an ensemble of multiple DTs. RFs produce robust and accurate classifiers that are able to generalise well on new data. RFs have a built-in feature selection; variable importance scores identify key input features in the model. 80 patients who received HLA incompatible renal allografts between 2003 and 2012 are included in the study. The 10 baseline (measured before transplantation) parameters comprised the input feature set for the model: recipient’s gender, total number of HLA mismatches between donor and recipient, the presence of both HLA Class I and Class II DSA, cross-match status, highest IgG DSA MFI level, and 4 total IgG subclass (1-4) MFI levels.

Results

The RF classifier developed in this study was able to predict early graft rejection (within 30 days) with 85% accuracy on 20 independent test samples (Table below). IgG4 level was the single most important factor, followed by the highest MFI IgG level, and the number of HLA mismatches (Figure below). This result was consistent with the variables previously identified by the DT model and a classical logistic regression.



| Random Forest performance measures | Training set | Test set |
|---|--------------|----------|
| Correct classification rate, <i>C</i> (%) | 91.7 | 85.0 |
| Sensitivity, <i>Sn</i> (%) | 93.9 | 92.3 |
| Specificity, <i>Sp</i> (%) | 88.9 | 71.4 |
| Positive Predictive Value, <i>PPV</i> (%) | 91.2 | 85.7 |
| Negative Predictive Value, <i>NPV</i> (%) | 92.3 | 83.3 |
| Area under the ROC curve, <i>AUC</i> | 0.914 | 0.819 |

Figure: Variable importance scores evaluated across ten RFs | Table: Predictive performance of RF model

Discussion

The predictions of our RF model are patient-specific and based on clinical indicators known prior to the transplantation, thus allowing for an accurate estimation of early transplantation outcomes in advance of the surgery. When integrated with existing electronic decision support systems, the RF can provide an accurate simulation tool to explore various clinical scenarios and identify patients at risk of ABMR prior to the operation, and thus leaving more time to make essential adjustment to treatment. Further work comparing the results on extended datasets from other centres would be beneficial.

Validating flow measurements of ABO-antibody titres in a single centre

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Introduction

Methods for the detection of ABO antibody titers vary between laboratories. There is a need for a universal antibody detection and quantification method that provides precise information in real-time. Accurate measurement of ABO antibody levels before and after ABO-incompatible organ transplantations is critical, to ensure adequate treatment for patients. In this study, our goal was to optimize and implement a multi-colour flow (MC-FC) assay in order to accurately detect and quantify the level of IgM, IgG and IgA immunoglobulins, individually and simultaneously.

Methods

We obtained samples from patients on the deceased donor kidney transplant waiting list. Samples were tested using the standard IAT (immunoglobulin agglutination testing) method used in our centre. Parallel testing of serum for ABO antibody utilising ABO- antibody-specific fluorochromes and MC-FC to give a 'relative median fluorescence intensity' (RMFI) of IgM; IgG & IgA. Correlation between testing methods was tested.

Results: We tested 13 patients with anti-A antibodies, 9 with anti-B and 21 patients with both anti-A and anti-B antibodies. We also excluded the one patient with AB blood group from the study. We saw that flow cytometer results were comparable to the gel card titer values; we looked closely at the correlation between the two assays to determine the validity of this new proposed MC-FC protocol in order to measure the specific individual immunoglobulins simultaneously.

| Characteristics of the Cohort Individuals | | | | |
|---|-----------|------------------------|----------|------------|
| Trial Participants | ABO Group | Number of Participants | Sex, M:F | Age |
| | O | 21 | 5:16 | 51 (26-70) |
| | A | 9 | 2:7 | 43 (31-51) |
| | B | 13 | 7:6 | 47 (29-65) |
| | AB | 1 | 1:0 | 32 |

The correlation between antibody levels obtained from the both gel card and MC-FC assays was examined using the Spearman rank correlation test and the correlation coefficient (rho) was assessed. The rho

values were 0.742 (p<0.001) and 0.351 (p<0.001) for IgG and IgM anti-B antibodies; and rho values were 0.873 (p<0.001) and 0.561 (p<0.001) for IgG and IgM anti-A₁ antibodies. The correlation coefficient for IgA anti-A and anti-B was 0.149 (p=0.452) and 0.202 (p=0.438) respectively.

Discussion

The experiments have shown the MC-FC has good intra-batch precision, coefficient of variation was less than 14% and the difference in values obtained from duplicate tests within experiments was less than 3%, which suggest good reproducibility of the method. The MCFC protocol showed greater sensitivity in detecting certain immunoglobulins than in the previously reported gel card method of testing and showed its analytical performance to be comparable to that of gel card testing, suggesting it's potential as an effective tool for the measurement of anti-ABO Immunoglobulins. Further studies are needed to clarify the target MFI ratio for transplantation and whether MCFC ABO Ab is preferable to gel card testing for a correlation with a clinical outcome.

Transplantation of kidneys from donors with liver failure and Paracetamol overdose

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Introduction

In the United Kingdom the median waiting time for kidney transplantation is over 3 years and unfortunately of those on the transplant list in April 2013, 3% died and 6% were removed from the list in the following year. There have been many initiatives to increase organ utility, including donation after circulatory death donors (DCD), and the fast track scheme for grafts which were previously rejected. These have shown comparable graft and patient outcomes to traditional donation after brain-death donors (DBD).

Case reports and series have shown that it is feasible to transplant organs from donors with chronic liver disease and paracetamol-induced liver failure with concomitant hepatorenal syndrome. In both situations the kidneys although malfunctioning at the time of retrieval, are potentially normal and able to restore function. We sought to evaluate the outcomes of transplant recipients who received these organs.

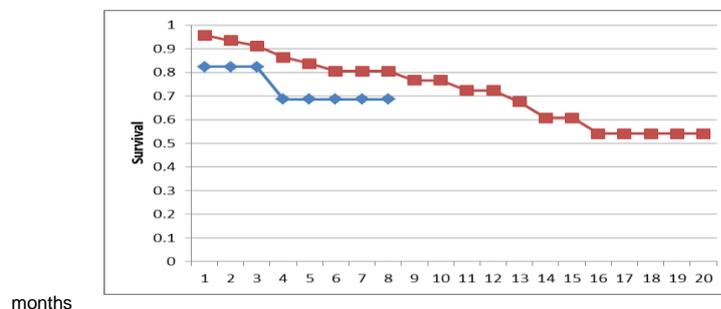
Methods

NHS Blood and Transplant ran a search of all donors where a cause of death was documented as either liver failure or paracetamol overdose. All available information on donor characteristics and graft outcomes was provided in the database. Kaplan-Meier survival curves were calculated with the available data on graft outcomes for liver failure and paracetamol overdose.

Results

There were 103 donors who fitted the inclusion criteria (59 liver failure, 44 paracetamol overdose). A total of 16 liver failure and 27 paracetamol overdose donors were used for transplant, providing 27 and 49 grafts respectively. Kaplan-Meier survival curves are shown in graph 1. There was primary non-function documented in a total of 3 recipients.

Graph 1: Kaplan-Meier estimated survival curves for liver failure (blue) and paracetamol overdose (red).



Discussion

This is the largest series of renal transplantation from donors with liver failure and paracetamol overdose. The long-term graft survival estimates (69% liver failure at 8 years, 77% paracetamol overdose at 10 years) are comparable to standard DBD (72% 10 year) and DCD (64% 10 year) outcomes. The use these organs for donation for renal transplantation may be a safe option.

P031

Anti-D Immunoprophylaxis in female solid organ transplant recipients to prevent Haemolytic disease of the fetus and newborn

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Introduction

Transplantation of an organ from a Rhesus D (Rh D) positive donor to a Rh D negative recipient is likely to result in the release of residual Rh D positive red blood cells from within the organ into the recipient's circulation. This may cause recipient Rh D sensitisation and anti-D alloantibody production. In female transplant recipients of childbearing potential this may lead to haemolytic disease of the fetus and newborn (HDFN) in subsequent pregnancies. NHSBT recommend that transplantation centres should consider a policy of anti-D immunoprophylaxis in the above patient group. The aim of our study was to determine current practice in transplant centres for anti-D administration.

Methods

Transplant coordinators in all solid organ transplant centres in England, Scotland and Wales were sent a questionnaire by email. The questionnaire included the following questions: 1) 1. Does your unit administer anti-D to female Rh negative transplant recipients (child-bearing potential) of Rh positive organs? 2. Which year (if known) did your unit commence administration of Anti-D? 3. How much anti-D is given? 4. If so, how is the dose calculated?

Results

Responses were available from 22 out of 29 centres (75.8%): 5 (22.7%) abdominal, 12 (54.5%) kidney, 3 (13.6%) cardiothoracic and 2 (9.1%) multi-organ transplant centres. Seven centres (31.8%) (1 multi-organ centre, 1 abdominal and 5 kidney) administer anti-D post-transplant to women of child-bearing age. Details of dosing were unavailable from two centres. Two transplant centres administer standard doses to all women (500 IU (kidney) and 1500 IU (abdominal)) and three kidney centres titrate the dose of anti-D according to immunophenotyping estimates of Rh D positive red blood cells in recipients plasma post transplantation.

Discussion

The majority of solid organ transplant centres do not routinely administer anti-D immunoprophylaxis to prevent HDFN in recipients of childbearing potential. In centres that do recommend immunoprophylaxis there is substantial variation in dosing regimens. More data are needed to guide clinical practice, including a multi-centre study of the incidence of anti-D formation in Rh D negative recipients of Rh D positive organs, and accurate assessment of the risk of HDFN complicating Rh D negative solid organ recipients' pregnancies.

P032

Ultrasound doppler vascular studies as part of renal transplant work-up: Unnecessary expense? Outcomes of a national survey of consultant surgeons

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Introduction

There is currently no agreed national guidance regarding iliofemoral and carotid doppler vascular studies prior to renal transplant (RTx) surgery. Recipient work-up varies between institutions based on established local guidelines. Ultrasound doppler studies have been used to evaluate the extent of peripheral vascular disease in target anastomosis vessels at an average cost of approximately £120 (GB) per scan. This study reports outcomes of a national survey involving UK RTx consultant surgeons to investigate current practice, and the relative usefulness of doppler studies in assessing recipient suitability.

Methods

An online survey was deployed, aiming to explore various factors influencing doppler study use, including indications, scan findings and overall efficacy in the assessment of recipient vascular disease. Opinion was sought on doppler studies relating to duration of RRT and further alternative imaging modalities, in particular where doppler assessment was thought to be sub-optimal.

Results

Response rate was 40% (n=35) representing 76% of all UK RTx centres. 15% of respondents perform carotid dopplers, estimating a cost of £20-£299. Iliofemoral dopplers are performed by 22%, estimating a cost of £20-£400. 31% of respondents felt that doppler studies were useful, with evidence of vessel stenosis being the most significant finding. A history of claudication/PVD was the modal indication (97%), followed by previous CVA/TIA (73%). 16% of respondents stated they had declined recipients based on doppler study imaging, as opposed to 69% following CT within the last 12 months. 72% recommend CT angiography for patients requiring further imaging. 97% would consider surgical exploration of target vessels irrespective of doppler or CT findings as an alternative to imaging.

Conclusion

Our study suggests most recipients are declined based on CT findings rather than ultrasound doppler studies. CT angiography should be considered as the primary imaging modality in patients requiring investigation prior to surgery. This in theory reduces work-up cost by approximately £240, whilst simultaneously providing a more accurate vascular assessment to assist surgery.

P033

TB Chemoprophylaxis post transplantation in West London

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Introduction

Active Tuberculosis (TB) is common post solid organ transplantation (SOT) with more atypical and insidious presentation. Incidence post SOT in Europe is reported to be between 0.7 – 5%. Isoniazid (INH) is commonly used for chemoprophylaxis in high risk patients post SOT with significant variation in dose and duration between transplant centres in UK. The aim of this study is to determine the incidence of TB post Kidney(KT) and Kidney Pancreas (KPT) transplantation in our centre where we use INH 150 mg once day together with pyridoxine 50 mg once a week as chemoprophylaxis in high risk patients whilst on immunosuppression.

Methods

In this retrospective single centre study, the largest of its kind in UK, all laboratory-confirmed cases of TB were identified from the records of patients underwent KT and KPT in our centre between November 2005 and November 2014 with follow up until November 2015. Patients who underwent multiple transplants were counted once only. All patients received a steroid sparing, tacrolimus based maintenance regimen with monoclonal antibody induction. Patients with previous TB or at high risk due to ethnic or geographical background received TB prophylaxis with isoniazid 150mg daily and pyridoxine 50mg once a week whilst they remain on immunosuppression. Patients intolerant of isoniazid received moxifloxacin 400mg daily.

Results

Total of 1424 patients were included (518 females and 906 males), mean age was 54.6 years (range 21-83 years) and mean follow up was 5.5 years (range 1-10 years). 47.2% were Caucasian, 30.7% were Asians and 11.2% were Afro-Caribbean. Total of 3 cases of definite active TB were identified. These were MTB isolated from lymph nodes. There was 1 case of a NMTB isolated from early morning sputum sample but treated empirically for MTB. Two patients were of south Asians origin and 2 were of other ethnicity. Three out of the 4 patients were on TB chemoprophylaxis. All 3 MTB showed resistance (2 were resistant to INH and 1 was resistant to moxifloxacin and pyrazinamide). Two of the NMTB cases were detected early within first 7 months post transplantation. The other two cases were detected at 49 and 93 months post transplantation. All 4 patients are alive and 3 out of 4 patients continue to have functioning grafts. All patients tolerated anti-TB treatment. It was unclear if INH resistance was associated with low dose isoniazid or whether this was primary infection with a resistant strain.

Discussion

Long-term TB chemoprophylaxis using low dose INH of 150 mg once a day was associated with a very low rate of TB disease in a multi-ethnic group of patients in our centre. Further studies are needed to evaluate if INH resistance can be avoided with a standard dose of INH and if shorter courses are similarly adequate.

P034

Efficiency savings through reduction of red blood cell cross-match and transfusion in renal transplantation

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Introduction

Blood products, including donated red blood cells (RBCs) are a valuable and limited resource. Transfusion of RBCs in the transplant recipient is not only undesirable from an immunological perspective, but is also expensive. Each unit of RBCs costs £122 to produce and store, a recipient "group and save" sample costs £22 to process, while cross-matching and issuing an RBC unit costs between £22-160, depending upon the antibody status of the patient. Our unit has recently switched from a policy of routine cross-match of 2 units of RBCs for renal transplantation to the use of "electronic issue", a process similar to virtual cross-match, where patients without red cell antibodies are allocated group-specific RBC units without a physical cross-match taking place. Up to 90% of the general population are thought suitable for electronic issue. We aimed to quantify the use of RBC cross-match and transfusion in our unit, to assess the efficiency savings that could be achieved through electronic issue, and also identify any variables that could predict the transfusion requirement of our transplant recipients.

Methods

Transfusion data for all renal transplants performed during a one-year period (April 2014 – March 2015) in our department were retrospectively analysed. Electronic issue was routinely performed for all recipients without red cell antibodies in the final four months of the study period. Results collated included: initial number of RBC units cross-matched and transfused in the immediate peri-transplant period; total number of units cross-matched and transfused during the index admission; proportion of patients receiving a transfusion; and the effect of admission haemoglobin on transfusion requirement.

Results

140 kidney transplants were performed during the study period. 32/140 (23%) of grafts were from a living donor (LD) and 108/140 (77%) were from a cadaveric donor (CD). 62/140 (44.3%) patients required a RBC transfusion during their index admission. In the initial peri-transplant period, the mean number of units cross-matched was 2.79 (range 0-10) and mean number transfused was 0.49 (range 0-4) per patient. There was no difference in transfusion requirements between the recipients of LD and CD grafts. LD transplant recipients were more likely to require a RBC transfusion if their admission haemoglobin level was <100g/L (75.0% vs 20.8%, $p=0.005$). No similar association was seen in recipients of CD grafts. Following the introduction of electronic issue, 24/46 patients (56%) had electronic issue performed rather than a physical cross-match. This resulted in a £1056 cost saving, and could lead to a 280 x 52% x £22 (£3,203) saving per annum in the future.

Discussion

The blood transfusion requirement in patients undergoing renal transplantation in our unit during the index admission is low. There is a clear benefit in optimising pre-operative haemoglobin in LD transplant recipients. Electronic issue has meant that patients no longer require multiple RBC cross-matches performed, which in turn will result in cost savings.

P035

HLA antibody in transplant recipients during transition from paediatrics

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Introduction

Adolescent transplant recipients in transition from paediatric to adult units are known to be at high risk of graft failure. Detection of HLA antibody is an important biomarker for graft failure but the frequency of allosensitisation has not been studied in this group.

Methods

Retrospective review of transplant recipients in transition to a single adult centre 1995-2015. Clinical and laboratory data was extracted from electronic patient records. Patients were screened for HLA antibody at transition and thereafter annually. The method of antibody screening evolved over the study period, since 2004 by Luminex. Two patients with no antibody screen at transition were assumed to be negative. Non-adherence in the adult clinic was assessed by two surrogate markers: non-attendance to clinic and undetectable CNI levels.

Results

There were 48 transition patients with a mean age of 18.5yrs, of which 42 were from a single paediatric centre and 7 were regrafts. Median follow-up was 5 years.

| | At transition (%) | At or after transition (%) |
|-----------------------|-------------------|----------------------------|
| No HLA Ab | 31 (65%) | 20 (42%) |
| HLA Ab | 17 (35%) | 28 (58%) |
| Donor specific HLA Ab | 10 (21%) | 17 (35%) |

Median eGFR at transfer (51 vs.73ml/min/1.73sqm, p=0.007) and graft failure (47% vs.10%, p=0.006) was worse in the group with HLA Ab at transition, although proteinuria was similar. 75% of graft failures were immunological. Acute rejection after transition was commoner in the HLA Ab group (47% vs.14% p=0.034). There were 345 recorded clinic non-attendances and multiple episodes in the same patient (>2) were associated with graft failure (40% vs.4% p=0.005) and HLA Ab (58% vs.14%, p=0.005). Undetectable serum CNI levels were common (74 episodes in 19 patients) but did not predict graft failure in this cohort.

Discussion

When transition patients enter the adult service they already have a high prevalence of allosensitisation that continues to rise. This is likely to be a factor in the subsequent high graft failure rate. Clinic non-attendance is associated with allosensitisation and graft failure.

Clinical relevance of C4d positivity in renal transplant biopsies without microcirculation inflammation or injury

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Introduction

Some renal transplant biopsies show C4d-positivity in the absence of microcirculation inflammation/injury and with only minimal acute tubular injury. Little is known on the outcome of these rare findings.

Methods

We reviewed cases from our archives that showed C4d positivity (Banff scores C4d2 and 3) in the absence of other features of antibody-mediated rejection (AMR)(ABO-incompatible transplants excluded), and compared outcomes with a group of C4d-negative (Banff scores C4d0 and 1) controls. Outcomes were graft loss and future clinical AMR.

Results

All cases (n=18) and controls (n=36) had the following features: Banff scores t,i, ti, g,ptc,v,cg = 0; ct/ci = 0 or 1; at most mild acute tubular injury. There was no significant difference in pre- or post-transplant parameters, including sensitization, mismatch number, time post transplant of biopsy, nature of biopsy (surveillance versus indication), or length of follow-up. Although cases more often had a follow-up biopsy than controls (83% versus 56%), there was no significant difference in the number of follow-up indicative biopsies. There was no significant difference in allograft survival between cases and controls (HR=0.34 (0.48-2.41);p=0.29). When comparing patients who were DSA+ versus DSA- at time of biopsy, there was no difference in allograft survival (HR=1.80 (0.12-26.70); p=0.59). In univariate analysis, there was no significant difference in AMR-free survival comparing C4d+ versus C4d- (HR=4.13 (0.90-19.07); p=0.06), but there was a significant difference when comparing DSA+ versus DSA- (HR=8.97(1.13-71.28); p=0.0017). Using multivariate analysis including the type of index biopsy (indication versus surveillance), DSA and C4d status, type of biopsy was not retained, DSA status was significant (HR: 22.93 (2.32-2226.69), p=0.0077) and C4d status was nearly significant (HR: 6.97 (0.99-48.81), p=0.052).

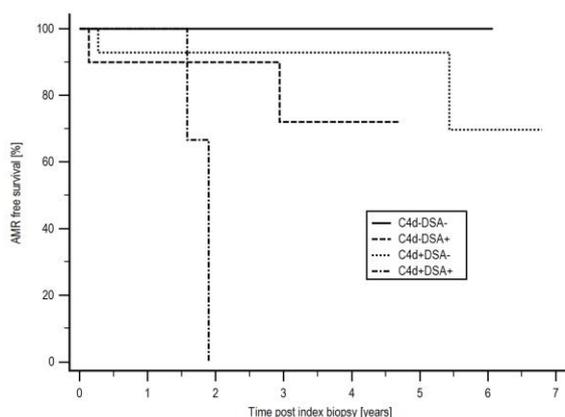


Figure 1. AMR free survival by C4d and DSA status

Discussion

In biopsies with minimal histological changes, DSA positivity indicates a risk of future AMR. Although not significant in this small study, C4d-positivity may also contribute to this risk.

P037

Immune complex-mediated glomerulonephritis with acute thrombotic microangiopathy following newly detected hepatitis B virus infection in a renal transplant recipient

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Introduction

Hepatitis B virus (HBV) presents a risk to both patients and staff in renal centres. To minimise the incidence of viral transmission, UK guidance recommends HBV immunisation for patients requiring renal replacement therapy. However, there is no specific UK guidance for HBV surveillance in kidney transplant recipients.

Case report

A 56 year old male with ESRD associated with hypertension and type 2 diabetes was successfully immunised against HBV prior to commencing haemodialysis in 2006. He received a DCD kidney transplant in 2009, at which time there was no evidence of hepatitis B infection. Initial complications included delayed graft function and acute T cell-mediated rejection requiring steroids and ATG. Thereafter he remained stable until April 2015 when he developed an acute kidney injury. Allograft biopsy revealed an acute thrombotic microangiopathy (TMA) with glomerulitis, peritubular capillaritis and C4d staining. He commenced treatment for presumed antibody mediated rejection, though no donor-specific antibody was detectable. Due to a full house immunoprofile, further tests were undertaken including virological screening, which revealed acute hepatitis B infection. No other cause for a TMA could be identified. He commenced entecavir, resulting in an improvement in HBV viral load and renal function; repeat biopsy demonstrated resolution of the TMA. HBV genotyping demonstrated a vaccine escape mutant, suggesting "past resolved" infection that reactivated with immunosuppression, though post-transplant acquisition cannot be ruled out.

Discussion

HBV infection is associated with numerous kidney diseases, but this is the first reported case of acute hepatitis B infection associated with immune complex-mediated glomerulonephritis and TMA. Furthermore, it highlights the potential importance of HBV surveillance in transplant recipients, which is not currently covered by UK guidelines.

P038

The effect of transplant nephrectomy on donor specific antibody levels

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Introduction

Transplant nephrectomy (TxNeph) of failed allografts can be performed for several reasons, and is usually associated with a reduction or withdrawal of immunosuppression (IS). There is only limited understanding of what happens to donor specific antibody (DSA) levels following TxNeph.

Methods

We conducted a retrospective analysis of patients undergoing TxNeph in our centre over a 10-year period (2004-14). A bead-based (Luminex) antibody-binding assay with single antigen testing was used to analyse HLA DSA levels before and after TxNeph with calculation of mean fluorescence intensity (MFI). We recorded the timing of immunosuppression withdrawal, and histology reports of the explanted TxNeph specimens.

Results

32 patients underwent TxNeph in our centre during the study period. Indications included: haematuria, resistant anaemia, sepsis, graft thrombosis, creating space for future transplant, need for a reduction in (IS), severe BK nephropathy and uncontrolled rejection. Donor type and pre- and post-nephrectomy antibody screening were available for 19/32 patients, and only these patients were included in the analysis. 14/19 patients (73.7%) had their immunosuppression reduced or stopped before nephrectomy. All 19 patients were found to have DSAs following TxNeph; 11/19 (57.9%) patients developed *de novo* DSAs. Of the 8 patients who had DSAs prior to TxNeph, the MFI increased in 6/8 (75.0%) and remained stable or decreased in 2/8 (25.0%). 6 patients had both class I & II DSAs, 11 patients had class I only and 2 patients had class II only. Histology of the explanted grafts demonstrated evidence of rejection in 12/19 patients (63.2%).

Discussion

The effect of TxNeph on DSAs is a complex subject, as the reduction or withdrawal of IS occurs contemporaneously to a decrease in the immunogenic stimulus, although some allogenic material usually remains in-situ in the form of the renal capsule and vascular stumps. Our series demonstrates that the majority of patients either develop *de novo* DSAs or have an increase in the DSA level following TxNeph. The rate of reduction or withdrawal of IS should therefore be carefully considered after TxNeph, taking into account the indication for surgery.

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Introduction

The UK kidney donor risk-index (UKKDRI) was developed to provide a simplistic clinical tool to help determine quality of an allograft and aid informed consent. It has been demonstrated that a high UKKDRI score is associated with inferior allograft outcomes. However, to our knowledge the UKKDRI score does not adjust for different immunotherapy protocols. The aim of this study was to determine if the UKKDRI can be applied to renal allograft recipients receiving a steroid sparing immunosuppressive protocol.

Methods

756 recipients of a deceased donor transplant between 2005 and 2015 were analysed. All patients received monoclonal antibody induction, with a steroid sparing protocol. 295/756 (39.0%) of donors were high risk (HR) and had a UKKDRI score ≥ 1.35 .

Results

Recipients of high risk ‘HR’ kidneys had inferior patient [HR: 1.71(1.1-2.7), $p=0.014$] and censored allograft survival [HR: 2.30 (1.5-3.5), $p<0.001$] compared with the low risk ‘LR’ kidneys as shown in the graph below. Overall rejection risk was lower in the ‘HR’ group [HR: 0.66(0.5-0.9), $p=0.015$] which suggests a role of recipient related factors. Despite fewer rejection episodes, allograft function was inferior at all time points in the ‘HR’ kidneys, $p<0.01$, as shown in the figure below.

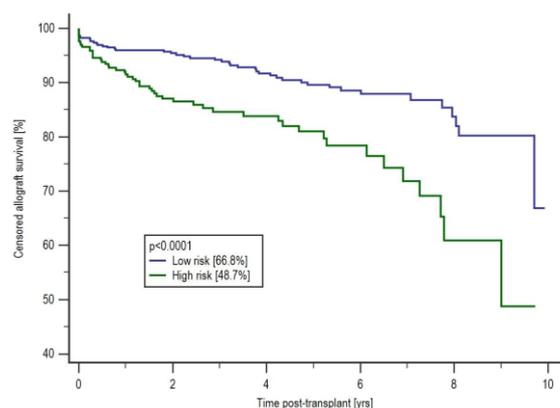


Figure 1. Censored allograft survival

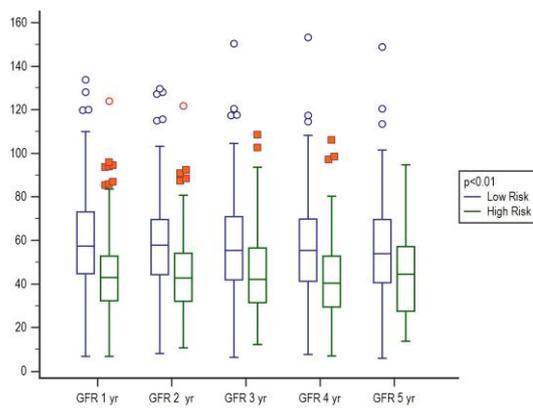


Figure 2. Comparison of eGFR in HR v LR kidneys

On multivariate analysis, where donor risk factors were defined by the UKKDRI score, variables known at the time of transplant associated with graft loss were: recipient diabetes ($p=0.0037$), preformed donor specific antibodies ($p=0.032$) and recipients of a ‘HR’ kidneys ($p=0.0001$)

Discussion

These data shows that recipients of high risk ‘HR’ kidneys as defined by the UKKDRI score have similar inferior allograft outcomes in the setting of a steroid sparing immunotherapy regimen. Hence the UKKDRI score may also be used in centres using such protocols to predict risk and inform patients.

P040

Clinical correlation between pairs of kidneys transplanted from the same donor

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Introduction

Concordance of allograft outcomes between kidneys transplanted from the same donor has previously been reported. However recipient characteristics become increasingly important after the immediate post-transplant period. The aim of this study was to demonstrate the correlation of outcomes between paired donor kidneys transplanted at a single unit receiving a homogeneous immunotherapy protocol and to define the time when recipient characteristics become more important.

Methods

226 (113 donor pairs) patients were analysed. Pairs were randomly assigned into 2 groups, ensuring there was an equal distribution of first and second transplanted kidneys in each group. Mean follow up was 4.91±4.6 years.

Results

Correlation of inter-pair allograft outcomes (assessed by attributable risk) are shown in the table below.

| Event | OR (95% CI) | p value |
|------------------------|-------------------|---------|
| Patient loss | 2.53 (0.43-14.75) | 0.15 |
| Allograft loss | 4.96 (1.48-16.61) | 0.013 |
| Delayed Graft function | 2.85 (1.33-6.12) | 0.0063 |
| Rejection | 1.81 (0.65-5.09) | 0.18 |
| De novo DSA | 0.76 (0.25-2.33) | 0.66 |

Assessment of the correlation in function (assessed by spearman's coefficient) is shown in the table below

| eGFR at given time point | rho | p value |
|--------------------------|------|---------|
| 1 month | 0.42 | <0.0001 |
| 3 months | 0.40 | 0.0001 |
| 6 months | 0.38 | 0.0005 |
| 1 year | 0.34 | 0.0063 |
| 2 years | 0.17 | 0.27 |
| 3 years | 0.18 | 0.28 |

There is a significant correlation in DGF, function in the 1st year and overall allograft survival in pairs of kidneys transplanted from the same donor. However, rejection, DSA development and function after the 1st year are more dependent upon recipient characteristics.

Discussion

Knowing the clinical outcomes of the contralateral kidney in the first year post-transplant may help in managing transplant recipients, as discordance might initiate investigation of dysfunction caused by recipient factors. For pairs transplanted at separate units, a fully accessible clinical database would need to be established to enable data sharing.

P041

Single donor sequential renal transplants and impact of different cross-match combinations

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Introduction

Cold ischaemic time (CIT) is a modifiable risk factor for deceased donor renal transplantation. Although many efforts have been made to reduce this e.g. virtual cross-matching (VXM) rather than full cross-matching (FXM), it is inevitable that when both kidneys are accepted from a single donor, the second transplant will have a longer CIT. The aim of this study was to determine if specific combination of cross-match types impacted on the outcome of either transplant.

Method

All 33 paired renal transplants from a single donor, sequentially transplanted, were identified over a 5-year period (2009 - 2014). Patients were allocated to three groups: Group 1- VXM in both transplants (V^1V^2); Group 2- VXM for the first and FXM for the second (V^1T^2); Group 3- FXM for both (T^1T^2). For each single donor the first and second transplants were compared for recipient demographics and one year outcomes including delayed graft function (DGF), biopsy proven acute rejection (BPAR), graft survival and serum creatinine.

Results

Ten pairs were performed in Group 1 (V^1V^2), 10 pairs in Group 2 (V^1T^2), and 13 in Group 3 (T^1T^2). All second kidneys endured significantly longer CIT's (8.5 vs. 14.1 hrs, 10.1 vs. 15.2 hrs & 13.5 vs. 18.0 hrs, $p < 0.05$). There was no significant difference in mean creatinine level (3, 6 and 12 months) between the first and second transplants in each group, nor was there any difference between first and second kidneys across each group. The BPAR rates were independent of kidney order and CIT (V^1V^2 25%, V^1T^2 5%, T^1T^2 33%).

Group 3 (T^1T^2) had the greatest rates of immediate graft function (10%, 40%, 46%) for both transplants. The DCD grafts had higher incidences of DGF which was independent of cross-match type or kidney order. Group 1 (V^1V^2) transplants, with the shortest CIT, had the highest rates of DGF for both DCD and DBD's (100% vs. 75%). The higher DGF rates did not translate into poorer outcomes at one year.

Conclusion

The cross-match combinations and differing CIT's do not impact on the outcomes of single donor transplants performed sequentially.

P042

Increase of serum IL-17A, IFN- γ and TNF- α is associated with acute rejection in kidney transplant recipients

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Introduction

Cytokines mediate several graft- host immune responses in Kidney Transplantation. We undertook to measure the levels of Th1- Th2 and Th17 cytokines in live donor renal renal transplant recipients and to correlate the cytokines level with graft outcomes.

Methods

Peripheral venous blood was collected from patients before transplant (Pre- tx), 1 month post transplant (Post- Tx) and at the time of suspected graft rejection. Serum was isolated and stored at -80°C . Serum level of IL-2, IL-4, IL-6, IL-10, TNF- α , IFN- γ and IL-17A were measured using BD™ cytometric Bead Array (CBA) Human Th1/Th2/ Th17 Cytokine Kit.

Results

This study includes 78 first kidney transplant recipients who were divided into two groups: Rejection group (R, n=38) and Non Rejection group (NR, n=40). The mean onset of rejection was 28.6 days (Range 3- 182 days). Age and sex matched healthy donors prior to nephrectomy were recruited as controls (n= 40). Serum cytokine levels were expressed as pg/ ml. P value <0.05 was taken as significant.

Patients with end stage renal disease had lower level of serum cytokines as compared to that of healthy control. There was significant increase in serum IL-17A, IFN- γ and TNF- α at the time of rejection as compared to their corresponding baseline level. There was no change of these cytokines level in post- 1 month sera of patients with stable graft function. IL- 6 and IL-10 levels did not show variation in any of the patients. IL-4 ad IL-2 could not be measured in stored serum by this method.

Discussion

There is increase in serum concentration of IL-17A, IFN- γ and TNF- α during acute rejection suggesting an increased activation of Th1 and Th17 subsets of T- cells.

P043

Correlation of serum C4d level with C4d immunohistochemistry in grafts during allograft rejection in kidney transplantation

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Introduction

Presence of C4d peritubular capillary staining in biopsies is considered as a non serologic evidence of antibody involvement in graft rejection. Isolation of graft biopsy is an invasive and relatively risky procedure. So, we intend to correlate C4d staining in biopsy with that of serum C4d level in patients with Kidney transplantation.

Methods

Blood samples were collected from patients before (Pre- Tx) and after kidney transplantation at 1 month, 3 months, 6 months, 12 months and at the time of rejection. Serum level of C4d level was quantified as ug/ml by ELISA (Quidel, USA). C4d staining in renal graft during rejection was performed by IHC (DAKO Invision, USA). P value <0.05 was taken as significant and results were expressed as Mean \pm Standard error of mean.

Results

Of 210 first Kidney transplant recipients, 41 (19.5|%) patients had indicated allograft biopsies. Thirty five (85%) kidney allograft biopsies had morphologic features of acute allograft rejection. Upon C4d staining, 20 (57%) of the rejected allograft biopsies showed diffuse C4d peritubular capillary staining.

There were no significant differences between baseline serum C4d levels in healthy control (7.046 ± 1.116) and patients with ESRD (7.537 ± 0.4953). Post transplant decrease in serum level of C4d was seen in all the patients, regardless of rejection.

Patients were stratified by the PTC C4d staining positivity irrespective of which, all the patients showed a similar pattern of C4d dysregulation following transplantation.

Discussion

Serum C4d level alteration is similar in rejection irrespective of PTC C4d staining positivity. Thus, serum C4d level doesn't correlate a positive PTC C4d staining in graft. So we concluded that serum C4d cannot be used as an alternative marker for biopsy C4d staining in diagnosis of allograft rejection.

P044

How hungry are you for a transplant?

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Introduction

Whilst developing a renal transplant care pathway, it became apparent that there may be huge inconsistencies with the pre-op care of emergency potential renal transplant recipients. This led us to look at the admission process for these patients.

Method

After discussion with some recently transplanted patients, a prospective questionnaire was given to all deceased donor transplant recipients from 23rd June to 19th October 2015.

Results

During the study period we performed 25 deceased donor transplants. 13 from DCD donors and 12 from DBD donors. 23 questionnaires were completed (92%). Despite reasonably consistent advice from the admitting transplant surgeon, in a significant proportion abstinence times were over 10 hrs for food with a median time of 12 hrs (range 6-48 hrs) and over 8 hrs for clear fluids with a median time of 11 hrs (range 3.5-40 hrs). Surprisingly 70% had a bed available on arrival. Unfortunately the rest waited in a variety of places including outpatients, the day room and seats in the corridor. The median time from patients arrival to theatre was 15.75 hrs (range 5.5-25.5 hrs).

Discussion

It is inevitable that bed availability is not immediate for potential transplant recipients and that unavoidable waiting between admission and theatre will occur. Patient starvation times are both inconsistent and excessive in some cases. This may have a negative impact on the peri-operative period.

The development of a specific emergency admission policy for transplant recipients is needed to optimise pre-operative care. This needs to include a specific waiting area with access to refreshments and a NBM policy that positively allows administration of light diet, but more importantly, clear fluids when possible.

We were very surprised by our findings and would encourage other units to check their patients aren't "too hungry for a transplant".

P045

An outbreak of *Pneumocystis jirovecii* in renal transplant recipients: Management, risk factors and outcomes

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Introduction

We describe an outbreak of 10 cases of *Pneumocystis jirovecii* pneumonia (PCP) in adult renal transplant patients attending renal outpatients' clinic. The index case was diagnosed in December 2014, and the last confirmed case was diagnosed in June 2015. The primary route of *P. jirovecii* transmission has yet to be proven, however outbreaks of infection suggest either inter-human transmission or a common environmental source. Public Health England has seen a steady increase in cases reported over the last few years. Our outbreak investigation aimed to identify the most likely mechanism of PCP acquisition. Clinical, epidemiological, molecular and environmental data were evaluated to elucidate the outbreak's origin and determine risk factors for both its acquisition and outcome.

Methods

Renal transplant patients with clinically and microbiologically confirmed PCP were included in the outbreak investigation. Genotyping of available *P. jirovecii* isolates was conducted to confirm a link between the cases. In order to assess for the presence of PCP in the renal transplant outpatients' clinic, the air was sampled both when the clinic was empty and also during patient occupation. A case-control study was executed in order to compare rates of clinic attendance as well as to assess the incidence of overlap of cases in clinic. To calculate a rate of attendance we looked at the number of clinic attendances / months in the study as the controls were in the study for longer than the cases. This was then split into two quartiles of attendance (low v high).

Results

Four of the 10 cases died; none of the remaining 6 lost their transplant. Of the four isolates available for molecular typing, all demonstrated an identical genotype confirming the spread of a single strain of *P. jirovecii* between patients. Air samples obtained from both the empty and occupied renal outpatients' clinic were negative for *P. jirovecii*. The overall rate of clinic attendance was significantly higher for cases versus controls ($P=0.019$). There was also a significant correlation between overlap in clinic with a case and later development of PCP ($P=0.027$), but not inpatient stays. The higher the number of clinic overlaps with a case, the greater the chance of developing PCP (P value for trend = 0.001). There was a trend towards increased risk of contracting PCP if the patients had had an increase in their immunosuppression in the preceding 6 months and low lymphocyte count, but no association in our cohort with underlying lung disease. Patients developing PCP had significantly higher serum creatinine levels in the preceding 6 months compared to the control group. Of note, the genotype involved in our outbreak differed to that found in a neighbouring renal unit's outbreak, whose patients we transplant.

Discussion

Our results demonstrate the spread of PCP in the outpatient clinic. The findings of this outbreak investigation indicate that contact with another case in clinic is a significant risk factor for developing PCP. The epidemiological evidence presented indicates person-to-person transmission of infection within the nosocomial environment. This raises a number of public health and infection control concerns. Results suggest the need for development of formal infection control policies within the department, and potentially nationally given the rising incidence of cases. Trying to establish clear risk factors may help enable individualisation of PCP prophylaxis, rather than using a blanket 6 months post-transplant schedule.

P046

Influence of smoking exposure on kidney allograft outcomes after kidney transplantation

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Introduction

The effect of cigarette smoking exposure on kidney allograft outcomes remains uncertain. The aim of this single-centre retrospective analysis was to determine graft outcomes in the contemporary era for kidney allograft recipients stratified by any smoking exposure (current or ex-smoker) versus no smoking exposure.

Methods

Data was extracted by the hospital informatics team for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events.

Results

Of the 1,140 patients, 24.0% had some documented smoking exposure and were classified as ever smoking in analysis. Males were more likely than females to be ever smokers (28.8% versus 17.0% respectively, $p < 0.001$) but there was no other association with any other baseline demographic. Patients with versus without any smoking exposure were associated with significantly increased overall graft failure (21.5% versus 14.2% respectively, $p = 0.003$), driven mainly by increased death-censored graft losses (13.9% versus 9.0% respectively, $p = 0.016$). The risk for rejection within the first year post kidney transplantation showed borderline significance with increased risk among patients with versus without any smoking exposure (14.6% versus 10.7% respectively, $p = 0.054$). Recipients with versus without smoking exposure were also at higher risk of having thrombotic microangiopathy (4.0% versus 1.7% respectively, $p = 0.029$), acute tubular injury (16.8% versus 12.1% respectively, $p = 0.032$) and chronic allograft damage (5.8% versus 2.8% respectively, $p = 0.016$). Creatinine levels at 3, 6, 12, 36 and 60 months were all significantly higher in kidney allograft recipients who demonstrated some smoking exposure in the past versus never smokers. In a Cox regression model, smoking exposure was shown to independently increase overall graft loss by 70% (1.697, 95% CI 1.241-2.320, $p = 0.001$) and death-censored graft loss by 69% (1.677 95% CI 1.078-2.611, $p = 0.022$).

Conclusion

Any smoking exposure among kidney allograft recipients is associated with increased risk for overall graft failure (driven by death-censored losses). We also demonstrated significant worse allograft function among at various time points for patients with smoking exposure. Further work is required to clarify this relationship between smoking exposure and graft outcomes but this requires improved documentation of current versus past smoking, and smoking pack years, to allow further stratification of risk and to adequately counsel patients.

P047

Outcome after kidney transplant in patients with chronic hypotension on Haemodialysis (HD)

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Introduction

5% of the haemodialysis (HD) population have chronic hypotension (i.e. hypotension in the absence of volume depletion, antihypertensive medication, heart failure or cortisol deficiency). The pathology of this condition is poorly understood with a limited relevant literature. The perioperative management of these patients is very challenging.

Methods

We retrospectively reviewed the records of all kidney transplants (KTx) performed at our centre over the last 5 years. We defined severe hypotension to be BP <100 mmHg during HD and between HD sessions.

We identified 14 patients with 15 transplants (one had 2 kidney Tx). 6 were from live donors and 9 from deceased donors (6 DBD & 3 DCD).

The mean donor age was 42 years old (13-76). Two were from expanded criteria donors with a history of hypertension. Three deceased donors had acute kidney injury.

The mean recipient age was 41 years old (19-69) and 8 of them were on midodrine and/ or fludrocortisone. Five of them had previous bilateral nephrectomy and two had unilateral nephrectomy.

All patients had adopt, MMF and prednisolone for immunosuppression. The cohort included 4 HLA incompatible Tx who treated with Therasorb and IVig before surgery and had Alemtuzumab for induction. We had two other high risk recipients treated with Alemtuzumab and eight patients treated with Basiliximab. Four patients had one previous Tx, three had two previous Tx and one had three previous Tx.

Eight of 15 KTx (53%) required ITU stay for intravenous (IV) noradrenaline to maintain BP at about 100 mmHg. Median ITU stay was 6 days (range 1-17). Four patients that didn't need ITU had IV Dopamine on the ward.

Results

7 (47%) Tx had primary non function (PNF), 5 had delayed graft function (33%) and 3 (20%) primary function. Nine patients (60%) had rejection (8 AMR and one TCMR).

Of the eight functioning kidneys four were from live donors and four from deceased donors. The median creatinine was 153µmol/L (76-253) with a minimum follow up of 3 months and maximum of 55 months. All the patients with a functioning kidney have normal blood pressure with no need for supportive medication.

Five cases had graft nephrectomy (1st intra-operatively due to severe hypotension after reperfusion and with high VA that necessitated cardioversion, 2nd due to renal venous thrombosis and the rest for PNF. Three patients died (1st 45 days post Tx for sepsis, 2nd after 27 months due to MI, 3rd after 42 months due to sepsis-none of them had a functioning kidney).

Conclusion

Hypotensive patients on HD represent a complex group that needs careful evaluation before proceeding to transplantation. They need good quality kidneys that have a high chance of primary function. Because of this they should not be offered kidneys from expanded criteria donors. Such patients require multidisciplinary approach at every stage of their Tx pathway. Guidelines are in great need in this area.

Chemoprevention of cutaneous Squamous Cell Carcinoma in renal transplant recipients: A case-controlled analysis

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Introduction

Organ transplant recipients are up to 200 times more likely to develop cutaneous squamous cell carcinoma (cSCC) than age-matched general populations. In some countries non-melanoma skin cancer (NMSC) is now the leading cause of death in long-term renal transplant recipients (LRTR). Factors affecting development of NMSC in LRTR include Fitzpatrick skin type (ranging from fair to dark skin), ultra-violet light (sun) exposure, and the type and duration of immunosuppression. Systemic retinoids have shown promising preventative effects against the development of cSCC, however their use has been associated with adverse side effects including liver dysfunction and dyslipidaemia, and a number of sources suggest they should be used with caution in patients with renal impairment (RI). Currently there are no consensus guidelines on their use in LRTR. There is little published data on whether they adversely affect kidney transplant function, or whether hepatotoxicity and dyslipidaemia are more common in LRTR. We aimed to determine the safety and effectiveness of acitretin as a suitable chemopreventative agent against the development of cSCC in LRTR.

Methods

We collected retrospective data from a large cohort (n=469) of LRTR (>7 years) attending our Annual Review Transplant Clinic, of which a significant proportion (n=108) had been diagnosed with NMSC. We identified patients (n=12) on treatment with acitretin for the prevention of cSCC. We matched these patients to an equal number of controls by age, total years from transplant and Fitzpatrick skin type. We compared GFR, liver function (LFTs) and lipid profile at 1 year pre, and 1, 3 and 5 years post commencing acitretin. We also compared the total number of cSCCs pre and post acitretin. Wilcoxon signed-rank test was used to compare blood chemistry values before and after acitretin treatment within cases, and a Mann-Whitney test was used to compare differences between cases and controls.

Results

Serum total cholesterol concentrations and LDL were significantly lower (p=0.007 and p=0.012 respectively) in patients prescribed acitretin at 5 years post treatment compared with baseline measurements. However, there were no other statistically significant differences in lipid profile, GFR or LFTs at baseline parameters and at 1, 3 and 5 years after starting treatment within cases or comparing cases and controls. During the five years after starting acitretin treatment the median number of new cSCCs per patient was 2 (range 0 - 4) which was significantly lower than the median number prior to treatment of 6 (range 3 - 10) p=0.005.

| | Baseline | 1 year post treatment | 3 years post treatment | 5 years post treatment |
|----------------------|--------------|---------------------------|----------------------------|----------------------------|
| GFR (Median (range)) | 50 (31 – 96) | 52 (31 – 93) p = 0.169 | 44 (20 – 114) p = 0.142 | 41 (23 – 113) p = 0.398 |

Table 1: Median GFR of cases at baseline and 1, 3 and 5 years after commencing acitretin.

Discussion

In our cohort, acitretin treatment did not adversely affect renal transplant function, liver function or lipid profiles when compared with baseline or matched untreated control data, and was associated with a statistically significant reduction in total number of new cSCCs during 5-year follow-up. Acitretin should be considered as a safe and effective chemoprevention agent in carefully selected LRTR with multiple SCCs who are under regular dermatology surveillance. Further research to assess whether its use may circumvent the need to reduce and or withdraw immunosuppression treatment in LRTR with cSCCs is warranted.

Comparing patient self-reported health status in kidney transplant recipients and waiting list patients using the EQ-5D-5L questionnaire: Results from the ATTOM study

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Introduction

The EQ-5D is a widely used patient-reported questionnaire for describing and valuing health in terms of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Patients’ responses to the EQ-5D can be converted to a score anchored between 1 (perfect health) and 0 (death). These scores can be combined with life expectancy to estimate quality-adjusted life years (QALYs). As part of the Access to Transplantation and Transplant Outcomes Measures (ATTOM) study, we measured health status in kidney and combined kidney and pancreas transplant recipients and matched control patients from the transplant waiting list in the UK using the 5-level version of the EQ-5D (EQ-5D-5L) and explored how scores vary with patient and treatment factors of interest.

Methods

The EQ-5D-5L was administered to incident transplant patients and prevalent patients from the waiting list at the time of recruitment into the ATTOM study. As health status is likely to be impacted in the period immediately following surgery, we also captured EQ-5D-5L responses in a subset of transplant recipients approximately 6 months after surgery. Using multivariable regression analysis, we explored the effect of age, gender, ethnicity, primary renal diagnosis, comorbidities and treatment factors on EQ-5D-5L scores.

Results

Mean EQ-5D-5L scores were similar for transplant recipients and waiting list patients at recruitment but higher in transplant recipients at 6 months following surgery. In multivariable analyses, age was not found to be a significant predictor of EQ-5D-5L scores in either cohort. A primary renal diagnosis of diabetic nephropathy and the presence of mental illness were associated with lower scores (poorer health status) in both cohorts. Among patients on the transplant waiting list, female gender, Asian

ethnicity and increasing time on dialysis were also associated with lower scores.

| | n | Mean EQ-5D score | 95% Confidence interval | P-value |
|---|------|------------------|-------------------------|-----------|
| Incident transplant patients at recruitment | 1809 | 0.77 | (0.77, 0.78) |] < 0.001 |
| Incident transplant patients at 6 months | 512 | 0.83 | (0.81, 0.85) | |
| Prevalent waiting list patients | 1704 | 0.77 | (0.76, 0.78) |] < 0.001 |

Discussion

The ATTOM study is a large UK dataset describing health status in both transplant recipients and patients on the waiting list. The results of our study are consistent with previous studies that have reported better health status among patients who have received transplants compared to patients receiving dialysis. Collection of comprehensive data on patient characteristics in the ATTOM study provides insight into additional factors beyond treatment modality that may influence health status. The results from this study can be used to refine and derive estimates of QALY gains associated with different forms of renal replacement therapy in different patient groups.

Outcomes for kidney allograft recipients who develop cancer

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Introduction

Cancer is a significant cause of morbidity and mortality after kidney transplantation, driven by the milieu of immunosuppression. Treatment for rejection involves increased immunosuppression and increases the risk for cancer. However, immunosuppression tapering in the context of post-transplant cancer can reciprocally lead to kidney allograft rejection and attrition. The aim of this analysis was to explore the relationship between cancer and allograft outcomes in a single-centre analysis of a well characterised clinical transplant cohort.

Methods

This was a retrospective single-centre analysis of all adult patients receiving a kidney transplant between 2007 and 2015. All patients received a standard triple immunosuppressive regime (tacrolimus, MMF, Prednisolone) with induction monoclonal antibody unless contraindicated. Episodes of cellular rejection were treated initially with steroids as first line and escalated as necessary with T-cell depletion therapy. Antibody-mediated rejection was treated the same with the addition of plasmapheresis +/- IVIG. Patients were followed up until September 2015 and electronic patient records were manually searched to facilitate data linkage between various sources to create a comprehensive database. Patients were divided into two groups depending on whether they developed acute rejection and rates of cancers compared.

Results

There were 1,140 patients who received a transplant during the study period with median follow up 4.4 years. The median age for the cohort was 47, males (n=681, 59.7%), Caucasian ethnicity (n=822, 72.1%), deceased-donor recipients (n=633, 56.4%), repeat transplants (n=111, 9.7%), diabetes as cause of end-stage kidney disease (n=117, 10.3%) and previous/active smoking exposure (n=274, 24.0%). The total number of new onset cancers was 69 (6.1%) of which skin cancers formed the largest group (31.9% of total cancers). The incidence of post-transplant cancer was significantly higher amongst the 164 patients (10.4%) who developed acute rejection compared to those without rejection (10.4% versus 5.4% respectively, p=0.016). Although subgroup analysis was limited by sample size, there was no correlation between type or grade of rejection and rate of post-transplant cancer (11.9% for cellular rejection and 10.7% antibody-mediated rejection, p=0.77). The episode of rejection preceded the diagnosis of cancer in the majority of patients (88.24%). Development of post-transplant cancer versus no cancer was associated with decreased patient survival (78.3% versus 93.8% respectively, p<0.001), death-censored graft survival (84.1% versus 90.2% respectively, p=0.082) and overall graft survival (63.8% versus 85.3% respectively, p<0.001).

Conclusion

This single-centre analysis demonstrates that patients who develop acute rejection are at increased risk of developing post-transplant cancer, even in the absence of T-cell depletion therapy. This is likely to be a consequence of the increase in immunosuppressive therapy given and suggests that there is a dose dependent relationship between immunosuppressive load and cancer risk. While the risk for rejection in the context of immunosuppression tapering is low, our data confirms development of cancer post-transplant remains a major cause of adverse clinical outcomes.

P051

Patients with ESRD due to Diabetes have higher variability of their tacrolimus levels and worse outcomes

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Introduction

Nonadherence to immunosuppressive medication is associated with rejection and graft loss and nonadherence to antidiabetic medication is associated with poor glycaemic control leading to microvascular complications and mortality. We have previously shown that inpatient variability (IPV) of tacrolimus trough levels can be used as a surrogate marker for adherence and that a high IPV can predict rejection and graft loss. In this study, we investigate the association between IPV of tacrolimus levels and transplant outcomes in a group of patients whose ESRD was caused by diabetes mellitus (DM).

Methods

We retrospectively analysed 668 patients who received a low risk kidney only transplant between 01/11/2005 and 01/09/2013. Patients who were defined as reaching ESRD due to diabetes mellitus (biopsy and non-biopsy proven) were compared to the patients with non-DM aetiology of ESRD, who were not diabetic and did not develop NODAT. Patients with diabetes who either were classified as having 'unknown cause of ESRD' or ESRD of other aetiology were excluded. All patients received alemtuzumab induction and tacrolimus monotherapy with a steroid sparing protocol with a target pre-trough tacrolimus level of 5-8ng/ml.

Results

105 patients were identified as having ESRD secondary to DM. 446 patients were used as controls. 117 patients were excluded from the analysis. The mean HbA1c was 8.19±1.20. Mean follow up 5.65±2.12years

| | DM | Non-DM | p value |
|---------------------------------|---------------------|---------------------|----------|
| COV 6 – 12 months | 19.56 (14.97-27.68) | 17.66 (12.85-24.21) | 0.0077 |
| Proportion in HV group | 63 (60.0%) | 213 (47.8%) | 0.0317 |
| COV all levels after 6 months | 25.79 (21.38-33.98) | 22.39 (17.10-29.62) | 0.0008 |
| Mean tacrolimus 6-12months | 7.31 (6.38-8.15) | 6.87 (6.05-7.67) | 0.006 |
| Mean Max tacrolimus 6-12months | 9.90 (8.10-11.10) | 8.80 (7.60-10.40) | 0.0025 |
| Mean Min tacrolimus 6-12months | 5.10 (4.38-6.20) | 5.10 (4.20-5.90) | 0.69 |
| Overall patient survival | 65.6% | 92.6% | p<0.0001 |
| Overall DWFG survival | 72.7% | 93.2% | p=0.0004 |
| Overall censored Graft survival | 71.2% | 90.6% | p=0.012 |
| Overall DSA free survival | 72.3% | 79.5% | p=0.013 |

Discussion

This study shows that patients defined as having ESRD due to DM have a higher variability of their tacrolimus levels and worse outcomes compared to those patients who have ESRD resulting from other causes. Whether the inferior outcomes can be attributed to poor adherence with medication, other co-morbidities or to changes in the pharmacokinetics and pharmacodynamics of medications that occur in patients with diabetes requires further exploration.

P052

Elevated pre-dialysis systolic blood pressure is associated with reduced patient survival in haemodialysis patients undergoing renal transplantation

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Introduction

Patients with end-stage renal disease undergoing haemodialysis have reduced survival relative to the general population. Renal transplantation reduces, but does not wholly remove, this mortality risk. A number of factors are associated with poor survival in haemodialysis patients. The effect of these variables on outcomes in patients subsequently undergoing renal transplantation is less clear. We analysed factors – modifiable and fixed, clinical and biochemical – affected both patient- and graft-related outcome following renal transplantation specifically in patients treated with haemodialysis immediately prior to renal transplantation.

Methods

We collected data for all patients on haemodialysis as renal replacement modality immediately prior to renal transplantation at our unit over the 5-year period January 2005 – December 2009. These patients were followed up for patient and graft survival until 31 October 2015. Demographic and laboratory variables were retrieved from the Strathclyde Electronic Renal Patient Record (VitalData). Differences in values between survivors and non-survivors were compared using independent samples tests (t-test, Mann-Whitney U); an adjusted Cox regression model was created to explore predictors of patient mortality, and this process was repeated for predictors of graft failure.

Results

252 patients were identified, with a mean age of 45.3 years, 59.9% male, 27.8% live-donor transplant. Over a median follow-up of 7.7 years, 18.6% died, 21% experienced death censored graft failure. Those patients who died were older (53.8 vs. 43.9 years, $p < 0.0001$), had higher systolic blood pressure (SBP) (mean pre dialysis SBP 145 vs. 136 mmHg, $p = 0.038$), and a longer wait time on haemodialysis before transplantation (median 8.7 vs. 5 years, $p < 0.001$). Diabetes, sex, phosphate, and albumin did not affect mortality in this selected cohort. Age (hazard ratio (HR) 1.05, $p = 0.03$) and SBP, HR 1.02, $p = 0.04$) were independent predictors of mortality following transplant in a Cox regression model. Death-censored graft failure was only predicted by serum creatinine at 3 months following transplant (HR 1.003, $p < 0.001$) but no pre-transplant variables, independent of transplant function.

Discussion

Haemodialysis patients who are older and have elevated systolic blood pressure appear to have poorer survival following renal transplantation; graft failure, however, is independent of these variables. In this co-morbid patient cohort with a substantial duration of renal replacement therapy whilst waiting for transplantation, elevated SBP is a potentially modifiable risk factor which influences post transplant outcomes.

P053

Kidney transplantation offers a significant survival advantage compared to waitlisting: A single centre experience

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Introduction

Kidney transplantation is associated with lower mortality and improved quality of life for patients with end stage renal disease (ESRD). Survival with ESRD in both dialysis and transplant populations have improved over the last decades and acceptance onto transplant programmes has become more liberal. The aim of this study was to investigate the benefit of renal transplantation in the current era and to identify factors influencing the degree of benefit compared to waiting on dialysis.

Methods

Single centre review of prospectively collected data of adult patients who were activated on the waiting list for renal transplantation from 11/2005 till 03/2015. All continuous data are presented as median (interquartile range).

Results

During a follow-up period of 51 months (28.1/82.4), 2219 patients were activated in our transplant waiting list (age 52.4 (42.3/61.6), 64.5% males). In this multi-ethnic group of patients (Caucasians 38.8%, South-Asians 30.7%, Afro-Caribbean 17%) glomerulonephritis (26.1%) and diabetic nephropathy (23.2%) were the most frequent causes of ESRD. At the end of the follow-up 1272 received a renal transplant (52.1% from a live donor). Patients that received a renal transplant were younger, aged 49.0 (39.0/58.7) vs 57.1 (47.7/64.9) compared to the wait-listed group. The median waiting time for a deceased-donor graft was 32.1 months (15.8/47.8). Multivariate cox regression analysis showed that transplantation (HR 0.63, 95% CI 0.47–0.84, p=0.001) and in particular pre-emptive transplantation (HR 0.49, 95% CI 0.34–0.68, p=0.01) as well as younger age on activation (HR 0.96, 95% CI 0.97–0.95, p<0.001) have a positive impact on overall survival. Diabetic Nephropathy (HR: 2.01, 95% CI 1.6–2.6, p<0.001) and dialysis vintage per month (HR: 1.03, 95% CI 1.01–1.05, p<0.001) were significant risk factors for mortality.

Discussion

This study indicates significantly lower mortality in the transplant cohort compared to the waitlisted. The survival advantage associated with renal transplantation is evident in this cohort with no difference between different ethnic groups. Pre-emptive transplantation in younger patients offers the most significant survival advantage.

P054

Reviewing and enhancing access onto the renal transplant waiting list

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Introduction

Transplantation is the 'gold standard' treatment for patients with end stage renal failure (KDIGO 2009). Planning should start when eGFR falls below 20mL/min/1.73m² dependent on the rate of decline (NHS England 2013). Recent data from NHSBT UK Activity Report 2014-15 shows that centres with smaller waiting lists reduces the potential number of DBD kidney offers and may increase the mismatch for patients receiving DCD transplants.

A recent audit showed patients were not being listed in a timely manner due to a number of factors.

Methods

A process mapping exercise was undertaken by the transplant and CKD team to establish barriers to listing. In response to the factors identified a care pathway for entry onto the waiting list was developed and presented at our local steering group to validate its structure and content.

A quarterly audit was introduced to establish a baseline of the current performance of the referring centres with the appropriate investigations and to clarify what tests.

Results

The process mapping exercise identified that between the dates Jun – Dec 2014:-

Total Referrals from the referring units was 41 patients

Average eGFR at referral was 15mL/min/1.73m²

Pre-emptive Referrals were 51%(21)

On haemodialysis at referral 39%(16)

On Perineal Dialysis at referral 9%(4)

Discussion

One referring centre does not have the facility to conduct Exercise Tolerance Testing which are required before listing most patients.

No one port of referral, following up of investigations, processing of bloods and workup prior to being seen in assessment clinic. Delays in receiving and processing bloods.

This Care Pathway has proved valuable in streamlining entry onto the waiting list. In our own centre we have changed a number of practices in the delivery of the service.

Outcomes of Cinacalcet versus pre-transplant Parathyroidectomy in renal transplant recipients: Single centre experience

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Introduction

Hyperparathyroidism (HPT) secondary to chronic kidney disease often persists after renal transplantation (Tx) and can be a cause of hypercalcaemia and acute graft dysfunction. Cinacalcet (Cx) has been shown to be effective in correcting hypercalcaemia and decreasing parathyroid hormone (PTH) levels with parathyroidectomy (PTx) as an alternative treatment often if Cx fails. However, there are concerns that PTx may be followed by a reduction in renal function, raising the question whether it must be performed prior to kidney Tx. At present, there are no studies suggesting the ideal timing for PTx in renal Tx patients with uncontrolled HPT. In this retrospective study, we aimed to investigate the differences in several renal Tx outcome measures and in classical markers of bone homeostasis by comparing HPT patients who underwent PTx before renal Tx with patients whose HPT was managed medically.

Methods

130 renal Tx patients treated with Cinacalcet and 49 patients who underwent PTx before renal Tx were selected from Pharmacy and Endocrine Surgical Records respectively over an 8-year period. We excluded patients with early (within 3 months) graft failure and a post-Tx follow up less than 6 months. We collected monthly renal function and bone marker measurements performed up to 24 months after Tx. The following 2-year post-Tx outcome measures were considered: graft failure, graft function (eGFR ≥ 60 mls/min), transplant renal artery stenosis (TRAS) requiring stenting within 12 months after Tx and rejection. Statistical analysis was performed by IBM SPSS Statistics ver. 20.

Results

117 and 46 patients were included in the Cx and PTx group respectively. PTH levels at the time of Tx were higher in the Cx vs PTx as expected (72.3 vs 1.6, $p < 0.001$). PTx was associated with significantly better bone profile markers (Calcium 2.50 vs 2.36, $p < 0.001$; Phosphate 0.85 vs 1.14, $p < 0.001$; Alkaline Phosphatase 107 vs 80, $p = 0.004$ at 24 months) during the study. No significant difference was found in rejection, TRAS and graft failure rates between the two groups. The Cx group showed a better mean eGFR (48.5 ± 17.9 ml/min vs 39.9 ± 17.8 ml/min at 24 months) throughout the 24-month follow-up period ($p = 0.015$, repeated measures ANOVA) compared to PTx group. This persisted after multivariate analysis ($p = 0.011$). Investigating the hypothesis that such a finding could be explained by a longer HPT duration in the PTx group, we compared the latter with a subgroup of 48 patients who were already on Cinacalcet before Tx. The results were similar ($p = 0.015$).

Discussion

Renal Tx patients with HPT who had PTx before Tx had significantly better bone profile markers up to 24 months after Tx compared with those treated with Cinacalcet. We observed better mean eGFR in the Cx compared to PTx group throughout the study. This may reflect the comorbidity of patients with more severe hyperparathyroidism in the PTx group since the difference in graft function emerged in the first 3 months post-Tx and was due to causes such as infection and vascular complications. Further studies are necessary to further evaluate this finding.

A review of the incidence, causes and impact of Neutropenia after renal transplantation

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Introduction

Neutrophils are crucial to a transplant recipient's defence against bacterial pathogens, which are an important cause of morbidity and mortality. We reviewed the incidence and nature of neutropenia following renal transplantation.

Methods

All patients receiving kidney transplants between November 2009 and July 2013 and for whom follow-up data were available for one year were included. Data was collected retrospectively for 195 patients. Neutropenia occurring within 6 months of transplantation was defined as a neutrophil count below $2 \times 10^9/l$ and severity was graded as grade 1 ($1-2 \times 10^9/l$), grade 2 ($0.5 - 0.9 \times 10^9/l$) or grade 3 ($<0.5 \times 10^9/l$) for each case.

Results

INCIDENCE: 38/195 (19.5%) patients developed neutropenia – grade 1, 15 patients (7.7% of all patients); grade 2, 9 patients (4.6%); grade 3, 14 patients (7.1%). The mean time to neutropenia was 52 days (14-175). The mean duration was 16 days (3-143). **POSSIBLE CAUSES & ASSOCIATIONS:** [1] **Kidney type:** Amongst the patients experiencing neutropenia, 20 (52.6%) received DCD kidneys, 5 (13.2%) received DBD kidneys, and 13 (34.2%) were live transplant recipients, compared with 91 (58.0%) DCD recipients, 27 (17.2%) DBD recipients and 39 (24.8%) live donor recipients without neutropenia. [2] **Drugs:** All 195 patients received cotrimoxazole. Neutropenia occurred in 35/182 (19.2%) of patients who received basiliximab at induction and 3/13 (23%) of patients who received alemtuzumab at induction. Almost all patients receiving basiliximab (182) received tacrolimus (3/182 received ciclosporin), mycophenolate (1g bd; 2/182 received azathioprine) and tapered prednisolone maintenance therapy, whilst patients receiving alemtuzumab (13) almost all received tacrolimus (1/13 received ciclosporin), myfortic (500 mg bd; 1/13 received azathioprine) and no steroid therapy. A total of 26/38 (68.4%) patients who developed neutropenia received prophylactic valganciclovir compared with 64/157 (46.5%) of the patients with no neutropenia. [3] **CMV infection:** 14/38 (36.8%) patients with neutropenia had CMV viraemia within the first 6 months compared with 29/157 (18.4%) of those with no neutropenia. **INTERVENTIONS:** Medications were reduced/ceased in 25/38 (65.7%) of patients with neutropenia. Multiple medications were altered in 14/38 (36.8%) patients (antimetabolite & cotrimoxazole 6/38, antimetabolite & valganciclovir 2/38, valganciclovir & cotrimoxazole 2/38, antimetabolite & valganciclovir & cotrimoxazole 4/38). A single medication was altered in 11/38 (28.9%) of patients (antimetabolite 6/38, cotrimoxazole 4/38, valganciclovir 1/38). Valganciclovir was commenced in 3/38 patients. **OUTCOMES:** Patient and graft survival at months was 38/38 (100%) and 35/38 (92.1%) respectively amongst patients experiencing neutropenia, and 154/157 (98.1%) and 149/157 (94.9%) respectively amongst patients not experiencing neutropenia. Contemporaneous bacterial infection was proven in 8/38 patients (23.5%) and suspected in a further 5/34 (14.7%). In the neutropenia group, the mean no. of admissions was 3 per patient (0-5) equating to an average of 13 hospital bed days each (0-53).

Conclusions

[1] Neutropenia is a common sequelae of transplantation. The incidence of neutropenia (19.5%) and severe neutropenia (7.1%) reported here are almost identical to published data (22% and 6% respectively; Am J Transplant 2009;9(8):1816-25). [2] CMV viraemia and the use of valganciclovir as prophylaxis or treatment were both associated neutropenia. The ubiquitous use of antimetabolites and CNIs prevented meaningful analysis of their association. [3] Rather surprisingly, neutropenia was not associated with worse patient or graft survival in this study, but was associated with high rates of bacterial infection.

P057

Outcomes in patients 70 years and over who received a kidney transplant compared to those who remained on the waitlist

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Introduction

Kidney transplantation is the optimal mode of renal replacement therapy for most patients with established kidney disease (ESKD). There is an increase in age of the incident ESKD population in the UK and older patients are more likely to have significant co morbidities with shorter life expectancy. Concerns still remain about transplantation in the older population in particular around complications that relate to undergoing major surgery and the immunosuppression burden. The aim of this retrospective study was to assess outcomes and complications for older patients (70 years and over) at a single centre, who had received a kidney transplant compared to those who remained on the transplant waiting list.

Methods

We evaluated all patients 70 years and over who underwent kidney transplantation or were waitlisted and had long term follow up at the centre between June 2005 and June 2015. Data examined retrospectively included mortality, incidence of cardiovascular events and cancer, infection and hospital admissions. Graft survival, episodes of acute rejection and kidney function were analysed for the transplanted patients.

Results

The study population consisted of 37 patients, 16 received a kidney transplant and 21 were placed on the transplant waiting list. Of the 21 who were waitlisted, 6 were removed and 6 suspended during the follow up period. Mean age was 72.5 years and the cohort consisted of 70% males, 42% white, 30% black, 24% Asian and 5% other ethnicities. There was no significant difference in time on the waitlist between the 2 groups with overall mean time of 25 months. Survival at the end of the follow up period was 87.5% and 80% in the transplanted and waitlisted cohorts respectively. There were 3 cancers diagnosed in the transplant group (metastatic oropharynx squamous cell cancer (SCC), skin SCC and basal CC) with none in the waitlist group. There were more infective episodes in the transplant compared to the waitlist group (7.5 vs. 1.6 infective episodes/100 patient years) and hospital admission rates were similar in the 2 groups. There were 2 and 6 cardiovascular events in the transplant and waitlist groups respectively. In the transplant cohort there were 5 (31%) episodes of rejection, all occurring in the first year. At 1 and 5 years, graft survival was 87.5% and 81.2%, patient survival was 94% and 87.5%, and creatinine was 127umol/l (eGFR 46ml/min) and 104umol/l (eGFR 49ml/min) respectively. 4 (25%) patients had complications post-operatively.

Discussion

Survival was similar in the transplanted and waitlist cohorts, which may be due to small numbers in the groups. The mortality in the waitlist cohort, who remained on dialysis, was lower than expected. There was a higher incidence of infections and cancers in the transplanted group, which are both complications associated with immunosuppression. We conclude that transplant outcomes are reasonable in this cohort of older patients with a high rate of complications, which are likely to be related to the immunosuppression and surgery. This may impact on quality of life and so further studies to explore this aspect compared to remaining on dialysis would be useful.

P058

Socioeconomic deprivation and barriers to live-donor kidney transplantation: a qualitative study of deceased-donor kidney transplant recipients

Poster withdrawn.

P059

Long-term pulse wave velocity and VO_2 peak outcomes with 12 weeks of aerobic or resistance training in kidney transplant recipients: A follow-up of the ExeRT Study.

Poster withdrawn

Stratifying skin versus non-skin cancer risk post-kidney transplantation according to patient characteristics

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Introduction

Cancer is a significant cause of morbidity and mortality after kidney transplantation and patients are appropriately counselled about the risk of developing post-transplant cancer. However, the majority of these cancers are skin cancers, which usually have a better prognosis compared to other cancers. It would be important to differentiate risk for development of skin versus non-skin cancer to better counsel patients and raise awareness for transplant professionals. The aim of this project was to stratify cancer risk varies depending on patient characteristics, with the aim to allow better counselling of patients regarding their post-transplant cancer risks.

Methods

Data was extracted from hospital informatics systems for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events. Immunosuppression utilised during this time for patients included basiliximab induction and standard maintenance immunosuppression of tacrolimus, mycophenolate mofetil and low-dose corticosteroids.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up 4.4 years post-transplantation. The median age for the entire cohort was 47, males (n=681, 59.7%), Caucasian ethnicity (n=822, 72.1%), deceased-donor recipients (n=633, 56.4%), repeat transplants (n=111, 9.7%), diabetes as cause of end-stage kidney disease (n=117, 10.3%) and previous/active smoking exposure (n=274, 24.0%). Over 4.4 years, 69 patients in our study cohort developed a post-transplant cancer of which 31.9% were skin cancers (including melanoma). Patients developing skin or non-skin cancer were older (53.6 years and 51.8 years) versus recipients who did not develop cancer (45.8 years, $p < 0.001$). Male kidney allograft recipients were more likely to develop both skin cancer and non-skin cancer post-transplantation compared to females ($p = 0.007$). Specifically, 81.8% of observed skin cancer cases were among male kidney allograft recipients. Patients with any smoking exposure had increased risk for both skin and non-skin cancers (3.3% and 6.9% respectively) compared to recipients who had never smoked (1.6% versus 3.3% respectively, $p = 0.005$). 91% of skin cancer cases occurred among kidney allograft recipients of Caucasian ethnicity. Recipients who developed post-transplant diabetes mellitus appeared to have a slightly increased risk of developing skin cancers (versus both pre-existing diabetics and non-diabetics), but not for non-skin cancers (5.4% versus 2.6% versus 1.5% respectively, $p = 0.042$).

Discussion

Cancer is a concern for patients post-kidney transplantation. The majority of the increased cancer risk comes from skin cancer. We have shown significant differences in cancer risk and in particular, skin cancer risk, according to different patient factors. Our data supports the rationale that clinicians should provide more tailored risk stratification of cancer post-transplantation.

P062

Pre-transplantation BMI and not BMI change may represent a risk factor for developing new onset Diabetes after transplantation

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Introduction

New-onset diabetes after transplantation (NODAT) is associated with poorer outcomes in kidney transplantation (Tx). Identification of modifiable risk factors is significant in order to reduce its incidence and impact on transplant outcomes.

Methods

We retrospectively examined consecutive non-diabetic adult patients, who underwent living donor (LD) kidney Tx from January 2011- December 2014. All patients received Tacrolimus-based immunosuppression and induction as per local protocol. We used the American Diabetes Association criteria for NODAT diagnosis except oral glucose tolerance test. We used non-parametric analysis.

Results

324 patients were included in the study. 30 recipients from LD developed NODAT (9.3%) during the study period and 7 during the first year (10.9%). There was no difference between the NODAT group and the NODAT-free group regarding gender ($p=0.175$) or ethnicity ($p=0.520$). The median age was 49 years (30-73). It was the first Tx for 76.7% of patients and pre-emptive for 30%. 60% of NODAT patients were on steroids and 33.3% had history of rejection. 30% of NODAT patients had history of CMV viraemia and 4 patients lost their graft. Regarding patients diagnosed with NODAT during the first year, there was no difference in age between the NODAT and the NODAT-free group ($p=0.144$). There was significant difference between the two groups regarding BMI at Tx ($p=0.049$). There was no significant BMI change among patients in each group during the follow up ($p=0.649$). The difference in BMI at Tx remained significant after correction for rejection ($p=0.05$).

Discussion

Despite the limitations of the current study, it seems that the pre-Tx BMI, but not the BMI change may represent a risk factor for NODAT. Tailoring clinical strategies may minimize the impact of this complication.

P063

HIV-positive deceased kidney donation

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Introduction

Solid organ transplantation is now the standard of care for many HIV-infected patients with end-stage kidney or liver disease. The relative shortfall in donated organs affects all transplant candidates, including those with HIV. One way to help alleviate this shortage would be the use of HIV-infected organ donors for HIV-infected recipients. The precedent for this approach was set in South Africa, where promising short-term outcomes have been reported in a small number of HIV-infected recipients of kidney transplants from HIV-infected donors. We sought to replicate this experience by accepting kidney offers from HIV-infected deceased donors for patients with HIV-infection on the transplant waiting list.

Methods

Donor selection criteria were as follows: stable and well-characterized HIV infection (HIV viral load < 50; CD4 count > 200) for at least 6 months prior to brain injury; no history of virological failure or drug resistance; preferably those where information about the donor virus (such as historical genotype patterns where possible and current viral load) could be obtained. Potential recipients were counselled about the potential risks of HIV-infected organ donation (including HIV superinfection, complications related to medication selection, transmission of latent opportunistic infection, or the possible increased risk of rejection) as compared to the risks of remaining on the transplant waiting list, and gave informed consent both at the time of listing and prior to transplantation. Agreement was obtained from the local transplant and HIV teams and from NHSBT.

Results

The donor was a 55 year old White DBD male. The cause of death was subarachnoid haemorrhage. The patient was known to have HIV infection since March 2008. Following an episode of pneumocystis pneumonia in April 2009 the patient had commenced antiretroviral treatment with tenofovir, emtricitabine and efavirenz and this remained unchanged since then. The HIV viral load had been < 50 since August 2012; the CD4 count had been > 200 since September 2009. The patient's HIV physician reported them to be adherent with medication and well since April 2009. Both kidneys were accepted and implanted into two local recipients with informed consent: a 60 year old Black-Caribbean male active 563 days on the deceased donor waiting list (recipient 1) and a 45 year old Black-Caribbean male active 306 days on the deceased donor waiting list (recipient 2). The cold ischaemic times were 18 hours and 22 hours 40 minutes respectively. Recipient 1 had delayed graft function and an episode of mixed T-cell and antibody-mediated rejection on day 5 treated with ATG. Recipient 2 had immediate function. Both patients received basiliximab induction and maintenance treatment with Neoral®, mycophenolate and corticosteroids. HIV remains undetected in both recipients. At 5 months post-transplant recipient 1 has a corrected eGFR of 44ml/min and recipient 2 has a corrected eGFR of 39ml/min.

Discussion

With careful donor and recipient selection and comprehensive informed consent prior to listing and at the time of transplantation it is possible to transplant kidneys from HIV-infected deceased donors into HIV-infected recipients, with promising early outcomes.

P064

Fatal case of Cowpox Infection in a renal transplant recipient

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Introduction

We report a fatal case of cowpox infection in a renal transplant recipient.

There have been reports of cowpox infections with similar clinical progress in immunocompetent patients with resolution and good prognoses. In immunocompromised individuals however, the illness can be more serious or fatal. Like smallpox, the cowpox virus is a member of the Orthopox DNA virus genus. The usual vectors are wood mice and bank voles. The transmission mode to humans is through broken skin, or cat scratches, causing lymphadenitis and necrotic eschars.

Case

A 17 year old boy, a renal transplant recipient through altruistic donation, was admitted for progressively worsening non painful cervical lymphadenopathy. He had CKD due to antenatally diagnosed dysplastic kidneys and had had haemodialysis, peritoneal dialysis and had two previous failed renal transplants. His neck lymphadenopathy progressed over 2 weeks, despite antibiotic treatment with oral and then intravenous broad spectrum agents. Eventually, airway compromise necessitated an intensive care admission and tracheostomy insertion. Two weeks after the initial neck swelling, he developed a vesicular dermatitis over the face and torso. This progressed to nodular, bullous lesions with necrotic centres. These necrotic eschars very quickly spread to the limbs within 24 hours. Tonsillar and skin tissue biopsy showed numerous eosinophilic intracytoplasmic inclusion bodies consistent with poxvirus infection, with cowpox identified on electron microscopy. The transmission was thought to have occurred through the family cat. The recommended antiviral treatment for a DNA virus would be cidofovir, but a sharp deterioration in renal function after only one dose despite adequate hydration was a major concern. Brincidofovir was given 18 days after presentation. His regimen also included vaccinia immunoglobulin on two occasions. Despite intensive treatment, he developed multi-organ failure and died 29 days after presentation.

Summary

We present a case of a kidney transplant recipient who contracted a cowpox infection which resulted in severe neck lymphadenopathy and widespread necrotic skin eschars. Despite reduction in his immunosuppressive medication, treatment with vaccinia immunoglobulin, and brincidofovir, he developed multi-organ failure and died. A high index of suspicion for unusual infection is required in immunosuppressed individuals; the use of nephrotoxic anti-viral therapies should be considered early in the illness.

P065

Viral infections in renal transplant recipients: our experience

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Introduction

Viral infections in the post transplant period are among the leading causes of patient morbidity. Incidence and severity of infection is directly related to the degree of immunosuppression and prior exposure status. Standard practice in our unit is use of Alemtuzumab or Basiliximab for induction and dual agent maintenance regimen with CNI and MMF. The purpose of this analysis is to establish the incidence and pattern of infections in our practice.

Methods

Patients undergoing kidney transplant between 01/01/2013 to 31/12/2013 were analysed retrospectively. 119 Patients were analysed for all types of viral infection. Only infections confirmed by laboratory testing were considered for the analysis.

Results

Review of data showed Alemtuzumab was given in 50 and Basiliximab in 45 patients. All had routine surveillance tests for BK viraemia and CMV was tested on clinical suspicion of CMV disease. 7 patients were investigated for atypical pneumonia of viral etiology (Influenza, Parainfluenza, RSV, Rhinovirus, Coronavirus & Humanmetapneumovirus). 34(35.41%) of them developed viraemia. 22(64.7%) were early and 12(35.29%) were late infections. BK & CMV accounted for 24(25%) cases of infection. 4 Patients developed EBV viraemia. 3 of them had prior exposure to EBV. One of these patients had EBV reactivated at a later date and showed low level(PCR<250) of viral replication while other developed PTLD after 5months and died due to bowel perforation from lymphoma of bowel. Recipient who had no prior exposure to EBV contracted EBV from donor (Early infection) and exhibited high EBV viral replication and succumbed to PTLD within 6months.

Discussion

Incidence of viraemia continues to be high in post renal transplant recipients. A separate study from our unit showed incidence of viral infections are higher in Alemtuzumab group as well as recipients who are neutropenic. A strong surveillance is needed for early recognition and early initiation of treatment is necessary to treat the infection successfully.

P066

Low grade acute rejection, or is it Polyoma Viral Nephropathy?

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Purpose

To study the associations of Polyoma Viral Nephropathy (PVN) with Acute Rejection (AR) in Kidney Transplant (KTx) Biopsies (Bx) and their outcomes.

Method

Retrospective analysis of all Bx reports of KTxs at a single centre between 01/2005 to 12/2014. PVN was confirmed histologically using immunohistochemistry for SV40 antigen. Immunosuppression protocol included basiliximab induction and maintenance with tacrolimus, MMF and prednisolone.

Results

Of the 826 patients studied, 1659 Bx were undertaken in 704 patients. Incidence of PVN was 21 (2.5%), occurring at a median duration of 7.3 months postTx (10 followed treatment of AR, 3 seen synchronously with AR, 1 preceded AR, and 7 cases not associated with AR). On univariate analysis, PVN (n=21) was significantly associated with AR- 14 (67%) vs. 227 (28%) and Interstitial Fibrosis/Tubular Atrophy- 8 (38%) vs. 104 (13%), compared to non-PVN group (n=805) respectively, and a trend of association was seen with Calcineurin Inhibitor Toxicity. Death-Censored Graft Loss (DCGL) (15% vs. 14%), and mortality (9% each) were similar at last follow-up. Sub-group analysis showed that PVN was significantly associated with low Banff grade rejections [Borderline: 6 (29%) vs. 134 (17%), and Banff 1a/1b (33% vs. 5%)], but not with higher grade Banff rejections (0.5% vs. 0.01%) or Humoral Rejections (0 vs. 0.9%), compared to non-PVN, respectively. DCGL was significantly lower in low Banff grade rejections (borderline/1a/1b) associated with PVN, compared to low Banff grade rejections in KTx cases without PVN [1(9%) vs. 24 (17%)], $p=0.05$. DCGL was higher in higher Banff grade rejections with or without PVN [1(100%) vs. 26 (55%)], respectively.

Conclusion

Although PVN is associated with treatment of low grade AR, this approach is justified because the graft loss of low grade AR without PVN is greater. Avoidance of depleting antibodies could account for a less poor outcome with PVN at our centre compared to literature.

P067

Screening for Atherosclerotic Disease in renal transplantation

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Introduction

There is evidence that atherosclerotic disease contributes to poor cardiovascular outcome following kidney transplantation. Current BTS and European guidelines have no specific recommendations on radiological screening for atherosclerotic disease, which is sometimes performed as part of pre-transplant screening. We evaluated recent transplants done in UHL trust to see if high risk patients could be identified for potential screening prior to transplantation.

Methods

We retrospectively analysed 53 kidney transplants that took place in UHL between October 2013 and April 2014. We identified risk factors of age, diabetes, smoking history, obesity and symptomatic peripheral vascular disease. We then assessed adverse outcomes in the form of intra-operative finding of atheroma, renal artery stenosis, renal artery thrombosis, renovascular thrombosis, deteriorating eGFR, cardiovascular events and transplant failure. Statistical significance was established using Fisher's exact test.

Results

We found that incidence of atheroma was significantly increased in patients with claudication ($p = 0.002$), and also in patients over the age of 55 who either had a smoking history ($p = 0.038$) or obesity ($p = 0.020$). The presence or absence of diabetes did not have a significant effect on outcomes. There was no increased incidence of atheroma in patients under 55 even in the presence of other risk factors. No individual or combination of risk factors lead to a significant increase in other measured adverse outcomes.

Discussion

Current practice at UHL (post-dating the patients in this report) is to perform iliofemoral ultrasound screening on patients who are either over 60, or over 55 with at least 2 of the listed risk factors. The evidence suggests that any patient with symptomatic peripheral vascular disease could benefit from such screening, in addition to patients over 55 with either a smoking history or a BMI of at least 30.

Normothermic machine perfusion in marginal DCD livers

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Introduction

The current organ shortage crisis has necessitated the increased use of marginal organs for transplantation. However, in the UK approximately 72% of offered DCD livers are declined during the screening, procurement or preservation process. Nonetheless, more than 25% of UK liver transplants are from DCD donors. These carry a higher risk of PNF, EAD and IC. Normothermic machine perfusion offers potential advantages for DCD organ usage. We present a case series of 5 marginal DCD organs that were successfully transplanted after being preserved using NMP.

Methods

As part of 2 different clinical trials, livers were preserved using NMP. Recipients were consented in advance whilst on the transplant waiting list. Flow dynamic and biochemical characteristics were used to measure organ viability including: pH>7.2(unsupported), HA flow>0.1L/min, Lactate<2mM, Glucose<10mM.

Results

The donor, preservation and recipient characteristics of these DCD livers is described below. The reason they fall outside standard DCD acceptance criteria is highlighted in bold.

1. Donor 38yr, CVA, **pH7.1, lac 7.2mmol, BE-13**, ALT 261IU/L, fWIT 28mins, TPT 12hr34min, NMPT 10hr13min. Recipient 42yr, BMI 27.5, ALD, MELD 17
2. Donor 64year, CVA, **pO2 6-8KPa for 72hrs prior to retrieval**, high dose noradrenaline, dobutamine and vasopressin, GGT 227IU/L, fWIT18mins, TPT15hr 48min, NMPT 14hr 1min. Recipient 35yr, BMI 22, PSC, MELD 8
3. Donor 73yr, hypoxic brain injury, ALT 250, GGT 666IU/L, **fWIT 35mins**, Logistical problems in the recipient hospital resulted in TPT 20hr 29min, NMPT 18hr 15min. Recipient 45yr, BMI 32.6, ALD, MELD 9
4. Donor 71yr, CVA, **fWIT 1hr 33min**, TPT 11hr 20min, NMPT 9hr 36min. Recipient 61yr, BMI 20.9, non-cirrhotic portal hypertension, MELD 12
5. Donor 52yr, CVA, BMI 32.7, fWIT 15mins, **2.2kg liver, discarded due to steatosis**, NMP commenced after 8hrs CIT, TPT 13hr 30min, NMPT 5hr 27min. Recipient 56yr, BMI 22.5, ALD, MELD 10

In all cases, perfusion-dynamic and biochemical parameters normalised within 4hrs and the livers were transplanted. No patient developed EAD and there was 100% graft and patient survival at 3months.

Discussion

Our early experience of using NMP in human liver transplantation suggests that it can enable marginal DCD livers to be objectively assessed and transplanted, with the potential to increase organ utilisation. Several of these livers would have been discarded if preserved using static cold storage. The results of on-going clinical trials are needed before reaching firm conclusions.

Key: PNF – primary non-function; EAD – early allograft dysfunction; IC – ischaemic cholangiopathy; NMP – normothermic machine perfusion; CVA – cerebrovascular accident; TPT – total preservation time; NMPT – NMP time; fWIT – functional warm ischaemic time; CIT – cold ischaemic time; HA – hepatic artery; ALD – alcoholic liver disease; PSC – primary sclerosing cholangitis; MELD – model for end-stage liver disease

P069

Do Hepatitis C positive liver recipients have worse survival outcomes if they receive hepatitis C positive livers?

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Introduction

An estimated 400,000 people in the UK are infected with Hepatitis C virus (HCV) and HCV associated liver cirrhosis is a common indication for liver transplantation. Organs from HCV+ve donors are a potential resource and are often allocated to HCV+ve recipients. We report the UK experience of using Hepatitis C positive livers.

Methods

An analysis was performed of recipients of deceased donor liver transplants in the UK between 2000 and 2015, using data from the UK transplant registry. Kaplan-Meier tables and Cox proportional hazards were used to compare graft and patient survival for HCV+ve and HCV-ve recipients who received livers from hepatitis C positive and negative donors.

Results

56 liver transplants were carried in the UK using HCV+ve livers. 17 went to HCV+ve recipients, 38 went to recipients of unknown HCV status and 1 went to an HCV-ve recipient. 507 HCV+ve recipients received HCV-ve livers. Unadjusted patient and graft survival analysis showed similar outcomes for HCV+ve liver recipients whether they received an HCV+ve liver or an HCV-ve liver. 5 year patient survival 82% HCV D+/R+, 70% HCV D-/R+ ($p=0.26$), and 5 year graft survival 82% HCV D+/R+, 74% D-/R+ ($p=0.39$). Unadjusted 5-year patient and death censored graft survival were higher for liver transplant recipients if they were HCV-ve compared to recipients who were HCV+ve ($p=0.0017$) and ($p=0.0031$) respectively.

Discussion

The UK experience suggests that patient and graft survival in recipients who have HCV is similar whether or not they are transplanted with livers from HCV+ve or HCV-ve donors.

P070

Liver transplantation survival in the elderly recipient \geq 70 year

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Introduction

Historically, the transplant community has been reluctant to offer liver transplantation to the elderly recipient \geq 70 years. This practice was based on concerns that the elderly have more co-morbidities and are at higher risk for major complications, and early death. In the last decade there has been an increasing referral of older patients for liver transplantation. The aim of this study was to look at long term survival in the \geq 70 year liver transplant recipient.

Methods

Single institution, retrospective analysis, of a prospectively maintained liver transplant database (February 1989 – February 2015) identifying liver transplant recipients \geq 70 years. Survival analysis was performed using Kaplan Meier (IBM SPSS v22) comparing the \geq 70 years to the 18 – 69 year old recipient. Data is expressed either as percentage or as a median and range. Minimum follow up was of one year.

Results

In the time period of study there were 3687 adult liver transplants of which 38 (1%) were done in the \geq 70 year old age group. The first \geq 70 year recipient was transplanted in 1997. There were 18 women and 20 men of median age 70 (70 - 74) years. Indications for transplantation were chronic liver disease in all. Aetiology was HCV-related cirrhosis (4/38, 10%), cryptogenic cirrhosis (3/38, 7.9%), PBC (11/38, 28.9%), ALD (6/38, 15.8%), HCC (2/38, 5.3%), PSC (2/38, 5.3%) and miscellaneous (10/38, 26.8%). The median MELD was 14.2 (5 - 56) and the median Child-Pugh score was 9.2 (range 5-13). The majority of elderly recipients were transplanted with a DBD graft (n=33, 86.8%), the remainder were transplanted with a DCD (n=4,10.5%) and one received a LRLT (2.7%). Whole grafts was used in 34 (89.5%), right lobe in 3 (7.9%) and 1 (2.6%) received a left lobe. 26 of 38 recipients are still alive (68.4%). The cause of death was cancer in 58.3% (n= 7/12) of which 2 were recurrent HCC and 5 were de novo cancer. There was no difference in 1,3,5 year survival between elderly (\geq 70y) and the younger recipient (< 70y) (97%, 80%, 73% versus 90%, 84%, 79%, respectively, p<0.05).

P071

Adapting the surgical Apgar Score for liver transplantation

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Introduction

The Surgical Apgar Score is a 10-point scale using the lowest heart rate, lowest mean arterial pressure, and estimated blood loss (EBL) during surgery to predict postoperative outcomes. The SAS has not yet been validated in patients undergoing liver transplantation, likely due to difficulties in estimating blood loss. Our primary aim was to develop a modified Surgical Apgar Score for liver transplant patients (SAS-LT) using appropriate volumes of intraoperative blood transfusion to replace the EBL parameter. We hypothesized that the SAS-LT would predict death or severe complication within 30 days of transplant.

Methods

Six hundred twenty-eight patients who underwent liver transplantation from July 2007 and November 2013 were included. Pre-, intra-, and postoperative variables were collected, including demographic data, comorbidities, indication for procedure, hemodynamic and transfusion data, major morbidity, and mortality. A modified Surgical Apgar Score (SAS-LT) was developed replacing EBL with volume of allogeneic and autologous red cells transfused. The SAS-LT was then compared to the MELD, SOFA, and APACHE III scores using multivariable logistic regression.

Results

One hundred patients (15.9%) had serious complications, and 5 patients (0.8%) died within 30 days. Using receiver-operating characteristics, the area under the curve (95% CI) was 0.56 (0.50, 0.62) for MELD score ($P = 0.059$), 0.62 (0.56, 0.67) for SOFA score ($P < 0.001$), 0.57 (0.51, 0.63) for APACHE 3 score ($P = 0.024$), and 0.57 (0.51, 0.63) for the SAS-LT ($P = 0.02$).

Discussion

The SAS-LT predicted early postoperative morbidity and mortality with similar accuracy to SOFA and APACHE scores. As the SAS-LT can be calculated based on simple intraoperative metrics, it may be one of the earliest tools to predict postoperative morbidity and mortality for liver transplant patients.

P072

Implanting DCD grafts correlates with a worse Quality of Life (QoL) compared to DBD grafts at 3 months and 1 year post liver transplantation in a cohort of UK patients

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Introduction

The use of grafts from donors after cardiac death (DCD) has increased annually to meet rising demand for OLT. In the UK the use of a DCD graft has been associated with a 2-fold increase in risk of mortality and graft loss up to 3 years post transplantation. Whether the use of a DCD graft impacts on a recipient's QoL remains to be elucidated and was the aim of this study.

Methods

Data was reviewed for patients undergoing liver transplantation between October 2007 and September 2014. Clinical data collected was recipient age, gender, UKELD scores, cold ischaemic time, type of graft (DCD and DBD only) and QoL score. QoL was grouped whether patients felt able to perform any kind of work or not. Chi Squared and linear regression models were performed on SPSS.

Results

459 patients 235M/219F/5 Unspecified were identified. 386 patients received a DBD graft, 69 received a DCD graft. Patients receiving DCD grafts had significantly poorer QoL at 3 months (76% unable to work vs 57%, $p=0.004$) and at 1 year (35% vs 19%, $p=0.008$). By 2 years QoL outcome were similar between the groups (18% vs 13%, $p=0.36$). When adjusted for other transplant factors the use of a DCD graft remained significant at 3 months and 1 year but not 2 years ($p=0.003$, $p=0.009$, $p=0.295$).

Conclusions

The implantation of DCD liver grafts is associated with a poorer QoL up to 1 year post transplantation. This likely reflects the increased risk of significant complications post-operatively associated with DCD grafts. The data suggests that new approaches, such as organ perfusion, are warranted in DCD livers.

P073

Outcomes in patients after combined liver-kidney transplant: a fifteen years experience from a single centre

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Introduction

Increasing number of combined liver and kidney transplant (CLKT) are being performed since the introduction of MELD system for allocation of deceased donor liver. The indications and timing for this type of transplant, however remain unclear. The aim of this study was to evaluate overall survival, kidney graft survival and renal function after CLKT in our centre.

Methods

Patients receiving a combined liver and kidney transplant from 2000 to 2015 were included in this study. Data was collected from a prospectively maintained database of liver and kidney transplant in our centre. Missing data were completed from patient's paper based records, electronic records and the hospital electronic record. Comparison made with patients receiving kidney transplant only matched by gender, age, ethnicity and date of transplant. We compared overall survival, graft survival and renal graft function between the two groups. Published liver transplant outcome from NHSBT was used as reference.

Results

20 patients received combined liver and kidney transplant between 2000 and 2015. The most common indication was Hyperoxaluria (25%) followed by Polycystic kidney and liver disease (20%). Eleven kidneys (55%) were transplanted pre-emptively.

One year overall survival for the CLKT group was 80% with 4 deaths within the first posttransplant year, and remained 80% after 5 years. All the deaths happened with functioning kidney graft. For kidney only transplant in the matched group 1 year and 5 year survival remained at 100% (.p=0.006) In the CLKT group 1yr and 5yr graft survival was 95% compared to kidney only group where this was 93% and 85% respectively (p=0.361). NHBT published data records 1 and 5 years survival after liver transplant as 92.1% and 78.8 % for our centre.

Discussion

Our data reflect an increased postoperative mortality in the patients receiving combined liver and kidney transplant. A majority of patients received preemptive kidney transplant in this group. A kidney transplant may have been added because of a favourable bias in the allocation of a kidney to these patients. Adding a second procedure may have contributed to increased mortality in this group. A lower kidney graft attrition rate (not significant) may reflect better quality graft allocated with CLKT. We propose a multicentre review of CLKT to confirm these results and review the policy based upon the findings of the study.

P074

Remote Ischaemic Preconditioning (RIPC) is feasible in liver transplant recipients but does not provide clinical benefit

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Introduction

Ischaemia Reperfusion (IR) injury is the injury that occurs when an organ's blood supply is interrupted and reconstituted. Remote Ischaemic Preconditioning (RIPC) has been shown to ameliorate liver IR injury in animal models. Its introduction into clinical practice has been limited. This study has investigated the feasibility of RIPC in a prospective controlled trial in liver transplant recipients

Methods

Patients selected for live transplantation were randomized to 3 cycles of 5 minutes lower limb ischaemia/reperfusion in the OR immediately prior to liver transplantation or a sham control (non inflated cuff).

Primary endpoints were patient recruitment and feasibility.

Secondary endpoints were 90 mortality and graft loss, aspartate transaminase (AST) levels on the 3rd post-operative day, ITU stay and incidence of post-operative haemo-filtration and infections.

Results

7 patients were unwilling to enroll and 4 were excluded secondary to minor peripheral disease. 40 patients (34M/6F) were randomised -20 RIPC/20 control. It was possible to perform RIPC in all patients randomized. No patient suffered a complication following RIPC.

Within 3 months, 1 patient died and 1 patient required re-transplantation – both in the control group. Median day 3 AST levels were non-significantly higher in the RIPC group (RIPC 260iU±298 vs control 251iU±322, p=0.926). There was no difference in ITU stay, haemo-filtration requirements or incidence of post-operative bacteraemias.

Conclusions

Liver transplant recipients are willing to undergo RIPC. Transplant logistics make trial completion a challenge. Conditioning does not cause harm to this patient group. Within this pilot no biochemical or clinical advantage to RIPC was demonstrated.

P075

Digital image, point of donation assessment of Steatosis using the Liver Image Quality (LIQu) score

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Introduction

Organ allocation and utilisation could be improved by a fast, reliable and quantitative point-of-use assay for donor liver steatosis. The required test should be able to be performed (i) at the retrieving hospital, (ii) outside normal working hours and (iii) without access to expensive capital equipment or highly skilled laboratory staff. It should fit within existing clinical practice and avoid significant inter-observer variation or subjective bias. Accordingly, we are developing an automated image analysis system to calibrate and quantify digital images of donor livers (taken with ordinary cameras and phones) with the aim of replicating expert visual assessment of steatosis.

Methods

A randomised set of 116 digital donor liver images from the National Organ Retrieval Imaging System (NORIS) database were independently scored for steatosis by two experienced surgeons using a 0-3 scale where 0 = good and 3 = poor. The digital images were then used as a 'training' dataset to identify predictive relationships between (i) readily measurable image analysis parameters and (ii) the surgeons' scores. Candidate image analysis parameters were combined into a single Liver Image Quality (LIQu) Score. A second randomised set of 94 images from the NORIS database (the 'test' dataset) was then independently scored by two surgeons and the software algorithm to validate the software algorithm.

Results

Consensus between the two surgeons' observations was judged as 'good' (Weighted Cohen's kappa test = 0.63) indicating that expert observers can make a consistent visual assessment of steatosis. With the 'training' dataset, liver images that the surgeons scored as <1 produced a computer score of 3.9 ± 4.1 ; images scored 1-2 by the surgeons produced a LIQu score of 47.8 ± 5.6 ; and images scored >2 by the surgeons produced a computer score of 87.4 ± 8.2 (mean \pm SEM). With the 'test' image group, images scored by the surgeon as 0 produced a LIQu score of 1.8 ± 5.4 ; score 1 matched a LIQu of 45.9 ± 7.7 ; score 2 matched LIQu score of 65.9 ± 5.9 ; and score 3 matched LIQu 93.4 ± 18.2 . The differences between all the groups were highly significant and the correlation between the surgeon and LIQu scores very good ($r^2 = 0.97$).

Discussion

These results suggest that it is possible to use quantitative image analysis to both assess images of donor liver for steatosis and mimic the scoring produced by expert observers. However, as the NORIS images had been acquired under non-standardised conditions (without calibration for ambient light intensity, colour balance, camera type, image resolution, magnification or framing of the specimen within the image) there was marked intra-group variation in the image analysis scores. Further validation work is underway using a simple LIQu kit to standardise image capture with biochemical measures of steatosis and clinical outcomes.

P076

Urinary Neutrophil Gelatinase-associated Lipocalin levels measured at abdominal closure accurately predict acute kidney injury post liver transplantation

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Introduction

The lack of early and accurate biomarkers of acute kidney injury (AKI) after liver transplantation has long impeded the prompt initiation of therapeutic measures before significant parenchymal injury has occurred. The diagnostic value of two promising biomarkers urinary neutrophil gelatinase-associated lipocalin (uNGAL) and albumin as early indicators of AKI in liver transplant recipients was examined.

Methods

Urine samples of 22 patients undergoing orthotopic liver transplantation were studied. Urinary NGAL and albumin were determined by ELISA pre-operatively, at abdominal closure and 24 hours post-operatively. The primary outcome was AKI defined by acute kidney injury network criteria (AKIN) within 48 hours of transplantation. The diagnostic value of these biomarkers was assessed using area under the receiver-operator characteristics curve (AUROC) analyses.

Results

12 patients developed AKI (54.5%). uNGAL was significantly raised in all post-operative time points compared to baseline values and peaked immediately post-operatively. uNGAL values measured at abdominal closure were significantly higher in patients with AKI ($p < 0.01$) as was urinary albumin at 24 hours post surgery ($p < 0.05$). The AUROC for uNGAL at abdominal closure was 0.867 (0.686-1). A cut off value of 411.66ng/mL gave a positive likelihood ratio of 9, a PPV of 90% and a NPV of 90%. The AUROC for albumin at 24 hours was 0.778 (0.540-1). A cut-off value of 39.97 mg/L respectively gave a positive likelihood ratio of 6.7, a PPV of 89%, and a NPV of 75%.

Conclusions

Urinary albumin and NGAL levels predict AKI post liver transplantation. UNGAL levels are a stronger and earlier predictor of AKI post transplantation than urinary albumin. uNGAL levels measured at abdominal closure may allow earlier supportive treatment to reduce the incidence of post operative AKI. A further large observational study is warranted.

P077

Factors causing delays in decision making in liver transplantation assessment and impact on patient outcomes

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Introduction

Liver transplantation assessment is a complex decision making process, which requires complex investigations and multidisciplinary decision making. Co-ordinating these and ensuring that they take place in a timely manner is important to (1) ensure patient satisfaction and confidence in decision making and (2) minimise unnecessary delay and thereby minimising morbidity and mortality in gravely ill patients. We sought to evaluate delays in the decision making process, their causes and the impact on patient outcomes.

Methods

Retrospective analysis of all liver transplantation assessments in 2014. Information was collected from clinical notes and electronic liver database. Data was analysed using t-test and Chi-squared, comparing those where an immediate decision was made to where there was a delay.

Results

A total of 323 liver transplantation assessments took place in 2014. A definitive decision at the time of first discussion in the multidisciplinary meeting was made in 229 patients (70.9%), and a delayed decision in 94 patients. The mean time from original discussion to final decision in those with a delay was 74 days (range 7-322 days).

The most common reasons for delay were cardiac investigations (38), review by another specialty (31), non-cardiac investigations (10) and monitoring of progress/exploring other treatment options (9).

There was no significant difference between those where there was an immediate or delay in decision making in terms of: outcome of listing meeting ($p=0.11$), transplantation and mortality on waiting list ($p=0.39$), and time to transplant ($p=0.26$). Of those in whom there was a delay, 67 (71.3%) were listed for transplant, 20 were declined and 5 (5.3%) died prior to a decision was made. 45 subsequently underwent liver transplant at a mean of 232 days after assessment.

Discussion

In the majority of patients an immediate decision regarding liver transplantation candidacy is made. However in those where there is a delay in reaching a final decision, this can constitute a significant time period and is associated with mortality before the decision is made. For those who are subsequently listed however, this does not appear to impact on mortality on the transplant waiting list or time to transplantation. The reason for delay is commonly awaiting further cardiac investigations or review by another specialty. A goal of transplant assessment services should be minimise the delay and ensure investigations and reviews take place in a timely manner, perhaps through risk assessment and pre-planned investigations prior to transplant assessment.

P078

The role of a national forum in determining suitability for intestinal and multi-visceral transplantation.

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Introduction

NASIT (National Adult Small Intestine Transplantation) is a national multi-disciplinary forum where patients being considered for an intestinal-containing graft can be discussed. This often includes patients with intestinal failure, but can also include other indications (for example, cirrhosis with extensive porto-mesenteric venous thrombosis where a liver transplant alone is not technically possible). NASIT is an opportunity to ensure a balanced discussion of all treatment options for this complex group of patients, with the benefit of experience and expertise of the members. The patients' needs and wishes remain at the core of all discussions. NASIT was founded in 1995 and today the core members include representatives from centres with appropriate intestinal failure and transplant experience. Each meeting is also open to referring teams to attend. The medical and surgical clinicians are joined by specialist nurses, dietitians, radiologists and trainees. It is a Department of Health requirement to have approval from NASIT prior to listing any adult patient for a small bowel or multi-visceral transplant. This article outlines the process of NASIT and demonstrates its individuality as a multidisciplinary forum.

Methods

This is a retrospective review of patients discussed at NASIT between January 2013 and September 2015. Minutes of the meetings and a central database were used to identify members present, the decisions made and the reasons for each decision.

Results

During the specified time period, 97 patients were discussed. Of these, 36 have been listed and transplanted, 5 are currently listed or awaiting listing. 2 other patients deteriorated on the list, were suspended and subsequently died. 15 patients are under surveillance for their condition and will be re-assessed in the future. 37 were deemed not suitable, 1 patient had no indication, 11 were deemed too high risk to proceed, 25 were treated via alternative means (for example, continuity surgery or interventional radiology to improve vascular access). 2 patients decided not to proceed to transplant.

Discussion

NASIT is an excellent example of collaborative working on a national scale. Intestinal and multi-visceral transplantation remains a complex procedure which is not without risk. The complex nature of this patient group means that a forum such as NASIT is essential to ensure the most appropriate outcome for each individual patient is achieved.

P079

Graft survival outcomes of DCD liver transplantation using organs declined by other UK centres

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Introduction

Aim of the study was to compare the graft survival of donors after cardiac death (DCD) livers, initially declined by other UK centres (imported) to those that had been institutionally allocated and utilised (local).

Methods

Retrospective analysis of prospectively collected data of DCD liver transplants performed at a single institute (2002-2015) and data provided by NHSBT for reason of organ decline. The graft survival of imported DCD was compared to local DCD livers. Survival analysis was performed using Kaplan Meier and survival compared using Log-Rank (Mantel-Cox) and Breslow models ($p < 0.1$) (IBM SPSS Statistics software v22).

Results

347 DCD liver transplants were performed during a 13-year period; 95 (27.4 %) grafts were imported. The main reported reasons for organ decline were donor-related (65%, $n=62$), no suitable recipient (15.7%, $n=15$), logistics (15%, $n=14$) and not stated (4.3%, $n=4$). Minimum follow-up was 8 months. 1, 3 and 5 year survival respectively for imported DCD grafts was 89%, 80 % and 75.4 % compared to local of 85%, 75% and 72.5 %. There was no difference in graft survival ($p= 0.263$, Breslow testing).

Conclusion

Imported DCD liver graft survival following decline by other UK transplanting units was not inferior to that of local DCD. The study suggests that UK DCD liver utilisation criteria should be revisited in order to standardise and optimise DCD liver usage.

P080

A worse Quality of Life (QoL) at 3 months post liver transplantation correlates with higher graft failure and mortality up to 2 years post- op in a cohort of UK patients

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Introduction

Lifestyle activity scores are used as an indicator for quality of life in annual follow-up assessments following liver transplantation. Whether the quality of life score at 3 months post transplant correlates with graft loss and patient survival remains to be elucidated.

Methods

Data was reviewed for patients undergoing liver transplantation between October 2007 and September 2014. Clinical data collected was recipient age, gender, UKELD scores, cold ischaemic time, type of graft (DCD and DBD only), graft failure, date of death and QoL score. QoL was grouped whether patients felt able to perform any kind of work or not. Chi Squared and linear regression models were performed on SPSS.

Results

459 patients 235M/219F/5 Unspecified identified. Patients with poorer QOL at 3 months had significantly higher chance of dying within 1 year (9.1% unable to work vs 1.1%, $p < 0.001$) and 2 years (10.6% vs 2.8%, $p = 0.002$). In addition, patients with worse quality of life scores at 3 months had higher chance of graft failure within 1 year (9.5% vs 1.1%, $p < 0.001$) and 2 years (10.6% vs 2.8%, $p = 0.002$) When adjusted for other transplant factors a poorer QoL at 3 months correlated with increased 1 and 2 year mortality ($p = 0.003$, $p = 0.005$) and 1 and 2 year graft loss ($p = 0.003$, $p = 0.004$)

Conclusions

A poorer quality of life at 3 months post transplant is associated with a higher risk of death and graft failure up to 2 years post transplantation and merits further investigation as an appropriate surrogate end-point in clinical trials.

P081

Transfusion requirements peri-operatively predict one year mortality following orthotopic liver transplantation while pre-operative anaemia does not.

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Introduction

Pre-operative anaemia and peri-operative transfusion requirements are associated with increased risk of mortality following many emergency and elective surgical procedures. In liver transplantation, there is a window to correct pre-operative anaemia and therefore this is key area of clinical concern.

Our aim was to investigate the association between pre-operative anaemia, peri-operative transfusion requirements and one-year mortality following liver transplantation in a single centre prospectively collated database.

Methods

Data was reviewed for patients undergoing liver transplantation between 1998 and 2012. Haemoglobin levels on the morning of the transplant were documented along with number of units transfused intra-operatively. Anaemia was calculated according to the WHO classification (Hb<13g/L for males and <12g/L for women). Values were adjusted for Recipient age, gender, cold ischaemic time and MELD score. Binary logistic regression and Mann Whitney U tests were performed on SPSS.

Results

793 patients (377M/416F) were identified. 216 patients died within the first year post transplantation of which 168 (78%) were anaemic. The median haemoglobin in patients that died was 10.6g/L vs 11.2g/L in patients that survived (p=0.002).

The mean number of transfused units in patients that died was 8 vs 4 in those that survived (p<0.001).

When adjusted for other transplant factors, number of units transfused peri-operatively correlated with 1 year mortality(p<0.001). Anaemia did not (p=0.894).

Conclusion

Pre-operative anaemia does not correlate with mortality in patients undergoing liver transplantation when adjusted for other transplant variables. This likely reflects the increased blood loss and complexity of operating in patients with end-stage liver failure.

P082

Increasing the donor pool for patients with fulminant liver failure by using donor rectus sheath fascia to enable greater donor recipient size mismatch

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Introduction

The only treatment option for patients with fulminant liver failure is super-urgent liver transplantation. There are occasions in which the urgency of the situation results in the use of livers from donors that may not be ideal. When particularly small recipients are listed super urgently for liver transplants their size becomes a significant limiting factor in the choice of donor. In our experience with multivisceral transplant recipients who often have a reduced abdominal domain, the use of donor rectus sheath fascia has been used to enable closure of the abdominal wall following transplantation. The use of this technique to enable size mismatch liver transplants has not been previously reported. We present a case using donor rectus sheath fascia to enable the use of a larger donor liver in a small patient with acute fulminant liver failure.

Methods

The donor procedure was performed via a midline incision (through skin and subcutaneous tissues) and then the rectus abdominus was excised in its entirety, including anterior and posterior sheath and peritoneum. It was then packed, as per a solid organ for transplantation, in UW solution and placed in an ice-box. The retrieval process allows closure (post organ retrieval) equivalent to a standard cadaveric retrieval. At the receipt hospital the rectus abdominus muscle belly was excised leaving the isolated rectus fascia and associated peritoneum. Following successful liver implantation, attempted primary closure of the abdomen resulted in increased ventilatory pressures. As a result the myofascial closure was augmented by insertion of the donor rectus sheath with continuous 2/0 prolene. The skin was primarily closed over this.

Results

A 19-year-old female patient with acute fulminant liver failure due to paracetamol overdose was super-urgently listed for transplantation. The recipient weight was 53.1kg and height 161cm; organs were accepted from a male donor weighing 75kg and height 186cm. The donor: recipient weight ratio was 1.41:1. The choice of a larger donor organ was made with a view to using donor rectus sheath fascia to facilitate abdominal wall closure. Post-operative recovery was unremarkable with no abdominal wall complications.

Discussion

We suggest that using rectus sheath fascia to facilitate closure post liver transplant allows for the use of larger livers in smaller recipients without the complications associated with compartment syndrome. This technique may increase the potential donor pool for super-urgently listed patients and reduce the chance of dying on the list or, enable earlier transplantation and the potential outcome benefits that this may bring. Of the multivisceral transplant patients in whom their abdominal wall has been closed using this technique we have not encountered any complications of this type of closure (n=5).

P083

The COPE project – research in organ preservation across six European countries

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Introduction

The transplant community is increasingly turning to deceased organ donors which previously would not have been considered suitable for transplantation, so called 'marginal' organ donors. However, the discard rate of organs from such compromised donors is extremely high and finding new ways of preserving them is crucial to ensure their safe and successful transplantation. COPE – Consortium for Organ Preservation in Europe - investigates organ preservation techniques including normothermic as well as oxygenated hypothermic machine perfusion in three multi-centre, international RCTs.

Methods

COPE started in January 2013 bringing together 14 partners across six European countries through an FP7 research grant. To investigate organ preservation techniques and their impact on marginal organs, COPE is running three RCTs across five countries comparing:

- Normothermic liver perfusion using the OrganOx *metra*[®] device with cold storage (liver trial)
- ECD kidneys reconditioned for a minimum of two hours with oxygenated hypothermic machine perfusion using the Kidney Assist[®] machine versus ECD kidneys transplanted after static cold storage (POMP trial)
- DCD kidneys of 50+ years preserved with oxygenated hypothermic machine versus hypothermic machine perfusion without oxygen using the Kidney Assist[®] device (COMPARE trial)

Based on these RCTs, COPE is gathering a consolidated biobank to identify biomarkers for organ quality assessment. Additionally, COPE is investigating new preservation solutions in hypothermic and normothermic perfusion in a pre-clinical setting using rat kidney and pig liver models.

Results

COPE's three RCTs are now recruiting across 5 direct project partners as well as 26 participating sites in the UK, Belgium, The Netherlands, Spain and Germany. The normothermic liver trial has passed its mid-way point in September 2015 and currently stands at 151 transplanted livers out of a target of 220 (as of 17/11/2015). The kidney trials show steady recruitment with 55 randomised kidneys in the POMP trial and 43 DCD 50+ donor pairs randomised in the COMPARE trial. Current design of sample collection includes several types of samples and tissues (blood, urine, liver and kidney tissue, bile duct tissue, perfusate and bile), several solutions or states for storage and assaying, and several time points across the donor and recipient surgeries.

Discussion

These developments and major progresses in trial implementation and sample collection enable a wide range of scientific questions with a total of 27 internal research proposals already received. The project team has accumulated a wealth of knowledge on complex trial logistics covering retrieval, organ allocation and transport as well as recipient transplant within the NHSBT and Eurotransplant framework. Logistical lessons learned as well as core research proposals focusing on proteomics; transcriptomics and metabolomics signatures in trial samples before, during and after machine perfusion will be described.

P084

Small airway disease in patients awaiting liver transplantation

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There are contradictory data on the existence of small airway involvement and tidal airway closure in liver disease (Funahashi et al, Thorax 1976; 31:303). Therefore, we set out to assess indices of small airway function in patients with end-stage liver disease awaiting liver transplantation.

We studied 51 consecutive, ambulatory, Caucasian patients (39 men) with end-stage liver disease, who were evaluated for liver transplantation. All of them were free from known history of concomitant pulmonary or any other disease and had (mean±SD): age=52±10, pack-years=23±24, FEV₁, %pred=96±18, FVC, %pred=103±18, DL_{CO}, %pred=76±18. Routine lung function testing, closing volume (CV), slope of the alveolar plateau ($\Delta N_2/L$), closing capacity (CC) and its alternative open capacity (OC) were measured. Flow limitation during tidal breathing was assessed with the negative expiratory pressure technique in upright and supine position.

The CV, %pred (119±62) was increased in 24/51 patients. Increase of the $\Delta N_2/L$, %pred (153±88) occurred in 29/51 patients. The CC, %pred (97±29) was increased in 10/51 patients. Measurement of the OC%pred (93±22), which was well performed by all patients studied, was decreased in 12/51 patients. Tidal airway closure was detected in 8 patients. Interestingly, none of the patients assessed was flow limited at rest.

In conclusion, there is an involvement of small airways and tidal airway closure in a minority of end stage liver disease patients awaiting transplantation. Flow limitation at rest was not detected in end stage liver disease patients.

P085

Bridging the gap to transplantation: Albumin dialysis versus plasma component exchange for chronic liver failure

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Introduction

National Institute for Clinical Excellence (2009) state the evidence on extracorporeal albumin dialysis for acute liver failure raises no major safety concerns. However, current evidence on its efficacy is inadequate in quality and quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

Patient A has a diagnosis of primary liver cirrhosis due to an auto-immune condition. Patient A has been treated on ITU receiving a 8 hour Single Pass Albumin Dialysis (SPAD) treatment for the past 3 years every 6 weeks, measurement of clinical outcomes for this treatment are symptom led.

Our objective is to implement a sustainable treatment within the renal ward to prevent an ITU admission; decrease symptoms experienced by Patient A and bridge the gap to transplantation.

Methods

In June 2015 the treatment of Patient A's condition was discussed with LINC medical who provide the renal unit with the HF440 for DFPP (Double filtration plasmapheresis). LINC proposed that Patient A could receive Plasma component exchange using the Evaclo filter. Evaclo is a plasma component exchange filter that removes small molecular weight proteins and large molecular weight water solutes. Education was provided and the treatment performed over a 4 hour period within the ward area as a day case. Pre and post blood results were taken for comparison, and no concerns were noted. Patient A was contacted weekly to assess symptoms and provide a comparison of health benefits between SPAD provided on ITU and SPAD provided using the Evaclo filter.

Results

Benefits to patient

- Treatment time halved
- Vascular access preservation
 - Reduction in blood product usage
- Nil fatigue
- Reduced impact on daily living

Benefits to Hospital Trust

- Nursing time reduced
 - Patient activity/flow within 24 hour period increased
- Provides more learning and education
- Overall cost saving of £616 per treatment

Discussion

Embedding PCE using the Evaclo filter within the ward area has demonstrated benefits for our patients in reduction of symptoms and enhancing quality of life, whilst bridging the gap between transplantation. This has benefitted the trust financially and provided nurse development and experience. This was done through education of staff from LINC Medical, discussion at clinical governance and multi-disciplinary team working. The next stage to development of the renal unit's plasma exchange/dialysis programme is to continue to expand the service. This will be achieved by presenting findings to the trusts executive board via a business plan. The renal unit will share positive clinical experiences with consultants in other specialities, where these treatment options available will be beneficial to other conditions.

P086

The use of alteplase in flow reconstitution in early hepatic artery thrombosis following liver transplantation

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Introduction

Since liver transplantation was introduced as a treatment for liver failure, hepatic artery thrombosis (HAT) has been a recognised complication. Occurring in just under 5% of orthotopic liver transplantations, it can increase the risk of morbidity, graft failure and mortality. Early HAT (within 2 months of transplantation) usually presents acutely with early graft dysfunction.

Methods

We present two cases in which reconstitution of arterial inflow were assisted by use of intra-arterial thrombolysis with Alteplase (Boehringer Ingelheim)(a recombinant tissue plasminogen activator).

Results

The two patients presented in this report were at increased risk of HAT, one having aberrant arterial anatomy and the other having had two prior transplantations. Both underwent the same management for the HAT – a thrombectomy using a Fogarty catheter followed by intra-arterial Alteplase.

Discussion

The HAT was discovered in both cases at the time of re-laparotomy following a challenging initial transplant. Both patients had early identification and management of the HAT. This is likely to have been a major contributor to the good observed outcome in both cases.

P087

Use of Transplant Adherence Questionnaire (TAQ) in UK transplant clinics: initial findings and recommendations for implementation

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Introduction

Maximising post-transplant patients' adherence to immunosuppressive therapies is critical to ensure successful transplantation outcomes. Optimal adherence requires life long commitment by the patient and substantial support from the healthcare team. Regular reviews of medication and adherence strategies are essential. Technical and psychological support enhances patient adherence.

Explaining the risks and consequences of non-adherence is challenging. The Transplant Adherence Questionnaire (TAQ) is an important tool to assess non-adherence; the results can be used to initiate a conversation about the patient's risk factors for non-adherence.

Methods

The transplant360 Task Force, a network of European transplantation healthcare professionals (<http://www.transplant360.com>), developed the TAQ, which is based on a validated self-report questionnaire (BAASIS). The patient completes the questionnaire whilst at the clinic, with or without help from a Nurse Specialist. The TAQ asks about the patient's medication schedule; how many doses of each medication were missed in the preceding 4 days; how many doses were not taken on schedule in the preceding 4 days; if special instructions (e.g. take with food) were followed; whether non-adherence is common at weekends; and if the patient had ever missed doses over the preceding 3 months.

Results

Nurse Specialists from 8 UK transplant centres offered the TAQ to patients. Data from 142 patients were collected and analysed. Most non-adherence was unintentional, due to the patient forgetting to take their dose(s), falling asleep, being busy or having their daily routine was disrupted. Patients need regular and consistent education so that they understand why they are taking medication and the risks of not adhering to their regimen. Ongoing psychological and technical support is essential to help patients take their medication on time. Adherence can vary over time, even in patients who have taken immunosuppressants long-term. Young adults are at special risk of non-adherence.

Discussion

The TAQ results proved very useful when discussing the risks of non-adherence to immunosuppressive therapies with post-transplant patients. It offered an objective way to discuss adherence with patients. Questions may be re-ordered and simplified. Recommendations for improving the accessibility and usability of the TAQ will be made.

A computerised version may be developed.

P088

Attitudes to living donation – the donor's perspective

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Introduction

The number of people choosing to donate a kidney for transplant to patients with kidney disease is increasing. Findings suggest living donors experience adverse consequences after the donation process. This study investigates a cohort of living donors' experience of donating a kidney.

Methods

A questionnaire survey sent by post to all 322 living donors receiving follow-up care from the Leeds renal transplant centre, assessing: demographic characteristics; decisional regret; decisional conflict (SURE); perceived knowledge, preparedness, and expectations of kidney donation; side-effects; knowledge of kidney patient before/ after process; quality of life (SF-12 QOL). Data were analysed using SPSS 23. Ethical approval was granted April 2015 (REC 15/SC/0238).

Results

Response rate was 50% (161/322); non-participants were younger than participants (mean years 48.2 ±12.3 versus 54.8 ±13.4; $p < 0.001$) and time since donation was 1 – 226 months (mean months 70.7 ±55.0 versus 71.5 ±57.1; NS). Participants were 53% female, 94% Caucasian, and 35% had up to 16 years of school education, 27% had additional vocational training, and 38% had additional formal education = 38%. Decisional regret was low (mean = 5.78; range 0-100) and 86% had no decisional conflict. About 48% felt they understood fully the issues of kidney disease and donation before their operation; 17% felt that the operation was worse than they expected, 21% felt the hospital stay was worse than expected, 11% experienced pain for a few months or more, and 12% felt their health deteriorated after donation. Currently, 91% rate their general health as good, with 21% feeling downhearted at least some of the time, and 11% feeling their physical and emotional health impacts on their social life at least some of the time. Comments provided suggest areas for improvement in staff training and information resources.

Discussion

The majority of our participants were sure they made the right decision to donate their kidney. A significant minority report an impact of the donation process on their wellbeing. This study provides evidence of the need for staff training and information to enable living donors to make informed decision about donation and support their well-being post recovery.

P089

Risk taking and decision making amongst live paired kidney transplant patients

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Introduction

The study explored risk taking and decision making amongst live kidney paired transplant (LKPT) recipients and their donor pairs and whether equity, justice and risk were reflected in this process. LKPT has contributed significantly to increasing the number of live donor kidney transplants and is associated with excellent clinical outcomes. However, little is known about decision making and risk taking amongst this cohort. At a time when patient centred care is driving global health policy, insight into these issues is crucial as a means to facilitating high quality decisions that articulate informed preferences amongst patients, their families and the transplant team.

Methods

Twenty LKPT recipients and their donors were subjected to a semi-structured interview. Data reduction to eliminate interview bias was performed on several levels through coding and categorisation to contrast with patterns, themes, decision making theory and empirical findings.

Results

Common to donor and recipient's decision making, was the constraining impact of renal disease upon the quality of the recipient's life, the ability to construct an identity of the unknown donor that was compatible with their own and disappointment (donors) and hesitation (recipients) regarding assimilated post-transplant living. The five overarching themes which impact upon LKPT recipient's decision making are as follows: restoration of health and well-being; recoup time lost to chronic illness; failure to reach age appropriate developmental milestones; experiences of fellow patients 'clinic friends'; altruistic goodwill towards a patient who needs a kidney transplant. The four overarching themes which impact upon LKPT donor's decision making are as follows: need to balance existing life commitments with the recipient's need for a kidney; equity in kidney exchange; justice for the recipient and risk (logistics of exchange and paired donor failing to donate).

Discussion

Donors and recipients follow different decision making pathways to participation in LKPT as highlighted by the themes identified above. An understanding of these pathways by the transplant team is the key to enhancing opportunities, addressing uncertainties and ensuring choices and actions are coherent, consistent, plausible and robust

P090

Poor HLA matching may reduce the beneficial effect of ABOi pairs entering the paired and pooled scheme

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Introduction

Paired/pooled donation (PPD) facilitates transplantation between UK donor-recipient pairs who are either HLA or blood group incompatible, in whom transplantation is either contraindicated or considered 'high risk'. In the current era, allograft survival in ABOi transplantation is comparable with ABOc. Chronic AMR remains the leading cause of allograft failure in ABOc grafts with the risk of de novo DSA and rejection depending upon the degree of HLA mismatch (MM). The aim of this study was to determine the impact of HLA mismatch on the outcomes of ABOi and living donor ABOc grafts. This in turn will help inform patients considering entering the PPD system with a well HLA matched but blood group incompatibility donor.

Methods

We performed a retrospective analysis of ABOi and ABOc grafts transplanted between 2005-2015. A low HLA MM was defined by a NHSBT MM level of 1 or 2, and a high MM as a level of 3 or 4. 55 high MM ABOi, 5 low MM ABOi, 428 high ABOc and 137 low ABOc were performed and all patients received a steroid sparing immunosuppressive protocol. Mean follow up was 5.3 ±2.8 yrs.

Results

Allograft outcomes are shown below.

| Event free survival | High ABOi | Low ABOi | High ABOc | Low ABOc | p value |
|---------------------|-----------|----------|-----------|----------|---------|
| Graft loss (GL) | 80.1% | 100.0% | 77.4% | 87.0% | 0.68 |
| Rejection | 60.5% | 100.0% | 69.6% | 87.6% | 0.0001 |
| AMR | 83.4% | 100.0% | 87.8% | 97.5% | 0.0088 |
| De novo DSA | 78.9% | 100.0% | 65.3% | 92.2% | 0.0001 |

The mean time to rejection was shorter in the high ABOi [0.97 (0.6-6.3) months] compared with the high ABOc [5.8 (4.4-7.8) months] group, p=0.0065. Directly comparing high ABOi with high ABOc grafts; overall rejection was increased [HR 1.72 (0.97-3.0), p=0.03], however there was no difference in GL [HR 0.77(0.36-1.68), p=0.48], AMR [HR 0.52 (0.21-1.30), p=0.07] and DSA risk [HR: 0.72 (0.40-1.32), p=0.35].

Discussion

Small numbers in the low ABOi group preclude statistical analysis however extrapolation from the low ABOc group suggest that low ABOi patients may have better outcomes than high ABOc grafts. It is therefore important when considering entering ABOi patients into the PPD that HLA mismatch requirements are stipulated if the original ABOi donor is well HLA matched, otherwise the ABOi recipient may be disadvantaged if they receive a poorly matched ABOc graft.

P091

Can Qrisk be useful to predict future cardiovascular co-morbidities and Type II Diabetes in living kidney donors prior to donation?

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Introduction

Living kidney donor transplantation has demonstrated significant survival benefits to individuals with End Stage Renal Disease (ESRD). However, Living kidney donation is associated with an increased risk of ESRD, although it is uncommon (1:500 to 1:3000). It also seems to increase the risk of Hypertension (HTN) (15-20 %), Gestational HTN and Preeclampsia. Long term cardiovascular risks associated with kidney donation are unclear.

Methods

Retrospective data was collected on Kidney donors (n=128) who underwent pre-Kidney donation assessment followed by Donor nephrectomy at Manchester Royal Infirmary between January 2009 to August 2014. Medical database and electronic case notes were used to collect the data on Gender, Age, Ethnicity, Smoking status, Body Mass Index, Lipid profile, Blood glucose and Isotopic GFR (Glomerular Filtration Rate). Data was also collected on Serum creatinine, Urine ACR and Blood pressure, both before and after surgery for a minimum of 1 year to maximum of 5 years. Both QDiabetes[®] diabetes and QRISK[®] 2-2015 Web Calculator were used to calculate the 10 year risk of developing Type 2 diabetes and cardiovascular event prior to donation.

Results

Among the cohort of 128 patients (m= 66, f=62), the mean age of donors was 45 ± 10 years. Majority of the donors (62%) were from 5th to 6th decade {n=13 (20-29 yrs), n= 27(30-39 yrs), n= 43(40-49 yrs), n=37(50-59 yrs), n=14(60-69 yrs.), n=2(70-79 yrs.)}. Most were Caucasians (83%). 42 % of the patients were overweight (BMI 25-30 Kg/m²) and 17 % were obese (BMI >30Kg/m²). 22.6% were smokers. Mean Body Mass Index (BMI) and cholesterol/HDL ratio were 27.34 ± 3.52, 4.08±1.49 in males and 25.80±3.6, 3.43±0.97 in females respectively. We used the QRISK2 tool to predict the 10 year risk of cardiovascular disease in donors. The mean Qrisk in men was 6.95% and 5.5% in women. 12.5% of donors had a Qrisk score of > 10% which is considered to be a trigger for intervention. These donors had a trend towards higher number of cardiovascular co-morbidities during follow up (hypertension, hypercholesterolemia) (p = 0.06). The QRISK figures were however lower than in the general population, which averages 8.66% in men and 6.57% in women. The mean Q risk scores for diabetes were 5.05% for men and 3.55% for women. This was again lower than the averages for the general population which are 6.12% (6.05-6.19) for men and 4.72% (4.66-4.78) for women.

Discussion

This study has demonstrated that QRISK for cardiovascular disease in living kidney transplant donors is generally lower than in the normal population. Donors with a QRISK of > 10% had more cardiovascular comorbidities recorded in follow up although no cardiovascular events were reported during this time frame. The QRISK for Diabetes was also lower than the general population. There were no new diagnoses of diabetes in these donors during the follow up period.

In conclusion calculation of the QRISK scores for diabetes and cardiovascular comorbidities may be useful in predicting the long term complications following living kidney donation. Donors with QRISK >10% should be considered for prophylactic interventions to reduce post donation cardiovascular risk. It also raises issues about the ethics of accepting donors at higher risk and how they should be cared for post donation.

P092

Are we declining the wrong kidneys?

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Introduction

The decision to accept or reject a deceased donor kidney offer is multi-factorial. Acceptance criteria vary between centres and this is related to the donor and potential recipient variables that can be difficult to define. Our study aims to analyse the outcomes of kidneys used elsewhere that were declined by our centre. Were we declining kidneys with subsequent good function?

Methods

A retrospective cohort study of all declined kidney offers from deceased donors made to our centre, between April 2014 and March 2015, were collected. We analysed the demographics, clinical data, type of offer, reason for declining and outcomes at other centres, where available.

Results

There were 77 declined offers from 52 (67.5%) DBD and 25 (32.5%) DCD donors. The donor male to female percentage ratio was 54.7:45.3. Mean age 54.3 years (range 1-82 years). The most common primary reasons for declining kidneys were donor past medical history (PMH) (33.8%), followed by poor function (PF) (32.5%) based on donor admission and/or retrieval creatinine, malignant concerns of donor (8.9%) and donor or donor-recipient age discrepancy (6.4%) . Median kidney donor risk index (KDRI) was 1.27 (range 0.64-2.73).

The offers to our centre were declined by a median of 6 other centres (range 0-12). 39/77 of our declined offers (50.6%) had at least 1 kidney accepted by other centres, these were declined by a median of 5 other centres (range 0-11) prior to acceptance. At 3 month follow up, 22/39 (56.4%) kidneys had a creatinine \leq 150 (57-150), 8/39 (20.5%) kidneys had a creatinine $>$ 150 (151-906) and 9/39 (23.1%) had no available results. Excluding the kidneys with unknown results, 9/11 kidneys (81.8%) declined by our centre for PMH and 5/9 (55.6%) of kidneys declined for PF were working at 3 months of follow-up with a creatinine \leq 150.

Discussion

Our sample size is small but this limited audit shows that we are declining some kidneys that have good early function at other centres. An internal review of acceptance criteria is ongoing. This review, with longer term follow up of declined kidney outcomes in other centres, will inform our future acceptance criteria.

However, it is important to note that during the study period, we have transplanted kidneys in our own unit that have resulted in creatinines $>$ 150 that have similar demographics to kidneys we have declined. We must not forget that there is a recipient at the end of a renal transplant, and for some patients and their nephrologists, a 50% risk of a creatinine at 3/12 being $>$ 150 when the donor has PF, is too great. This is not true for all, and patient preference, health on the waiting list and choice should always be part of any decision to accept or decline a kidney.

P093

Altruistic kidney donation: the donor's perspective

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Introduction

Although all living kidney donors are offered yearly reviews post-transplant, the restricted contact time and medical focus limits understanding of the motives and experiences of the subset who donate altruistically. We surveyed all altruistic kidney donors at one centre, to better understand what leads people to donate in this way, their satisfaction with the process, and how best to support them before and after donation.

Methods

A 10 question survey was posted out to all altruistic kidney donors (n=35) whose donation took place at one renal transplant unit since 2006. Respondents could choose to reply by post or online. The survey used 5-point Likert scales to cover satisfaction with outcome, the standard of care received before and after transplant, and the influence of donation on wellbeing and relationships. Free text responses were sought to describe motivations, what improvements to care could be made, what contact they received from the recipient and how they felt about this contact or lack of it.

Results

We received to date 19 responses, (54% response rate). Explicitly altruistic motivations were commonly reported, with 74% of respondents stating that they wanted to help, be of use or do some good for the life of another. Respondents were unanimous in declaring no regrets about donation. All respondents rated highly the care they received before donation transplant, although 35% thought they could have been better supported by the transplant team post-transplant. 63% of donors received contact from the recipient, which made a substantial positive impact. Of those who received no such contact, 50% were disappointed and 83% stated that they would like to know if the recipient was happy and well. None received information concerning transplant rejection or failure. All respondents considered donation to have either improved their wellbeing to some extent, or to have made no overall difference.

Discussion

It is encouraging that none of the donors regretted the decision to donate, nor did any consider the donation to have influenced their wellbeing in a negative way. The positive impact of receiving contact from the recipient was noted by all individuals in this position, and has implications for the advice given to recipients of altruistically donated kidneys. The expectations of post-donation care may well have differed between individuals, accounting for some differences in the perception of the standard of this care, but the reasons for this should be explored further.

P094

Psychological benefits of transplantation versus Haemodialysis

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Introduction

Over recent years there has been an increasing reliance on expanded criteria deceased donor kidneys for transplantation, yet their use remains controversial. The aim of this study was to determine whether there were differences in psychological and health-related quality of life outcomes between haemodialysis patients and transplant recipients.

Methods

Haemodialysis patients (HDx) and Recipients (Rx) from our 2014 cohort were asked to complete a questionnaire within 12m of their transplant. Transplant patients were subdivided into living donor recipients (LTx) and standard (STx) and expanded criteria deceased donor recipients (ETx). The questionnaire included validated measures of life satisfaction, mood, distress and health-related quality of life (HRQoL).

Results

248 questionnaires were completed (98 HDx vs. 150 Rx (26 LTx, 59 STx and 58 ETx)). There was a significant difference in age between HDx and Rx patients (58.4 vs. 53.4 yrs; $p=0.016$) and between the STx and ETx groups (48.6 vs. 59.0 yrs; $p<0.001$). Life-satisfaction and mood were significantly lower in HDx patients when compared to Rx patients (15.0 vs. 24.0; $p<0.001$; 2.0 vs. 0.0; $p<0.001$ respectively). There was no significant difference between deceased donor and living donor kidney recipients (23.0 vs. 26.0; $p=0.287$; 0.0 vs. 0.5; $p=0.747$ respectively) or between STx and ETx groups (24.0 vs. 21.0; $p=0.050$ and 0.0 vs. 0.0; $p=0.405$ respectively). Distress was significantly higher in HDx patients when compared to Rx patients (14.0 vs. 12.0; $p=0.001$). HRQoL was significantly lower in HDx patients (33.0 vs. 40.0; $p<0.001$). There was no difference in distress or HRQoL between deceased donor and living donor kidney recipients (12.0 vs. 9.0; $p=0.893$; 39.0 vs. 45.5; $p=0.094$ respectively) or between the STx and ETx groups (12.0 vs. 12.0; 39.9 vs. 38.1; $p=0.356$ respectively).

Discussion

This study has demonstrated that transplantation conveys a psychological and health-related quality of life advantage over remaining on dialysis, regardless of whether the transplant is from a living donor, or from a standard or expanded criteria deceased donor. There are no significant differences in outcome between recipients of living donor and deceased donor kidneys. The positive findings from this study, in addition to favourable graft and patient survival outcomes, further endorse the use of expanded criteria deceased donor kidneys.

P095

Psychological benefits after living donor kidney transplantation

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Introduction

Living donor kidney transplantation remains the gold standard treatment for end-stage renal failure. There is an assumption amongst the transplant community that the physical benefits are met with a corresponding psychological benefit, however there is very little within the recent literature that has focussed specifically on quantifying this. The aim of this study was to measure how recipients of living donor kidney transplants benefit psychosocially from transplantation.

Methods

A sample of living kidney donor recipients were asked to complete a questionnaire at 3 different time points: pre-operatively and 3 and 12 months after transplantation. The questionnaire contained validated measures of wellbeing, distress, mood, stress, health-related quality of life (HRQoL), life satisfaction, self-esteem and anxiety.

Results

51 recipients participated in the study (mean age: 42.9yrs, SD 14.7). Wellbeing, distress and HRQoL scores all improved significantly over the first year after transplantation ($p < 0.001$, $p < 0.001$ and $p = 0.001$, respectively). For each measure the significant difference occurred between pre-operative and 3 month scores. Very little change was demonstrated between 3 and 12 months ($p > 0.05$ for all measures). Mood scores steadily improved over the 3 time points (2.0 vs. 1.0 vs. 0.0; $p = 0.037$). Stress, anxiety, life-satisfaction and self-esteem scores did not improve significantly over the first year after transplantation ($p = 0.368$; $p = 0.096$; $p = 0.105$; $p = 0.396$, respectively). There was no difference in outcomes between those who were on dialysis prior to transplantation and those who were transplanted pre-emptively.

Discussion

This study has demonstrated that benefit following kidney transplantation is quantifiable by improvements in wellbeing, distress, HRQoL and mood. Stress, anxiety, life-satisfaction and self-esteem scores do not improve. This may reflect the ongoing burden of chronic illness, such as multiple hospital visits, reliance on medications and the threat of complications and transplant failure.

P096

Comparison of baseline proteinuria and short and long term outcomes in live kidney donors – 10 year U.K cohort study

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Introduction

Living kidney donation has significantly improved recipient and graft survival world wide. With a move to increase these numbers further, it becomes mandatory to have a better understanding of the long term outcomes and risks of kidney donation.

Aim

Baseline proteinuria and short and long term outcomes in live kidney donors.

Methods

National Health Service and Blood and Transplant, U.K (NHSBT), obtains informed consent from all patients undergoing a transplant in the UK for continuing data collection and subsequent analyses. The study protocol was reviewed and passed by the Renal Registry (RR) projects advisory group, UK. From January 1, 2001 until December 31, 2013 inclusive, all live kidney donors were included in the study. No formal sample size estimate was produced for the study; all eligible patients records were used. December 31, 2014 was considered the study end, meaning that all patients had at least one year of follow-up. Datasets, based on regular returns from individual transplant centres across the UK, were obtained from NHSBT.

Results

There were 9750 donor records available. Out of which 9500 donors were tested for proteinuria at baseline. 8858 had no evidence. 437 had trace, 182 had 1+, 18 had 2+ and 5 had 3+ proteinuria. There were no significant relationships between baseline proteinuria and 1, 5 and 10 year mortality and morbidity outcomes.

Multiple logistic regression models adjusted for age and sex was used to analyse baseline comorbidities and proteinuria at 1 year. The baseline comorbidities analysed were gender, ethnicity, GFR risk groups (1. meeting the recommended levels. 2. up to 5 mls/min/m² less than the recommended levels and 3. more than 5 mls/min/m² less than the recommended levels), different BMI bands, BMI <18.5, 18.5 -<25, 25-<30, 30-<35, 35-<40, 40+, cardiovascular disease, kidney stones or renal mention, microscopic haematuria, hypertension, diabetes, depression, asthma, hypercholesterolemia and any morbidity.

Proteinuria was more prevalent and statistically significant in male donors (P=0.012). Ethnicity was of borderline significance, with white ethnicity having less frequent proteinuria (P=0.052). BMI bands suggested a trend towards an increase in frequency of proteinuria as BMI increased (P=0.037); Higher proportion of kidney mention patients had proteinuria at 1 year and this was statistically significant (P=0.031). Patients with any baseline morbidity were more likely to have proteinuria (P=0.009).

Conclusion

Baseline proteinuria did not have significant association with morbidity or mortality at 1 year. However, certain baseline comorbidities were significantly associated with proteinuria at 1 year.

P097

Living kidney donation - donor perspective

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Introduction

Living Kidney donation is an important source of organs in most transplant centres. Positive experience of the donor in the whole process is a key element in the success of any transplant programme. Laparoscopic kidney donation was introduced in our centre in 2009 and at the time of the study 129 operations had been performed.

Methods

Postal questionnaire was sent out to 129 donors. The questionnaire consisted of 2 components – personal information and service information.

Results

78 out of 129 donors (60.5%) answered to the survey. The mean age of the responders was 53.8 years old (range 20 to 83 years). 64.8% of female and 54.7% of male donors answered to the questionnaire. 59% of donors who responded were in full or part time employment. 22/78 donors were retired. 44/78 donors came forward as a result of information from the Renal Unit (23) and the media (21). 24/78 donors were non-directed altruistic. 98.7% of responders were satisfied with the information we provided. All had a chance to ask more questions. 27 donors met with patients who had donated kidneys in the past and the majority found it useful. 32/78 donors had between 6-10 visits to hospital before donation. After donation 67/78 donors felt as fit as they were before donation. Mean time for going back to work was 40.7 days. 34/78 donors felt that there should be more financial support for donors. 69/78 would recommend a friend or family member to donate a kidney. Almost all responders scored the individual aspects of the process 9-10 out of 10. Overall experience of kidney donation was scored 9.4 out of 10. Psychological or psychiatric assessment was not popular among donors.

Discussion

The study allowed us to evaluate our service from the donor's perspective. Less visits to hospital and some help with financial loss and travel costs is expected by some. Donor satisfaction, education from the Renal Unit and media involvement are important for increasing donor numbers as experienced in our Unit.

P098

Giving a kidney but getting a problem? Outcomes for living donors at least 20 years after donation

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Introduction

There has been a 700% increase in the annual number of living kidney donors (LD) in our region in the past 5 years. As the demand for living kidney donors increases, concerns have been raised regarding the long-term outcomes of these individuals. Prior to 2010 there were relatively few donors resulting in a paucity of data available for our growing prevalent donor population. We reviewed the outcomes of all the living donors in our region who donated at least 20 years ago.

Methods

The Renal Transplant Database has prospectively recorded all transplant procedures and outcomes for every transplant that has taken place in our centre since 1961. LD transplant recipients from 1961-1995 inclusive were identified. The electronic care record was interrogated for those for whom donor details were available. Recorded data included demographics, alive or deceased, (if deceased the date and cause of death), any medical record of cardiovascular disease, hypertension, diabetes, and renal disease.

Results

During this time period 743 transplants were performed with 58 (8%) from living donors. 33 (57%) of the donors were male. Mean age at donation was 42 yr. (range 17-65 yr.). Follow-up ranged from 20-50 yr.

Initial review identified 13 of these donors. The majority (10/13) are alive, current mean age is 65 yr. (range 43-84yr.). The age at death of the 3 donors who died was between 72 yr. and 81 yr. The time since donation ranged from 22 yr. to 50 yr. The causes of death were lung malignancy and pneumonia. 6 of the 13 donors had documented hypertension and the majority of patients required at least 2 antihypertensive agents. Approximate onset of hypertension could be identified in half of these patients having occurred between 16 and 25 yr. post donation. 3 patients had documented cerebrovascular disease, 2 had suffered probable type 2 myocardial infarctions, and 4 developed Type 2 diabetes mellitus. 11/13 patients had renal function results available within the past 5 years, none had an eGFR below 40 mls/min/1.73m², (7 had an eGFR \geq 60 ml/min/1.73m² and 4 an eGFR 40-59 mls/min/1.73m²). None had persistent proteinuria. One donor required a short period of haemodialysis during an episode of sepsis-induced multi-organ failure but subsequently recovered independent renal function.

Discussion

Long-term renal outcomes for the living kidney donor population in our region are excellent, despite hypertension, (typically developing beyond 15 yr. after donation), being common. Further evaluation of the complete donor population is required to provide more accurate information for the informed consent and selection of potential donors.

P099

Living donor kidney transplantation: Reasons for cancellation and potential prevention strategies

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Introduction

Living Donor Kidney Transplantation (LDKT) enables timely and pre-emptive transplantation and results in both patient and graft survival benefits compared to those receiving deceased donor organs or remaining on dialysis. Last minute LDKT cancellations result in missed pre-emptive opportunities, delays in transplantation and patient anxiety.

The purpose of this study was to identify patients who had a cancelled LDKT between 2002-2015, perform root cause analysis and devise strategies to prevent avoidable cancellations.

Methods

We performed a retrospective review of LDKT in our unit with analysis made of number and cause of cancelled procedures. Causes were then grouped into three categories: Recipient Issues, Donor Issues and Resource Issues. Time to transplantation following cancellation was also collected.

Results

We identified 115 cancelled LDKT operations over a 13 year period. We present data on an initial 48 patients with the remaining 67, those referred in from satellite units for transplant, not yet reviewed. 58% of the sample was male, 42% female and 13% planned preemptive transplants. The majority (84%) of cancellations were due to recipient issues with donor related 12% and hospital resource 4%. Reasons for cancellation amongst recipients included acute infection (36%), medical complications including hypertension and anaemia (32%), positive crossmatch (12%), personal issues (2%) and anaesthetic concerns (2%). Following cancellation 46/48 (96%) patients were successfully transplanted at a later date with a median time to retransplant of 81 days. The time from initial cancellation to transplantation was greatest in the recipient issues group at 147 days compared to 26 days for the donor issues group and 20 days for the resource issues group.

Discussion

Approximately 10/48 (21%) cancellations were felt to be avoidable eg anaemia in a dialysis patient. Strategies to ensure that improved timely surveillance and optimization of recipients occurs in the period prior to transplantation are needed. Education and strategies for recipients to self-monitor their health and clinical status and report illness or concerns could be developed.

Students for organ donation: Taking the message to the students by the students

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Introduction

The increasing shortfall of donors to patients on the waiting list continues to be the main focus of the transplant community. A targeted approach is required to raise awareness and recruit potential donors. The student population is well represented in Manchester and our research revealed that students are ill informed about organ donation and that many had not formed an opinion. A new society was born in Manchester to focus on this target group. The aims were to: educate about organ failure, raise awareness of the need for donors and empower individuals to be proactive.

Methods

Two medical students were inspired to act by a placement at the Renal Transplant Unit at the MRI . Through collaboration with transplant surgeons at Manchester Royal Infirmary (MRI) and funding support from the University and NHSBT has enabled the launch of “Students For Organ Donation” (SFOD) starting in the academic year of 2014-2015. The society was founded by students, will be led by students and will be guided by the experts, with the intention that the need for organ donation will be taken on and propagated by the student population. Publicity for the society was achieved through the University’s portal system and social networking with 150 members . A 14 member organising committee was divided into sub groups. Transplant surgeons and specialist nurses carried out training through open lectures and focussed tutorials for the committee. A unique brand and logo was designed to feature on publications, merchandise and social media. In September 2014 a stand at the fresher’s fair increased recruitment further and helped introduce the society to the 600 attendees. NHSBT provided merchandise including key rings, pens, leaflets and stickers and were incorporated into welcome packs. University funding and support helped to hold a further well-attended event in October. This educational and emotional evening consisted of talks from surgeons, donor families and a transplant recipient The society has also collaborated with the University “Scalpel” group to hold a lecture on kidney and pancreas transplant. The society is currently working on an open student debate event and a ‘going into schools’ initiative.

Result

Over the past year the society has: received formal endorsement from NHSBT, grown in number of members. attained a large social media following, been invited to speak at the national NHSBT meeting and helped to recognise the need for focussed strategy in the cause for raising awareness. The initiative to take the message to schools has led to the formation of a specialist steering group to plan visiting high schools and colleges in the region

Discussion

This novel, student led, society has achieved significant steps in raising awareness about organ donation in a short period of time and through the support of MRI, NHSBT and the University have great aspirations for the future.

Better the donor you know? A qualitative study of renal patient attitudes to 'Altruistic' live-donor kidney transplantation

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In the UK there is a short-fall between individuals requiring a renal transplant and kidneys available for transplantation. Non-directed 'altruistic' living kidney donation has emerged as a strategy for bridging this gap between supply and demand, with the number of non-directed living kidney donations increasing each year. This study aimed to explore the attitudes of potential recipients to non-directed 'altruistic' live-donor kidney transplantation.

Semi-structured interviews with 32 UK deceased-donor kidney transplant recipients were performed between February 2014 and July 2015. Interviews explored attitudes to directed and non-directed live-donor kidney transplantation. Interviews were recorded, transcribed verbatim and anonymised. Transcripts were analysed using the constant comparison method.

Individuals could be categorised into four mutually exclusive groups according to their attitude to receiving a non-directed 'altruistic' live-donor kidney transplant (LDKT):

- i) those willing to accept a LDKT from any living donor,
- ii) those willing to accept a specified directed LDKT only,
- iii) those willing to accept a non-directed 'altruistic' LDKT only, and
- iv) those not willing to accept an LDKT from any type of live-donor.

For those not willing to accept a non-directed 'altruistic' LDKT, the following themes were identified:

- i) Prioritising other recipients above self;
- ii) Fear of acquiring an unknown donor's characteristics, and
- iii) Concern for the donor – unnecessary risk. Gaps in knowledge about non-directed living kidney donation also emerged. For those willing to accept a non-directed 'altruistic' LDKT live-donor transplant the following themes were identified:

- i) Prioritising known above unknown persons;
- ii) Belief that they are as deserving as other potential recipients, and
- iii) Advantages of a LDKT.

Barriers and facilitators affect recipients' willingness to accept a non-directed 'altruistic' LDKT. These insights provide the transplant community with targets for intervention, through which concerns of potential recipients might be addressed.

P102

Are living kidney donors happy? A comparison with the UK population

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Introduction

With the rising number of successful Living Donor Kidney Transplants being carried out, there has been growing interest in understanding the well-being of live donors. This study aims to measure living kidney donor well-being and compare it to the UK population.

Methods

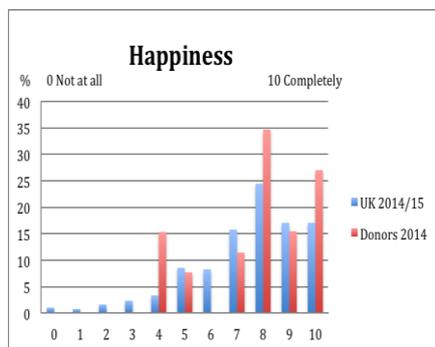
Living kidney donors (LDx) from our centre from January 2014 to December 2014 were requested to complete a well-being questionnaire in October 2015. The questionnaire included an assessment of life satisfaction, happiness, anxiety and whether life is worthwhile. These are the same questions included in the Integrated Household Survey by the Prime Minister to assess the nation's happiness in 2011*.

Results

26 questionnaires were successfully returned and completed. The average age for Donors was 51.1 years with a range from 21 years to 68 years. 15 of the Donors were female and 11 were male. 23 Donors were white. 1 was black. 1 was Chinese/oriental. 1 was defined as other. The mean score for life satisfaction was 8.54 (SD1.77), for Happiness 8.19 (SD 1.65), for Anxiety 2.96 (3.19) and for feeling that things are Worthwhile 8.38 (SD 1.66). The scores for the UK were 7.6, 7.5, 2.9 and 7.8 respectively. Life satisfaction and happiness were significantly different between the groups (P=0.012 and 0.042 respectively) where as Anxiety and feeling things are Worthwhile were not (P=0.923 and 0.087 respectively)

Discussion

Even though the sample was small, the results from this study indicated that living donors have a better life satisfaction and happiness score than the UK population.



*<http://www.ons.gov.uk/ons/rel/wellbeing/measuring-national-well-being/index.html>

P103

Young recipients receiving kidneys from older donors have poorer allograft outcomes

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Introduction

An increasing number of marginal donors are being used in order to expand the donor pool. Age is one of the major criteria in defining 'extended criteria'. In terms of allograft life-years, aged match kidneys ie old donors to old recipients may be highly appropriate, however in younger patients, receiving a kidney from an older donor may result in premature graft failure and the risk of requiring retransplantation, this compounds the waitlist number and on an individual level makes allocation more difficult in the setting of sensitisation from the failed allograft.

Methods

The aim of this study is to determine the allograft outcomes of young recipients (YR) receiving a transplant from an old (OD) versus a young (YD) deceased donor. 60 years old was defined as old in both donors and recipients.

Results

417 YD (Mean age: 42.2±13.1) were transplanted into YR (Mean age: 43.6±10.5); 115 OD (66.4±4.3) were transplanted into YR (50.6±7.8). Mean follow up is 4.67 ±2.20. Allograft outcomes are shown below.

| Event | HR (95 % CI) Old v young donors in young recipients | p value |
|-------------------------|---|---------|
| Patient survival | 2.14 (1.01-4.51) | 0.015 |
| All graft loss (GL) | 2.65 (1.43-4.93) | 0.0001 |
| DWFG | 2.46 (0.95-6.41) | 0.018 |
| Death censored GL | 2.60 (1.54-4.36) | 0.0001 |
| Rejection free survival | 0.58 (0.38-0.89) | 0.033 |

Mean eGFR at 1 year and 5 years in the YD to YR group was 57.0(44.7-73.24) and 53.22(39.6-67.5) compared with 40.8(32.7-53.6), p<0.0001 and 38.6(25.1-60.5), p=0.01 in the OD to YR groups. A further analysis showed no difference in all GL [HR: 0.90(0.6-1.5), p=0.69], DWFG [HR: 1.67(0.8-3.7), p=0.20], death censored allograft survival [HR: 0.59(0.3-1.1), p=0.12] and rejection [HR: 1.23(0.6-2.4), p=0.54] in YD into OR when compared with OD into YR pairs

Discussion

Donor organ quality needs to be taken into consideration during the acceptance and informed consent process for young recipients who are more likely to require a functioning allograft for a longer period than older recipients.

P104

Patient empowerment: driving a service forward

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Introduction

As healthcare professionals we strive to promote patient centred services. In practice this can be challenging to both develop and deliver. This poster describes how active listening and patient engagement has driven the development of an interactive patient forum for pre and post pancreas transplant recipients, families and carers.

Methods

Direct patient feedback expressed a need for peer support, answers to real time questions, and help in addressing feelings of uncertainty and isolation for individuals undergoing pancreas transplantation. A simple scoping exercise involving post-transplant pancreas recipients confirmed that significant numbers of individuals agreed these feelings and needs were real and under supported. With patient engagement we established Pancreas recipient seminars, supplemented by facilitating access to certain forms of social media.

Results

To date a total of 150 individuals have, by invitation, attended three pancreas seminars. The seminars were evaluated positively via a questionnaire, with requests for more such seminars and increased access to social media cited as the way forward. Many others are now accessing a Facebook page established by patients for patients, family and carers.

Discussion

Whilst health care professionals can provide information, support and guidance to pre-transplant patients, the seminars highlighted the value of an additional forum where patients can explore their feelings, questions and expectations with others going through a similar experience. This ability to meet and chat with fellow patients and receive information and education from the MDT as a group, provides not only a better understanding, but a greater feeling of support and solidarity through shared experience and the chance to chat about the positive and negative aspects of pancreas transplantation.

While the evolution of a Facebook page created by and for patients awaiting a kidney pancreas transplant undoubtedly has great benefits, as health care professionals we need to retain awareness of the unintended consequences of relying solely on social media as the main conduit for patients to share with one another. Through facilitating the seminars, we are able to influence the information exchanged between patients, to make sure it was medically accurate, and does not propagate misleading generalisations or assumptions.

A challenge we experienced as health care professionals was conveying empathy and responsiveness to the needs of our patients while keeping professional boundaries clear in the less formal, non-clinical environment.

An unexpected outcome of this patient engagement process was that of empowering individuals choosing pancreas transplantation to re-visit their decision in a relaxed non-threatening environment. For a couple of individuals, this opportunity resulted in a decision not to proceed to transplant, for others a decision to change direction and explore living kidney donation, but for the majority they maintained their decision that this type of transplant was what they wanted.

P105

Living donor kidney transplant as an option in a patient with Type 1 diabetes mellitus with malignant melanoma considered ineligible for simultaneous kidney and pancreas transplant: an ethical dilemma

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Introduction

Melanoma is a high-risk skin cancer which is considered a contraindication to solid organ transplantation due to risk of recurrence or metastases with post-transplant immunosuppression. Melanoma is becoming increasingly common in the UK in all age groups and is likely to pose an increasingly common dilemma for transplant specialists in the allocation of scarce allografts.

Methods

This case involves a 53 year old Caucasian, fit man awaiting a spontaneous pancreas and kidney (SPK) transplant for type 1 diabetes. The patient was haemodialysis-dependent, but had poor dialysis clearance despite optimisation so transplant was considered the best option. This patient developed stage IIb melanoma was suspended him from the transplant register for 5 years. The patient challenged this decision – as the 10 year survival rate on dialysis currently stands at 50%, statistically a 55% chance of survival at 10 years from melanoma (without immunosuppression) was possibly in the patient's favour.

Results

Due to the unusual nature of this case, the patient is currently being evaluated for a live-related single kidney transplant. Theoretically, this should reduce the dose of immunosuppression required, reducing the risk of melanoma recurrence and/or metastases. He could then be reconsidered for a pancreas transplant in 5 years. This would also eliminate the risk of potential organ wastage from the national donation registry.

Discussion

There is a significant gap in knowledge of the prognosis of pre-transplant melanoma, making it very difficult for clinicians to accurately predict prognosis for individual patients. This case demonstrates an example of the ethical dilemmas faced when transplantation is contraindicated due to melanoma, but would potentially be life-prolonging when compared to dialysis in a patient who is fully educated about the risk involved.

Lessons from Lanarkshire: Requirement and validity of consent in deceased organ donation and transplantation

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In the context of deceased organ donation, the requirement for consent and the validity of consent are easily confused. Requirement concerns the circumstances in which consent must be given and the individuals who are qualified to give it. Validity concerns the nature of consent and the elements which are necessary for it to be lawful. Requirement is largely governed by legislation. Validity is exclusively a matter of common law.

Recent interpretations of both are significant for all involved in organ donation and transplantation.

- (a) Requirement. 'Appropriate consent/authorisation' by, or on behalf of, a deceased donor under the Human Tissue Acts is well- understood in connection with organ donation, but is also essential for aspects of research related to 'relevant material'/ 'parts of the body' removed from such donors. Considerable uncertainty and difficulty has surrounded the application of donor consent to research projects aimed at improving outcomes for transplant recipients, particularly early interventions designed to maintain organ viability. It is now becoming clear that such research projects, being part of the clinical process of transplantation, are not within the scope of the Human Tissue Acts and are thus not subject to the requirement of donor consent, once appropriate consent to organ donation has been given. This applies even if such interventions occur before removal of the organ.
- (b) Validity. The validity of all forms of consent will be affected by the recent landmark judgment of the UK Supreme court in *Montgomery v Lanarkshire Health Board (Scotland)*. This confirms that, for consent to medical treatment to be valid, it is no longer sufficient for the decision as to disclosure information to a patient to depend on medical judgment. Autonomy requires that the patient must be in a position to decide personally what is material to. The 'materiality' test is that, for consent to be valid, a reasonable person in the patient's position must have been made aware of any specific material risks to which he or she would be likely to attach significance and of any reasonable alternative or variant treatments. The doctor should also be reasonably aware that a particular patient should attach significance to such risks.

In this paper we discuss the reasoning behind these important recent developments and their possible implications for organ donation and transplantation. While recipient-related research will benefit from current interpretation of the Human Tissue Acts, the materiality test will impose an obligation to ensure, in all forms of consent, that it is sufficiently well-informed to satisfy the law. This may prompt the need to reconsider how consent can be made valid in every case and is likely to have effects on clinical practice which may not be beneficial for organ donation and transplantation.

P107

UK renal patient attitudes to 'Transplant Candidate Advocates' as an intervention to increase uptake of living kidney transplantation: a qualitative study

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A reluctance to ask friends and relatives to consider living donation is a barrier to live-donor kidney transplantation for many potential recipients. One way to overcome this is through the use of 'Transplant Candidate Advocates' (TCAs): individuals (for example, healthcare professionals, previous donors, existing transplant recipients) to advocate for a renal patient awaiting transplantation, discussing living donation with potential donors on the transplant candidate's behalf. In the USA 'live donor champions' have been successfully piloted, whereby a friend, family member, or community member advocates for the candidate. We aimed to understand the attitudes of UK renal patients towards the use of advocates, prior to a possible trial of their use.

Semi-structured interviews with 32 UK deceased-donor transplant recipients were performed and analysed using thematic analysis. Participants were purposively sampled as individuals who had not received live-donor kidney transplants, and therefore were most likely to be the target group for TCAs, but had received deceased-donor transplants and had therefore been fit for transplantation. Participants were selected to differ in age, gender, ethnicity, primary renal disease, socioeconomic position and previous renal replacement therapy. Interviews explored attitudes to the proposed use of TCAs.

For those who felt TCAs might be helpful the following themes arose:

- i) National identity – overcoming perceived 'Britishness';
- ii) Professionals being better equipped to have discussions about donation; and
- iii) Easier for a stranger to ask.

For those who thought the use of TCAs was unacceptable or unhelpful, the following themes were identified:

- i) Perceived coercion;
- ii) Ineffectiveness; and
- iii) An extension of asking personally.

Understanding patient attitudes will help ensure an intervention based on TCAs is designed to address some of the anticipated barriers to their use. Identifying reasons TCAs are seen as unacceptable (or ineffective) also allows alternative interventions to be designed to support individuals awaiting transplantation.

Are we performing enough pre-emptive paediatric renal transplants? A national and single-centre comparative study

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Introduction

Pre-emptive renal transplantation (PRT) from living-related donors (LRD) is the gold standard therapy for children with ESKD, dramatically improving allograft survival and quality of life. We aimed to analyse the local and national pre-emptive renal transplantation rates of children in the United Kingdom.

Material and methods

Retrospective local and national database review of living donor and/or pre-emptive renal transplantation rates, including UK Transplant data from 1 January 2003 to 31 December 2014. Local database case analysis of those not pre-emptively transplanted.

Results

1,262 paediatric renal transplants were performed nationally over 12 years, of which 326 (26%) were from our single centre (local). There were 32% national and 40% local pre-emptive renal transplantation rates with nationally 47%(21%) and locally 57% (27%) living donor (and preemptive living donor) rates. Of the total pre-emptive transplants, there were 60% nationally versus 68% locally living donor rates. Out of the 60% local non-pre-emptive renal transplants performed, 13% could have been pre-emptively transplanted when independently reviewed (excluding those patients who presented in ESKD or were on dialysis within 3 months of presentation, anephric pre-transplantation (native nephrectomies for FSGS, Wilms' tumour etc.), non-adherence or social reasons).

Conclusions

Paediatric nephrologists and members of the multi-disciplinary team need to ensure that renal transplant work-up is always performed promptly in appropriate children with chronic kidney disease to ensure that the goal of pre-emptive renal transplantation is achieved nationally and locally, where possible. National analyses indicated significant correlation between number of candidates for pre-emptive transplantation who were not transplanted pre-emptively and mean waiting times on UK deceased donor transplant waiting list. By increasing pre-emptive transplantation from living donors, patients whose only option is deceased donor listing, will face lower waiting times, improving overall patient care and outcomes

P109

Serious adverse event reporting in the OutSMART Study: workload intensity for nurses

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Introduction

The Optimized Tacrolimus and MMF for HLA Antibodies after Renal Transplantation Study (OutSMART) is a phase IV, type A trial (risk no higher than standard care). The study is testing whether HLA antibody screening is a feasible way to help prevent kidney transplant failure, and if a targeted treatment plan will keep the kidney transplant working for longer without causing unacceptable side effects.

A serious adverse event (SAE) can be defined as any adverse event or adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect. This does not include planned hospital admissions. OutSMART also requires all pregnancies and important medical events to be reported.

SAEs must be reported to the sponsor within 24 hours of becoming aware of an SAE. To do this, a 3 page form is filled out with details of the SAE and this is signed by the PI and sent to the sponsor. Almost all SAE reports require several follow-ups before they are closed.

Methods

On 12/11/2015 there was a review of the number of SAEs submitted for OutSMART for the host site and the time spent doing them by research nurses.

Results

There are currently 486 participants in OutSMART at the host site. At present, a total of 170 SAEs have been reported for 93 patients. Each initial SAE takes approximately 90 minutes to fill out. This equates to 255 hours, or 6.8 weeks (in a 37.5 hr week) of full time work. This does not include follow up reports, which require much time and chasing; currently 130 of the SAE reports require one or more follow-up reports.

Discussion

There is a considerable amount of time spent reporting and following-up SAE reports within the OutSMART study. The method of SAE reporting should be considered when developing a study, including whether the reports are generated on an online system or completed on paper. To help minimise the workload associated with SAE reporting for research nurses, there should also be well defined SAE exclusion criteria in the protocol, for example reporting for specific cohorts, exclusion for specific unrelated events or within a specific time length. As Type A studies are considered as standard risk, SAE reporting in these studies could be more selective.

The feasibility and workload intensity should be considered during the design and set-up of studies.

P110

Evaluation of follow up renal biopsy after histologically proven rejection in renal transplantation

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Introduction

There are no national guidelines to guide follow-up management of acute rejection following renal transplantation. Local policy since 2009 has been to conduct a follow up biopsy to assess response to treatment and to guide further immunosuppression management. This study examines what benefits are gained from this policy and if these outweigh the potential risks of biopsy.

Methods

A retrospective review of all adult patients transplanted in this unit between 2009-2015 was undertaken, and the study group were those patients:

- Under care of the adult transplant unit throughout the period of study
- Histologically proven rejection (Banff 2-4) within 6 months of transplantation
- Received follow up renal biopsy

Data was collected on all patients including primary renal diagnosis, baseline immunosuppression and renal function prior to each biopsy, histopathology and alterations to immunosuppression in light of biopsy results. These were analysed using Microsoft Excel.

Results

473 adult patients were transplanted during the study period. 283 needed a biopsy for graft dysfunction. Of these, 191 showed no evidence of rejection on initial biopsy and of the 92 where there was evidence of rejection 69 also had a follow-up biopsy. Follow up biopsies were not performed in 23 for clinical and logistical reasons. Of these patients, 50.7% (n=35) showed histological evidence of on-going acute rejection (Banff 3-5) on follow up biopsy, resulting in active management (alteration/increase of immunosuppression or methylprednisolone in 40%) Further follow up biopsy was conducted in 80% (n=28) with 7 patients not biopsied due to clinical improvement. Of those who received a second follow up biopsy, 78.5 % (n=22) showed improvement or complete resolution. Of the remaining 6 patients with ongoing evidence of rejection, one had their immunosuppression increased and two received further courses of methylprednisolone.

Mean duration between initial and first follow up biopsy was 22.9 days (SD 22.3) and between first and second follow biopsy 48.4 days (SD 54.5). 43 patients showed improvements towards baseline creatinine following initial biopsy with a further 11 following repeat biopsy, of which 6 had received intervention. In total 323 biopsies were performed on the population, with only 7 recorded complications, 6 episodes of haematuria and 1 AV fistula which required embolization.

Discussion

The study shows that doing routine follow up biopsies following treatment of biopsy proven acute rejection does change immunosuppressive treatment in 40% the patients. Effective treatment of acute rejection should improve long term graft function. In our experience repeat biopsies do not result in significantly excess complications. Whilst an economic analysis has not been done there is sufficient evidence to continue this practice.

P111

Renal Transplantation beyond 70 years of age: single centre experience

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Introduction

Renal transplantation improves quality of life, health and patient survival. As such, it is considered the gold standard renal replacement therapy (RRT), for all suitable patients. As the average age of patients with ESRD has increased, there has been a corresponding increase in the number of elderly patients receiving a kidney transplant.

Methods

We did a retrospective analysis of prospectively collected data from the Transplant Outcomes Database, regarding patients who received a kidney transplant when aged 70 years or older, between January 2005 and September 2015, capturing in particular, patient and graft survival outcomes. Our cohort included 102 patients. 71 (69.6%) were male, with a median age of 74 (range 70.10 and 86.9). 81 patients (79.4%) had received a graft from a diseased donor and 21(20.6%) from a live donor. Median follow up was 4 years and 2 months for the patients that were alive until the end of our study period, and 1 year and 8 months for those that died during the ten year period.

Results

At the end of our study, 25 (24.5%) patients had died. 11 (44%) from sepsis, 2 (8%) from mesenteric infarction, 4 (16%) from cardiovascular events, 6 (24%) from malignancy, 1 (4%) with post operative bleeding and 1 (4%) with CVA. 17 out of the 25(68%) had a functioning renal graft.

Patient survival at 3 and 5 years was 86.2% and 79.4% respectively. Graft loss was seen in 15 (14 %) patients; 2 due to primary non-function(PNF), 1 due to BKV nephropathy, 8 due to infection, 1 due to malignancy, 1 due to acute myocardial infarction, 1 due to acute rejection not responding to treatment, and 1 due to cardiac failure. Graft survival at 3 and 5 years was 83.3% and 71.5 % respectively.

Mean serum creatinine at 3 months, 12 months and 3 years were 179.7, 143.0 and 138.4 $\mu\text{mol/l}$ respectively. Mean eGFR at 3 months, 12 months and 3 years were 47.0, 36.1 and 35.0 ml/min respectively. Delayed graft function (DGF) was observed in 39 patients (38.2%). Biopsy proven acute rejection rate was 12.7% and PNF was seen in 2 patients (2.0 %).

Discussion

Renal transplantation in patients 70 years of age or older has good outcomes for both patients and graft survival. Our experience supports renal transplantation in this age group, and age itself, should not be considered as a contraindication to transplantation. As the death with functioning graft is still the main cause of graft loss in this patient population, patients over the age of 70 should have detailed pre-transplant evaluation. The main cause of death in this patient population is infection, indicating the need for review of immunosuppression protocols due to immunosenescence.

P112

Survival advantage in the elderly with kidney transplantation: a single centre experience

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Introduction

Patients with established renal failure (ERF) are aging. Of patients starting dialysis at our centre a third and a half are over the age of 70 and 65 years respectively, with a total dialysis population of 1500 patients. Age is not contraindication to transplantation but age related co-morbidity is an important limiting factor. Mortality rates in dialysis populations are declining and comparative published data regarding the outcome of transplantation in the elderly are historic. The aim of this study was to benchmark the survival advantage of transplantation in the elderly in a modern era.

Methods

A single centre prospective cohort of patients above the age of 65 was studied with a protocolised tacrolimus-based steroid avoidance treatment from the time of activation on the wait-list 01 November 2005 till 31 March 2015.

Results

354 patients (70.4% male) were medically fit to be activated on the transplant waiting list. One third of those patients (34.5%) received a transplant while the rest continued with dialysis, median (IQR) follow up time 4.0 (1.9/6.1) years. The transplant recipients were younger, median age (IQR) in years 67.7 (66.2/69.7) vs 69.5 (66.8/72.6) ($p=0.001$) and started dialysis at a younger age 66.4 (64.5/69.1) vs 68.2 (65.3/71.7) ($p=0.004$). Ethnic case-mix was comparable in both groups (38.8% Caucasian, 31.5% South-Asian, 16.8% Afro-Caribbean transplanted vs 45.1%, 32.8%, 17.2% wait-listed respectively) and both groups had similar comorbidities. A multivariate time-dependent Cox regression analysis, adjusted for age, ethnicity, gender, time on waiting list, diabetes (DM), dialysis vintage, modality type and duration, revealed a positive effect of transplantation (HR:0.56 - 95%CI 0.31 to 0.94, $p=0.04$) on survival. DM (HR:1.83 - 95%CI 1.13 to 2.9, $p=0.011$) and dialysis vintage in years: (HR:1.14, 95%CI 1.04 to 1.125, $p=0.01$) were significant risk factors for mortality. Excluding pre-emptive, live-donor transplantation, the survival advantage still remains evident.

Discussion

In our multi-ethnic cohort of patients transplantation offers a significant survival advantage while comorbidities and frailty is likely influential with increased age.

P113

Predicting the trajectory of renal transplant function decline and planning for transplant failure

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Introduction

Recently published literature evaluating the rate of decline of native renal function has proven useful in renal replacement therapy (RRT) planning including timing of vascular access creation and listing for transplantation. No such similar data exists for decline in function of failing renal transplants. This study aims to evaluate both the rate of graft decline to end-stage and current practice with regards to future RRT planning in patients with failing renal transplants.

Methods

Two cohorts of transplant patients in the West of Scotland were evaluated. Firstly, all renal transplant patients who had a graft which failed between January 2005 and January 2015 had eGFR recorded at 6-monthly intervals for the 5 years prior to graft failure. The trajectory of renal decline was calculated and classified into four groups as described by O'Hare et al, 2012 (persistently low eGFR $<30\text{ml/min}/1.73\text{m}^2$ (pattern 1); progressive loss of eGFR over the 2 years prior to failure from baseline $30\text{--}59\text{ml/min}/1.73\text{m}^2$ (group 2); progressive loss of eGFR over the two years prior to failure from baseline $>60\text{ml/min}/1.73\text{m}^2$ (group 3; accelerated loss); loss of function from eGFR $>60\text{ml/min}/1.73\text{m}^2$ in the 6 months prior to graft failure (group 4; catastrophic loss). Causes of graft loss in those patients with catastrophic decline were also assessed. Secondly all prevalent patients with a functioning graft on 1st October 2015 were evaluated (n=1540) and eGFR recorded. Planning for RRT (modality, vascular access and future transplant planning) were considered for all patients with eGFR $\leq 15\text{ml/min}$.

Results

472 patients had graft failure in the past 10 years. 100 patients were excluded as graft loss occurred <30 days following transplantation and 26 were excluded due to inadequate data/ loss to follow-up. Of the others 51.2% (n=177) had rate of graft decline following pattern 1; 33.2% (n=115) had pattern 2; 9.5% (n=33) followed pattern 3 and 6.1% (n=21) followed pattern 4. Patients with catastrophic loss of function had been transplanted more recently in the patients in the other 3 groups (median: 2 years vs. median 8 years; $p<0.001$). Of the patients with catastrophic loss, two-thirds had acute rejection (several in the context of non-compliance). Only one had recurrence of their primary renal disease. Of the 1540 prevalent transplant patients, 17.0% (n=262) have eGFR $\leq 30\text{ml/min}$ and 3.3% (n=51) have eGFR $\leq 15\text{ml/min}$. Only 60.8% (n=31) of patients with eGFR $\leq 15\text{ml/min}$ had documented evidence of future RRT planning (19 haemodialysis (HD), 6 peritoneal dialysis, 2 palliation, 4 pre-emptive live donor transplantation). Of those choosing HD only 8 patients (42.1%) had a functioning AVF. Only 23.5% (n=12) were re-listed for cadaveric transplantation.

Discussion

The trajectory of renal decline in patients with failing transplants differs from the pattern of native renal decline, however in the majority of cases it is predictable well in advance of graft loss. Current vascular access planning and re-listing for transplantation at an early stage is suboptimal. It is hoped that knowledge regarding the rate of decline in graft function can better inform RRT planning decisions.

Outcomes for kidney allograft recipients with language barriers post-transplantation: a comparative analysis

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Introduction

Black, Asian and Minority Ethnic (BAME) patients make up an increasing number of recipients of kidney allografts in the United Kingdom. Some of these patients have poor English skills and language barriers have been acknowledged as contributing to health inequalities in the NHS. No study has ever compared patient and/or kidney allograft outcomes between recipients with versus without language barriers. This study aimed to test the hypothesis that non-native English speakers may have poorer outcomes after kidney transplantation compared to native English speakers.

Methods

Data was extracted by our hospital informatics team for all kidney allograft recipients transplanted between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events. Patients were linked to data held with the Language and Communication Services to identify patients who ever required interpreting services. SPSS version 22 was utilised for all statistical analysis.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up to 4.4 years' post-transplantation. Ethnicity breakdown of the cohort was; Caucasian (72.1%), black (5.5%), south Asian (17.6%) and other (4.7%). Interpreters had been requested for 40 kidney allograft recipients, with commonest languages required including Urdu/Punjabi (n=25), Arabic (n=2), Bengali (n=2), Gujrati (n=2) and single cases of 9 other languages. Patients who required interpreting services were more likely to be of south Asian ethnicity (80.0% of users versus 15.4% of non-users, $p < 0.001$) and female (60.0% of users versus 39.5% of non-users, $p = 0.008$). Comparing recipients using versus not using interpreting services, we observed less events of any rejection (2.5% versus 14.8% respectively, $p = 0.014$), cellular rejection (2.5% versus 13.5% respectively, $p = 0.023$) and antibody-mediated rejection (0.0% versus 3.8% respectively, $p = 0.217$). Specifically looking at south Asians who were primary users of interpreting services, those using versus not using interpreter services had less episodes of rejection (3.1% versus 14.8% respectively, $p = 0.053$). There was no difference between the groups for development of post-transplant diabetes, cardiac events, cerebrovascular accidents or cancer. Finally, users versus non-users of interpreting services had equal patient survival (92.5% versus 92.9% respectively, $p = 0.551$), death-censored graft survival (90.0% versus 89.8% respectively, $p = 0.615$) and overall graft survival (82.5% versus 84.1% respectively, $p = 0.461$).

Discussion

Kidney allograft recipients with poor English skills who require interpreting services do not suffer adverse patient or kidney allograft outcomes compared. Interestingly, we observed less rejection in these patients. The major confounder to this analysis are patients who have poor English skills but do not utilise interpreting services (due to family relatives interpreting on their behalf.) Despite this limitation, our results are encouraging for kidney allograft recipients who do not speak English comfortably and supports use of professional interpreting services for long-term clinical follow up post kidney transplantation to achieve suitable standard of care.

P115

Does kidney re-transplantation have a favourable effect on patient survival?

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Introduction

Despite improved long-term outcomes of kidney transplants graft loss remains a major problem, which results in many patients returning to dialysis and being considered for re-transplantation. The aim of this study was to evaluate the survival benefit of re-transplantation, on patients that are re-activated on the transplant list after a failing first renal graft.

Methods

A single centre review of prospectively collected data of all patients who were previously transplanted and then re-activated on the waiting list (WL) for renal transplantation, from November 2005 till March 2015. Survival was analysed as the time from initial placement on the waiting list to death.

Results

A total of 256 participants were included in our study (62.4% males). One hundred forty (54.7%) received a kidney transplant (49.3% from a live donor) within the study period, 20 were transferred to other centres, while the rest continued with dialysis. The median (IQR) time of follow up was 52.3 (27.4/86.6) months. Median time (IQR) on renal replacement therapy (RRT) and dialysis were 13.1 (8.7/20.1) and 2.7 (0.8/6.5) years, respectively. Re-transplanted patients (Tx) were younger compared to control group (WL). The median age in years (IQR) was 43.7 (36.6/53.5) vs 48.6 (39.9/56.2) respectively ($p < 0.001$). Re-transplantation incurred a significant survival advantage compared to remaining active on the waiting list with a 1, 5 and 9-year survival of 96.9%, 94.3% and 89.2% vs 96.3% 88.1% and 66.1% respectively (Log rank test, $p = 0.003$). Multivariate cox regression analysis with time varying covariate showed that renal re-transplantation (HR 0.26, 95% CI 0.1–0.9, $p = 0.029$), time on RRT (HR 1.06, 95% CI 1.01–1.10, $p = 0.024$) and age on activation (HR 1.04, 95% CI 1.01–1.08, $p = 0.035$) had a significant effect on survival.

Discussion

Kidney re-transplantation seems to have a favourable effect in survival in patients who are re-activated on the waiting list after losing their first graft.

P116

UKKDRI score predicts the development of TRAS post deceased donor transplantation

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Introduction

Transplant renal artery stenosis (TRAS) is a heterogeneous disorder with different subtypes and aetiologies which include traditional cardiovascular and transplant specific risk factors. Whether the increasing use of extended criteria donors, who have a higher incidence of intrinsic cardiovascular risk factors will impact on the incidence of TRAS is not known. The aim of this study is to determine if a high UK kidney donor risk-index (UKKDRI) score is associated with TRAS.

Methods

We performed a retrospective analysis of all transplants performed at our centre between 2005 and 2015. 209/1479 (14.1%) of all patients had proven TRAS by formal angiography.

Results

TRAS prevalence was significantly higher in deceased donors (DD) compared with LD, 152/209 (72.7%) of TRAS developed in DDTx recipients, $p < 0.0001$. The mean time to TRAS diagnosis was 3.5 ± 3.6 months. Demographics were available on 150 deceased donors with TRAS and these were compared with 605 TRAS negative deceased donors.

| Donor characteristic | | TRAS+ N=150 (%) | TRAS- N=605 (%) | p value |
|----------------------|---------------|--------------------|--------------------|---------|
| Gender | Male | 94 (62.7) | 291 | 0.023 |
| | Female | 56 (37.3) | 314 | |
| Age | Mean yrs | 56.91 \pm 12.97 | 49.50 \pm 15.72 | <0.0001 |
| Ethnicity | Caucasian | 139 (92.7) | 542 (89.6) | 0.33 |
| | Non-caucasian | 11 (7.3) | 63 (10.4) | |
| Graft status | DBD | 117 (78.0) | 492 (81.3) | 0.42 |
| | DCD | 33 (22.0) | 113 (18.7) | |
| SCD/ECD status | SCD | 54 | 336 | <0.0001 |
| | ECD | 92 | 262 | |
| Donor \uparrow BP | Yes | 65 | 168 | 0.0003 |
| | No | 85 | 437 | |
| UKKDRI score | High | 81 | 213 | <0.0001 |
| | Low | 69 | 392 | |

Discussion

A high risk UKKDRI score may enable identification of patients at risk of developing TRAS and knowing donor characteristics may allow a focused screening strategy for TRAS post deceased donor transplantation.

P117

Outcome of renal transplant from donors with excessive alcohol consumption

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Introduction

Prolonged excessive alcohol intake can cause tissue fibrosis as in liver cirrhosis; as a consequence, this will lead to organ function impairment. It is not clear whether excessive alcohol intake will cause similar changes in the kidney. We report the outcome of renal transplant function and histological findings in the pre-perfusion biopsy from donors with history of alcohol abuse with or without liver cirrhosis.

Methods

A retrospective database search of last consecutive 225 kidney donors offered and transplanted in our unit; donors with excessive alcohol intake were included in the study and divided into two groups; alcohol abuse with or without liver cirrhosis. The presence of interstitial fibrosis or glomerular sclerosis in the pre-perfusion renal biopsy and the renal function were evaluated.

Results

Excessive alcohol intake donors with liver cirrhosis (n=15) and those without liver cirrhosis (n=27). Median age was 58 and 46 years, history of Diabetes Mellitus (n=1 vs n=0) and hypertension (n=2 vs n=5) respectively. Renal function six months post-transplant showed mean creatinine value of 161 $\mu\text{mol/L}$ (95% CI 93-227 $\mu\text{mol/L}$) vs 147 $\mu\text{mol/L}$ (95% CI 122-172 $\mu\text{mol/L}$). The presence of fibrosis in the pre-perfusion renal biopsy was 63.6% vs 37.5% and glomerular sclerosis of 54.5% vs 45.8%.

Discussion

Recipients who had renal transplant from donors with alcoholic liver cirrhosis showed worse renal function at six months post-transplant than those with alcoholic abuse only. The presence of interstitial fibrosis in the pre perfusion biopsy from donors with a history of alcoholic liver cirrhosis was higher and this may have negative impact on the graft quality and survival.

P118

Black ethnicity as a risk factor for poor kidney allograft outcomes post-transplantation

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Introduction

Registry studies, largely from the United States, have consistently demonstrated inferior outcomes for black patients undergoing renal transplant. However, this has been challenged by a recent Canadian publication reporting equivalent outcomes compared to white counterparts. The aim of this study was to determine outcomes for black patients in a large contemporary UK cohort.

Methods

Data was extracted from hospital informatics systems for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events. Immunosuppression utilised during this time for patients included basiliximab induction and standard maintenance immunosuppression of tacrolimus, mycophenolate mofetil and low-dose corticosteroids.

Results

We collected data for 1,140 patients who received a kidney allograft, with median follow up 4.4 years post-transplantation. Ethnicity breakdown of the cohort was white (72.1%), black (5.5%), south Asian (17.6%) and other/unspecified (4.7%). Black ethnicity versus non-black ethnicity demonstrated equivalent patient survival (6.3% versus 7.1% respectively, $p=0.531$) but significantly worse death-censored graft survival (22.2% versus 9.5% respectively, $p=0.003$). In total, black patients had worse overall graft survival compared to non-black patients (25.4% versus 15.4% respectively, $p=0.032$). Black patients had borderline significance for increased risk of any rejection episode within the first year post kidney transplantation compared to non-black patients (19.0% versus 11.2% respectively, $p=0.053$). There was no difference when comparing black versus non-black ethnicity to post-transplant events including cardiac events, cerebrovascular accidents or cancer but black patients did have increased risk for post-transplant diabetes (16.7% versus 8.7% respectively, $p=0.048$) and peripheral vascular disease (6.3% versus 1.1% respectively, $p=0.009$). Despite the unadjusted difference in graft survival, in a Cox regression model black ethnicity was not independently associated with graft failure when adjusted for other variables.

Discussion

Analysis of our dataset demonstrates that Black kidney allograft recipients have worse overall graft survival but black ethnicity itself does not appear to be a risk factor for graft loss. This is likely to be due to differing demographic or transplant specific factors, and unappreciated confounders, within this cohort. Further work, including analysis of national data from NHS Blood & Transplant, should be undertaken to provide clarity on kidney allograft outcomes for black patients in the United Kingdom.

P119

South Asian kidney allograft recipients and post-transplant outcomes

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Introduction

South Asians are the biggest minority ethnic group in the United Kingdom and a sizable proportion of patient. Recent literature exploring South Asian kidney allograft recipient outcomes has identified an increased risk for major cardiovascular events post-transplantation but similar incidence of post-transplantation diabetes. However, this cohort was from Canada and there is no contemporary literature looking at a cohort in the United Kingdom. The aim of this analysis was to compare South Asian kidney allograft recipient outcomes post-transplantation to determine if outcomes differ between South Asians and other ethnic groups.

Methods

Data was extracted by our hospital informatics team for all kidney allograft recipients transplanted between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up to 4.4 years post-transplantation. The median age for the cohort was 47, males (n=681, 59.7%), Caucasian ethnicity (n=822, 72.1%), deceased-donor recipients (n=633, 56.4%), repeat transplants (n=111, 9.7%), diabetes as cause of end-stage kidney disease (n=117, 10.3%) and previous/active smoking exposure (n=274, 24.0%). Ethnicity breakdown of the cohort was; Caucasian (72.1%), black (5.5%), south Asian (17.6%) and other (4.7%). We identified an increased risk for post-transplant diabetes among south Asians versus non-south Asian recipients (16.9% versus 7.6% respectively, $p < 0.001$) but equivalent episodes of cardiac (6.5% versus 6.0% respectively, $p = 0.444$) or cerebrovascular events (2.5% versus 2.3% respectively, $p = 0.532$). There was no difference in incidence of rejection, cancer or hospitalisation for septicaemia when comparing south Asian to non-south Asian kidney allograft recipients. Overall there was no difference comparing south Asian versus non-south Asian kidney allograft recipients for patient survival (93.5% versus 92.8% respectively, $p = 0.417$), death-censored graft survival (89.6% versus 89.9% respectively, $p = 0.486$) and overall graft survival (84.1% versus 84.0% respectively, $p = 0.541$).

Discussion

South Asian kidney allograft recipients have increased risk for post-transplant diabetes but equivalent risk for cardiac events compared to non-south Asian recipients, which contrasts with recent data from Canada. Reassuringly, hard outcomes such as mortality and kidney allograft loss are equal for south Asian versus non-south Asian kidney allograft recipients. This data can be utilised to counsel south Asian candidates for kidney transplantation and informs transplant clinicians involved with their post-transplant care.

A single centre observational review of the outcomes of transplantation in the older population

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Introduction

There is an ongoing disparity between the number of patients awaiting transplantation and the number of organs available. Meanwhile, the number of patients transplanted over the age of 60 has been rising. This study sought to evaluate the outcomes of older recipients and to identify patient, donor or process factors influencing these outcomes.

Methods

The renal electronic records system (VitalData) was used to retrospectively identify patients over age 60 at the time of transplantation during a 5 year period (1/1/2010 – 1/9/14). Data was collected from paper and electronic patient records across the three Trusts providing follow up. Data regarding the recipient (primary renal disease, comorbidity, age at transplant, renal replacement therapy, CMV status), donor (age, CMV status, type), transplant process (mismatch score, induction agent used) and outcome (serial serum creatinine values, graft failure, mortality, infections, biopsy proven acute rejection, and hospital admissions) were collected. Statistical analysis using Cox proportional hazards was performed using SPSS.

Results

95 patients were identified, providing follow up of 91,850 patient days (mean 967 days/patient; range 4–1917). The minimum follow up period for functioning grafts was 10 months. The mean age of patients at transplantation was 67 years (range 60–80). The mean donor age was 56 years (range 9 – 76). **Current status:** 76/95 (80%) have a functioning graft; 8/95 (8%) remain alive without a functioning graft, 8/95 (8%) died with a functioning graft; 4/95 (4%) died subsequent to graft failure. **Rejection:** 5/95 (5.2%) developed acute cellular rejection (with no graft failures). 12/95 (12.6%) developed vascular rejection, of which 11 received ATG (with 2 graft failures). 1/95 (1%) developed antibody mediated rejection (treated effectively with increased maintenance immunosuppression). **Infection:** CMV viraemia (CMV PCR titre > 3.2 log¹⁰ IU/ml) occurred in 38/95 (40%) patients of which 5 had ganciclovir resistance. 13/95 (13.7%) developed BK viraemia and/or nephropathy. **Admissions:** A total of 303 hospital admissions occurred (median 3, range 0-14) totalling 2,739 bed days (median 12, range 0-263). The average length of stay per admission was 7 days. **Malignancy:** 13/95 (13.7%) developed malignancy post transplantation (7 skin cancers, 2 prostate cancers, 1 renal cell carcinoma, 1 mesothelioma, 1 lymphoma, and 1 leiomyosarcoma; the latter 3 patients died from their malignancies). **Overall Mortality:** 12/95 (12.6%) patients died within the study period. Those with functioning grafts died from cancers (3), cardiac causes (2), pneumonia (1) and CMV (1). Those with non-functioning grafts died from CVE (2), PE (1) and cardiac causes (1). 30 day mortality was 1/95 (1%). A cardiac history ($p=0.014$) and a history of malignancy pre-transplant ($p=0.043$) were associated with an increased likelihood of death during the study period.

Discussion

Although data from a matched cohort of younger patients was not available, this review suggests that the transplantation of older patients at this centre was associated with outcomes in keeping with those achieved for the population as a whole. Patients with a prior history of heart disease or malignancy had statistically poorer outcomes than those without, however no statistically significant difference in outcomes was seen across different age brackets (60-65 vs >65) when other factors were accounted for. This study supports the hypothesis that age alone should not be a contraindication to transplantation and that clinicians should accept patients onto the waiting list on a case by case basis.

P121

A comparison of hospital admissions 12 months post-renal transplant for those aged ≥ 65 years and those aged < 65 years

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Introduction

Transplantation in the older population was previously avoided due to concerns over mortality and morbidity. In more recent years transplantation in the elderly population has increased with collective reports of survival advantage compared to those remaining on the transplant waiting list. However less is known about the burden of hospital admissions and optimal immunosuppression regimes in this population.

Methods

All patients over 65 years of age that received a kidney transplant in 2012 and 2013 and were followed up for at least 12 months in a large single UK transplant centre were identified. Information collected and analysed included mortality, hospital admissions, length of stay, immunosuppression regimes and graft outcomes. These were compared with a cohort of patients under 65 years of age from the same period and follow up.

Results

A total of 35 patients over 65 and a random selection of 60 patients under 65 years were included. 20% of the over 65s died within 12 months compared with 7% of under 65s. 77% of over 65s had at least one hospital admissions in 12 months compared with 57% of under 65s. The 30day readmission rate was 50% for over 65s versus 23% for under. The over 65s had a longer hospital stays at 38.8 bed days/year versus 19. The main causes of hospital admissions for over 65s were infections (n=20, 38% admissions), drug toxicity (n=11, 22% admissions) and surgical and cardiovascular complications (n=5, 10% admissions for each). No admissions were related to rejection. The most common reason for admission in younger patients were infections (n=22, 31% admissions), biochemical (n=13, 19% admissions) and surgical complications (n=8, 11% admissions). Rejection treated with pulsed methylprednisolone accounted for 4 admissions which was 6% of total admissions. Transplanted patients over 65 had higher admission rates of 1.5 per patient/year compared to USRDS data for CKD4/5 patients whose admission rate was 0.87.

Discussion

Patients transplanted over 65 years of age have more hospital admissions with increased number of hospital bed days compared to younger patients. Those aged 65 years or over that were transplanted had a higher hospital admissions incidence compared to CKD4/5 patients over 66 years of age not transplanted. Some of these hospital admissions may be prevented with increased vigilance for drug toxicity and reiteration of drug education. There may be some scope to review immunosuppression protocols in the over 65s.

Three month post transplant protocol biopsies: retrospective review of findings and outcomes

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Introduction

Protocol biopsies (PB) are undertaken without clinical indication to detect subclinical histological changes. Detectable changes vary and are dependent on immunological risk, type of immunosuppression used and timing of PB. The peak incidence of subclinical acute rejection (SCAR) is in the early post transplant period with increasing rates of chronic changes later on. Many of the detectable changes are amenable to intervention and there is equivalence in published evidence in whether this leads to improved outcomes. Due to this equipoise and concerns about complications, there is variation in practice of performing PB across the UK.

We perform PB at time zero and 3 months post transplant with guidance for intervention depending on PB findings at 3 months. The aims of this study were: 1) to analyse histological findings and complications, 2) to assess whether there were any factors associated with positive findings, and 3) to assess long term outcomes following PB at 3 months.

Methods

We evaluated all patients who were transplanted and had long term follow up at the centre between August 2009 and August 2014. Standard induction therapy included basiliximab and steroids; maintenance immunosuppression included tacrolimus with early steroid withdrawal for those stratified to low immunological risk.

Results

The study cohort consisted of 125 patients, of whom 99 had a protocol biopsy. Mean age was 54 years old. There were 80(64%) males, 77(61%) deceased donor transplants and 83(66%) were stratified to low immunological risk.

Protocol biopsy findings consisted of 63(64%) normal, 11(11%) borderline rejection, 6(6%) acute rejection, 9(9%) calcineurin inhibitor (CNI) toxicity and 10(10%) interstitial fibrosis/tubular atrophy, which were all <25% of cortical area. Complications: 6 (6%) episodes of haematuria, which spontaneously resolved and 8(8%) inadequate biopsy samples.

None of the factors analysed, which included type of transplant, immunological risk, CMV status and kidney function at time of PB, were associated with a positive finding on PB at 3 months.

For all patients the mean creatinine (Cr) at 1 year was 135umol/l with a significant difference in Cr in those who had a PB at 3 months compared to those who did not have a PB (113 vs. 213umol/l, $p < 0.05$). Mean Cr in those with a positive finding on PB compared to a normal PB at 3 months was 129 vs. 108umol/l ($p = 0.05$) at 1 year and 121 vs. 129umol/l at 3 years.

Discussion

The most common positive finding on PB at 3 months was SCAR or borderline rejection (17%). SCAR was treated with pulsed methylprednisolone and an increase in maintenance immunosuppression. Immunosuppression was reduced in patients on 3 agents with a normal PB.

There are no factors associated with positive findings on the PB, which suggests that no criteria can be applied to select those who should undergo a PB.

Overall long term outcomes are good in patients who had a PB at 3 months and renal function is better than in those who did not have a PB although these groups are not directly comparable with likely confounding factors.

We conclude that PB at 3 months is safe and yields findings amenable to intervention with good long term results.

P123

A case series of perioperative blood pressure and fluid management in paediatric renal transplant recipients

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Introduction

The optimal perioperative blood pressure and fluid management in paediatric renal transplant recipients (pRTR) is currently unknown. This case series aimed to investigate the effects of nine perioperative blood pressure and fluid management strategies on two outcomes: one-week postoperative estimated glomerular filtration rate (eGFR) and postoperative length of stay (LOS) in the hospital.

Methods

73 pRTR transplanted over three years from 2012 to 2014 were studied retrospectively. Data sources included patient blood test results, preoperative checklists, anaesthetic records, clinic letters and discharge summaries. Two-sample t-tests, one-way analysis of variance (ANOVA), Pearson's correlation and multiple linear regression were performed using SPSS.

Results

The following strategies did not significantly affect eGFR and LOS: donor systolic blood pressure (SBP), intraoperative median SBP z score of the recipient, intraoperative fluid volume, intraoperative fluid type, intraoperative crystalloid type and the presence of postoperative hypertension.

Preoperative peritoneal dialysis (PD) was significantly associated with shortened LOS compared to preoperative haemodialysis (HD) (P = 0.002), but was not significantly associated with postoperative eGFR.

Aorta-inferior vena cava (IVC) anastomoses were associated with significantly higher postoperative eGFR (P = 0.001) but longer LOS (P = 0.02) compared to iliac vessel anastomoses.

The presence of postoperative fluid overload significantly increased LOS (P = 0.01) but did not significantly affect postoperative eGFR.

Discussion

Preoperative PD was associated with shorter LOS than HD, supporting its use over HD prior to paediatric renal transplantation. Aorta-IVC pRTR had higher postoperative eGFR than iliac vessel pRTR, encouraging continued use of the former type of vascular anastomosis. Both aorta-IVC anastomoses and the presence of postoperative fluid overload were associated with longer LOS. Future research into goal-directed fluid therapy, such as perioperative cardiac output or Doppler flow monitoring, that would reduce perioperative fluid overload and thereby LOS is recommended.

P124

The effect of delayed graft function in kidney transplantation on long-term renal function

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Introduction

Delayed graft function (DGF) is defined as the need for renal replacement therapy within a week of renal transplantation. DGF is associated with increased hospital stay and costs. It is not clear from the literature whether DGF has a long-lasting effect on renal allograft function. The purpose of this retrospective observational study is to determine the effect of DGF on renal transplant function in the short and long term.

Methods

Analysis of 353 renal transplants for deceased donors after brain death (DBD) and after circulatory death (DCD), between 2005 and 2011 at a single centre was undertaken. Serum creatinine at 1, 3 and 5 years following transplantation was compared between patients who had immediate and delayed graft function.

Results

Of the 353 patients included in the study, 40.2% of patients (n=142) had DGF, 4.0% (n=14) had primary non-function, and 6.5% (n=23) had graft failure or patient death before 1 year post-transplantation. 316 patients were available for analysis at year 1. At year 3, 127 patients' allograft function was censored, leaving 189 patients for analysis. At year 5, a further 78 patients' allograft function was censored, leaving 111 patients for analysis. Patients who experienced immediate function were on average 6 years younger than patients with DGF ($p = 0.0001$). There was also a higher proportion of DCDs in the DGF group compared to the immediate graft function group (82.1% vs 21.3%, $p=0$). At 1 year, renal function was significantly worse in patients who had DGF (mean creatinine $175 \pm 105.0 \mu\text{mol/L}$), compared to patients with immediate graft function (mean creatinine $1135 \pm 56.7 \mu\text{mol/L}$, $p = 0.0001$). At year 3, renal function remained significantly worse in patients who had DGF (mean creatinine $196.2 \pm 196.0 \mu\text{mol/L}$), compared to immediate graft function (mean creatinine $144.1 \pm 83.9 \mu\text{mol/L}$, $p = 0.0138$). At year 5, the renal function between the groups was comparable. The mean creatinine in the DGF group was $218 \pm 231 \mu\text{mol/L}$, and $159 \pm 130 \mu\text{mol/L}$ in the immediate function group. There was no statistical difference in serum creatinine at 5 years between the groups ($p = 0.883$, $n = 111$).

Discussion

These outcomes from a single centre strongly suggest that DGF impacts renal graft function in the short and medium term. This difference appears to become non-significant at five years. The mechanisms leading to these observations are likely to be complex and warrant further investigation.

P125

Post-transplant focal Glomerulosclerosis: the effect of treatment on histopathology lesions and podocyte foot process effacement

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Background

Post-transplant Focal Segmental Glomerulosclerosis (FSGS) is associated with increased risk for renal allograft failure. It has been reported in the literature that podocyte foot process effacement (FPE) may precede FSGS recurrence in kidney transplant recipients (KTR). There have been only limited data to support that successful management of post-transplant FSGS is associated with resolution of podocyte FPE.

Methods

Patients with a primary diagnosis of FSGS as well as KTR's with non-biopsy proven primary diagnosis that developed post transplantation proteinuria with evidence of segmental or focal glomerulosclerosis on light microscopy or diffuse FPE on electron microscopy (EM) were included. 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. Baseline EM results were obtained from renal biopsies performed prior to therapy and Post-treatment FPE was assessed from renal biopsies performed following the completion of treatment. The degree of FPE was categorized into minimal, segmental and extensive.

Results

10 transplant recipients (8 male) with a mean age of 51 years (range 23-67) were treated for biopsy proven post-transplant FSGS. All patients underwent pretreatment graft biopsies (mean glomeruli per biopsy sampled=20.4+/-11), that included tissue processed for EM. The histology diagnoses included 3 tip lesion 1 collapsing and 2 NOS variants of FSGS, while 3 patients had only podocytopathy, with extensive FPE on EM with an absence of a constituted FSGS lesion. Upon completion of treatment 9/10 KTR's had a biopsy. A resolution of FSGS lesions was found in 4/9 patients, while in 5/9 EM showed improvement in FPE. Histopathology findings correlated to the clinical outcomes, as 9 out of 10 patients achieved remission after the conclusion of treatment (4 complete and 5 partial).

Conclusion

FPE appears to be the earliest histology finding in Post-transplant FSGS. Clinical response to treatment is related to resolution of histopathology lesions and improvement in FPE. Further studies can elucidate the diagnostic and prognostic value of EM in Post-transplant FSGS.

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Kidney transplant recipients requiring critical care admission within one year of transplantation

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Introduction

Kidney transplantation is the gold standard renal replacement modality for ESRD. With the increasing age of the recipient population, carrying significant comorbidities, and the use of more marginal organs, there is potential for increased critical care admissions.

Method

We performed a retrospective analysis of kidney transplant recipients admitted to ITU within one year post transplantation, between January 2009 and December 2013.

Results

Of 1002 kidney transplants, 53 (5.3%) patients were admitted to ITU within one year; 32 (61%) in the immediate post-operative period (Group 1) mainly from cardio-respiratory derangements with mean ITU stay of 3.7 days (1 - 34) and zero mortalities. 21 patients (39%) admitted later in the post-operative period (Group 2) principally from sepsis related complications with a mean ITU stay of 18 days (1 – 101), majority requiring intensive therapy including mechanical ventilation and immunosuppression reduction and incurring ITU and hospital mortalities of 33% and 48% respectively. Haemorrhage with re-exploration was higher in group 1. Diabetes mellitus, cardiac co-morbidity, prolonged ITU stay, nutritional support, nosocomial infections and MODS are variables higher in the Group 2 patients who died.

Conclusion

The incidence of ITU admissions 1 year post kidney transplantation was 5.3%. Majority occurred in the early post-operative period, mostly on pre-emptive basis for cardio-respiratory monitoring and support. This category is potentially preventable with optimisation of preoperative management. Later admissions were mostly consequential to sepsis related complications and recorded a high mortality rate associated with MODS. Clinical management should focus on the prevention of MODS to improve outcome.

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Management of failing kidney transplants: a single centre's experience

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Introduction

There is evidence that kidney transplant recipients (KTRs) with poor graft function receive suboptimal care when compared to patients with native renal disease. With this in mind, the British Transplantation Society published their first guidelines on this subject in April 2013. The aim of this study was to analyse the management of recipients with failing kidney transplants (FKTs) and adherence to these recommendations at our unit.

Methods

As of 1st November 2015, there were 61 FKTs in the Wessex Kidney Centre with an eGFR \leq 20ml/min (6.3% of the total Wessex KTR population). We examined whether this cohort had been referred for low clearance clinic review or access for dialysis and had a documented decision regarding re-transplantation. In addition, we reviewed the most recently measured Hb, K, HCO₃, PO₄, Adjusted Ca and blood pressure (BP) control in these patients.

Results

The cohort was 56% male with a mean patient age of 56 years and a mean allograft age of 160 months. The mean eGFR of these failing allografts was 15.1ml/min (SD 3.3ml/min). Only 38% of the cohort had a documented decision with regards to re-transplantation and only 21% of the cohort had been referred for low clearance clinic review. Of the 13 FKTs referred to low clearance clinic, 12 (92%) had then been referred for dialysis access. In comparison, of the 48 FKTs that had not been referred to low clearance clinic, only 7 (15%) had been referred for dialysis access.

| | Hb (g/l) | K (mmol/l) | HCO ₃ (mmol/l) | PO ₄ (mmol/l) | Adj Ca (mmol/l) | Systolic BP (mmHg) | Diastolic BP (mmHg) |
|-------------------------------|------------|------------|---------------------------|--------------------------|-----------------|--------------------|---------------------|
| Target Range | \geq 100 | \leq 5.0 | \geq 20 | \leq 1.5 | \geq 2.20 | \leq 130 | \leq 80 |
| Mean | 109 | 4.7 | 21.4 | 1.37 | 2.36 | 133 | 77 |
| Standard Deviation | 14.7 | 0.6 | 3.3 | 0.29 | 0.14 | 12 | 21 |
| % of FKTs within target range | 74 | 62 | 72 | 64 | 90 | 52 | 66 |

Conclusions

Adherence to current guidelines is reasonable in our unit and we are meeting targets for Hb, electrolyte and BP control in the majority of FKTs. However, less than half of our FKTs had been referred for low clearance clinic review. A larger proportion of FKTs had been referred for dialysis access if they had been seen in low clearance clinic (92% vs 15%). Since the mortality rate of patients returning to dialysis after graft failure is high, we suggest that all FKT patients are reviewed in low clearance clinic in addition to frequent optimisation of their medical management.

Blood pressure (BP) control in kidney transplant recipients: a single centre experience

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Introduction

Cardiovascular disease is the leading cause of death among kidney transplant recipients (KTRs), however there remains uncertainty regarding optimal BP targets. Current UKRA, KDIGO and KDOQI guidelines advocate BP control to 130/80 in KTRs; UKRA/KDIGO advocate tighter control (125/70) in proteinuric KTRs. We examined BP control and proteinuria in all KTRs under longterm follow up at one centre, and adherence to these recommendations

Methods

As of 1 March 2015, 839 KTRs were attending for regular clinic review (excluding recent KTRs<1yr). We performed a retrospective database review of BP, proteinuria, renal function and antihypertensive use.

Results

The cohort was 60% male with mean allograft age 10 ± 0.28 years. Mean decline in eGFR was $0.83\text{ml}/\text{min}/\text{m}^2$ per year ($p=0.0004$). Mean SBP was 134 ± 0.56 , DBP 79 ± 0.37 . 48% had SBP <130, 62% DBP<80, 39% both. 78% received ≥ 1 antihypertensive, 42% 2-3, 4% ≥ 4 agents. Only 9% had PCR measured. In those with PCR ≥ 50 , 19% had BP treated to 125/75. Dipstick proteinuria was recorded in 58% and showed a significant association with SBP ($p=0.01$). There were significant correlations between reducing eGFR and increasing PCR ($R^2=0.11$, $p<0.0001$), and between PCR and ACE/ARB use ($p=0.0002$). There was no correlation between CNI level and BP (CyA $p=0.88$, FK506 $p=0.49$). There was a significant stepwise decrease in renal function (sCr $p=0.005$, eGFR $p=0.01$) and increase in dipstick proteinuria ($p=0.03$) when data were analysed in SBP groups <120, 120-140 and >140. In terms of DBP, the stepwise decrease in renal function remained (sCr $p=0.01$, eGFR $p<0.0001$) when data were analysed in groups <70, 70-90 and >90. DBP ≥ 90 had the most significant impact on eGFR. DBP was not associated with proteinuria.

Discussion

The optimal BP target remains uncertain. Adherence to current guidelines is reasonable in our unit but could be improved. This study again demonstrates that SBP is the key risk factor for proteinuria, however increases in DBP >90 were most strongly associated with graft dysfunction.

Management of the failing renal transplant patient: a local audit

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Introduction

Failed renal transplant patients comprise 4% of the dialysis population. There is a concern that the management of failing transplant patients in the run-up to dialysis may be suboptimal compared with patients with native renal disease. There is also a lack of robust data for the optimal weaning of immunosuppression following graft failure. We describe a local audit of the management of patients' with failing grafts with respect to anaemia, bone disease, vascular access and immunosuppression.

Methods

Patients who returned to dialysis after a failed transplant between August 2005 and August 2015 were identified from our local renal database. Patients were included if time from established CKD stage IV to dialysis start was greater than 3 months. Information on blood tests, medications and vascular access referrals were taken from the database and clinic letters.

Results

49 patients (32 male, 37 cadaveric transplants) returned to dialysis over the designated period. Mean time (years) from transplantation to return to dialysis was 10.9 (range 0.4-30.2), and from established CKD stage IV to return to dialysis 2.9 (range 0.3-7.0). **Anaemia** 39% of patients were anaemic (Hb<105g/dl) at CKD IV, this increased to 76% by return to dialysis. 41% of patients did not have iron studies checked within 6 months of CKD IV. 24% of anaemic patients at time of return to dialysis were not on erythropoietin therapy, and 8% of these had been anaemic since development of CKD stage IV. **Bone Disease** 71% of patients had PTH levels checked within 6 months of CKD IV and 88% were on alfacalcidol by return to dialysis. Of the 6 patients not on alfacalcidol at return to dialysis, 2 had PTH greater than 4 times the upper limit of normal, and 2 had not had PTH checked. **Vascular Access** 46 patients transitioned to haemodialysis. Of these, 28 patients (61%) required new vascular access of whom 17 (61%) returned via a new fistula and the remainder via a tunnelled central line. Median time (years) from CKD IV to dialysis was 3.7 in the fistula group (range 0.5-11.5) and 1.2 in the tunnelled central line group (range 0.4-6.2). **Immunosuppression** At return to dialysis, 69% of patients were on dual or triple agent immunosuppression. After 12 months, 49% were on no immunosuppression, 33% on steroid only and 4% on 2 immunosuppressive agents.

Discussion

Aspects of our management of the failing transplant patient are suboptimal, particularly the investigation and management of anaemia and vascular access planning for patients returning via haemodialysis. There is variation in the weaning of immunosuppression in these patients, and there is a need for more robust guidelines for it. In the future we plan to review these patients in a specific low-clearance clinic to optimise their return to dialysis consistent with established guidelines.

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Are the outcomes of deceased cardiac donor (DCD) renal transplants affected by the recipient sex status?

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Introduction

The influence of recipient gender on transplant outcomes is controversial. However, within animal models data indicates a greater female tolerance to ischaemic re-perfusion injury (IRI). With DCD organs being exposed to greater degrees of ischaemia during the transplantation process, any potential protective effect of the female sex should be evident within this group. Thus, the aim of this study was to determine if recipient gender impacted on outcomes in DCD renal transplantation.

Methods

Retrospective analysis of all adult renal transplantation, over a four year period (2011-2014), was performed. Baseline demographic characteristics and outcomes were compared by sex status for all DCD transplants. Outcome measures included serum creatinine at one year, biopsy proven acute rejection (BPAR) rates and one year graft survival. The rates of DGF and their outcomes were also analysed.

Results

One-hundred-and-seven DCD transplants were identified with females accounting for 43%. The overall donor and recipient case mix was not significantly different and mean BMI were matched for each sex (26.1 vs 27.1). The serum creatinine at one year was statistically lower in female DCD kidney recipients compared to males (116.8±7.05 vs. 135± 5.73, $p<0.05$) and was independent of donor organ sex. The DGF rates were equal for male and female DCDs (50% vs. 51%) and no significant difference were seen for BPAR rates (11% vs. 7%, $p>0.05$) or one year graft survival (89% vs. 97%). Outcomes following DGF showed a significantly lower creatinine for the female recipients (125.8±9.94 vs. 137.1±7.26, $p<0.05$) but BPAR (17.4% vs. 12.9%) and one year graft survival (91.3% vs. 100%) showed no sex differences.

Conclusion

The female sex status offers a lower creatinine at 12 months following transplantation of DCD kidneys but no differences in DGF rates were observed between male and female recipients. Thus, from this study no difference in tolerance to IRI between male and female DCD recipients.

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Development of polycystic kidney disease in a cadaveric renal transplant

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Introduction

Here we present a case of a cadaveric renal transplant recipient who developed multiple cysts in the transplanted kidney, with appearances suggestive of a polycystic kidney.

Case Report

The patient is a 63 year old gentleman with end stage renal failure secondary to autosomal dominant polycystic kidney disease. He received a cadaveric renal transplant in July 2003. The patient had a complex post-transplant period with urological complications and developed chronic graft dysfunction, with the transplant failing twelve years later. Of note also, in 2007 the patient had an open appendicectomy for a mucinous cystadenoma of his appendix. As part of his assessment for a further transplant, this time from a live donor, the patient has undergone a computed tomography scan. This has revealed an enlarged transplanted kidney with multiple cysts up to 4.5cm in size. Previous ultrasonography in 2014 detected multiple simple cysts in the kidney, however earlier scans did not detect these. The donor was a 66 year old male with hypertension, but no history of renal disease and preserved function with a creatinine of 73. The other recipient of the kidney died in 2008 of pneumonia, but had good transplant function prior to this.

Discussion

There have been rare cases of donated polycystic kidneys and the question has been raised previously as to whether known polycystic kidneys should be used for transplantation when renal function is preserved [1]. In this case, the transplant functioned for 12 years despite other complications, supporting the notion that polycystic grafts may have reasonable survival times. The donor was 66 years of age and it is unusual to develop cysts after this age in polycystic kidney disease. To our knowledge, there are few reports of polycystic change occurring de novo in transplanted kidneys and it is of further interest that the patient has autosomal dominant polycystic kidney disease himself. He will now require a transplant nephrectomy prior to receiving a new transplant due to the enlarged size of the kidney. Histopathological examination will therefore be possible enabling further assessment of the kidney.



Reference

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Recurrence of Tubulo-Interstitial Nephritis without Uveitis, in a patient with previous TINU syndrome post transplantation

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Introduction

Tubulo-interstitial nephritis and uveitis (TINU) syndrome is a rare and poorly understood condition. We are describing the clinical course of a 26 year old renal transplant recipient, whose primary renal disease was TINU syndrome, presenting with a flare up of tubulo-interstitial nephritis following a reduction in immunosuppression nine years after transplantation. Aim of this report is to try to connect possible negative influence of reduction of immunosuppression on the recurrence of this disease and highlight possible patho-physiology.

Methods

We report a case of Recurrent Tubulo-Interstitial Nephritis without Uveitis, in a Patient with Previous TINU Syndrome Post Transplantation; A 26 year old gentleman who was diagnosed with TINU syndrome at the age of eight. He developed end stage renal failure and underwent live donor related renal transplantation at the age of 17 . 1st recurrence of TINU occurred 36 months post -transplant and treated with increased immunosuppressive drugs. Renal function worsened again to eGFR of 25 (mls/min/1.73m2) at 76 months post-transplant .No further drug history was reported apart from immunosuppressive medications.

Results

Transplant ultrasound was unremarkable. Virology tests; CMV, BK virus and EBV were all negative, with negative donor specific antibodies and negative TB tests. Urine protein creatinine ratio was unremarkable. Immunology and serum ACE were negative. Biopsy at the time showed chronic sclerosing allograft nephropathy and immunosuppressive drugs were decreased subsequently. Following that there was a decline in renal function over the next 3 months down to an eGFR of 18 (mls/min/1.73m2). A further renal biopsy showed granulomatous interstitial nephritis and moderate interstitial fibrosis. This was consistent with a further relapse of Tubulo-Interstitial Nephritis without uveitis. His renal function improved following the re-introduction of Tacrolimus.

Discussion

The recurrence of TIN, despite the absence of uveitis, in this patient following a reduction in immunosuppression is a rare occurrence and has not previously been reported in this context. The relapse of TIN in our renal transplant recipient following a reduction in immunosuppressive treatment certainly lays weight to the existence of a circulating autoantibody capable of causing recurrence of the disease that was dependent on reduction of immunosuppression drugs.

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Kidney biopsy allows the diagnosis of pancreas rejection in simultaneous pancreas-kidney (SPK) transplant recipients with isolated pancreas dysfunction

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Introduction

Simultaneous pancreas and kidney (SPK) transplantation provides an excellent treatment for patients with diabetes and associated end stage renal failure. Elevation of pancreatic enzymes (amylase (AMY) & lipase (LIP)) post-transplant may indicate rejection, but pancreatic biopsy poses a challenge due to the intra-peritoneal location of the graft. We wished to determine the efficacy of kidney biopsy to secure a diagnosis of rejection in patients with isolated dysfunction of the pancreas.

Methods

We performed a single centre, retrospective review of allograft biopsy practice and outcome in n=200 consecutive SPK recipients transplanted between 2001-2015. We sought to ascertain: 1. The frequency, timing, method (percutaneous versus open), & indication for allograft biopsies (kidney and pancreas). 2. The frequency of complications. 3. The frequency of rejection in kidney biopsies performed in patients with isolated elevation in AMY and LIP in the absence of an increase in creatinine.

Results

59.0% of SPK recipients underwent biopsy, 47.5% kidney, 2.5% pancreas, 9.0% both. Biopsies were most commonly undertaken in the first 6 months post-transplant (median time of biopsy = 118 days). Significant complications were rare; for kidney, the complication rate was 4.4% for percutaneous biopsy and 0.0% for open biopsy. For pancreas, the complication rate was 10.0% for percutaneous biopsy and 11.8% for open biopsy. N=41 patients underwent kidney biopsy with isolated elevation of pancreatic enzymes. 61.0% (n=25) of these biopsies demonstrated rejection. Of the remaining n=16, only 1 underwent a pancreas biopsy. 69% of the remaining patients were treated empirically for rejection, 82% of these responded.

Discussion

1. Kidney biopsy allows the diagnosis of rejection in more than half of patients with isolated pancreas graft dysfunction, confirming its utility as a first line diagnostic test in this patient group once the vascular supply of the pancreas has been assessed.
2. Pancreas biopsy was not associated with a high frequency of complications, suggesting that it could be undertaken more frequently when the cause of allograft dysfunction is unclear.

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The assessment of ex-vivo human pancreata using magnetic resonance imaging

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Introduction

Outcomes following pancreas transplantation are closely linked with the pre-operative condition of the organ. Increased fat content is recognised as leading to poorer outcomes following implant. However, current assessment of the allograft prior to implantation is entirely subjective, leading to inevitable variation between surgeons and potential underutilisation of suitable organs.

Magnetic Resonance Imaging (MRI) provides the ability of viewing tissues non-invasively, leading to a possible method of critically analysing organs and therefore providing an objective method of assessing pancreata prior to implantation.

We aimed to conduct a preliminary study to assess the feasibility of conducting MRI on ex-vivo human pancreata and explore the potential advantages of MRI assessment in the evaluation of the organ prior to transplantation.

Methods

Those pancreata deemed unsuitable for transplantation underwent MRI on a Philips Achieva 3.0T system. Pancreata were scanned in 3 bags containing UW preservation solution, surrounded by a further bag of ice. MRI protocols were developed to acquire high-resolution 3D volume images of water and fat, and of T1 and T2 weightings within the specimen at 4°C. With experience of technique scan times reduced from 3 hours to 20 minutes.

Results

Images from water and fat protocols at equivalent sections of an ex-vivo pancreas, deemed unsuitable to transplant are presented, indicating excellent differentiation and identification of fat and “other” tissue within the specimen.

Conclusions

MRI appears to be a feasible method of assessing ex-vivo human pancreata with respect to fat content. Based upon the calculated protocols used in this study and the results presented, it is possible that in the future, MRI could be a valuable tool in aiding clinicians to objectively assess suitability of pancreata prior to implantation without adversely prolonging cold ischaemic times.

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High postoperative tacrolimus variability predisposes to early pancreas graft loss

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Introduction

The therapeutic index for tacrolimus (Tac) is relatively narrow and can vary postoperatively in pancreas transplant patients secondary to drugs, diabetic gastroparesis and changes in bowel motility. Variable blood drug concentrations have been shown to be a risk factor for rejection and long-term allograft nephropathy in kidney transplantation. We hypothesised that inpatient Tac variability (%Coefficient of Variance; %CoV) would influence early patient outcomes after pancreas transplantation despite our use of Aleumtuzumab depleting antibody induction.

Methods

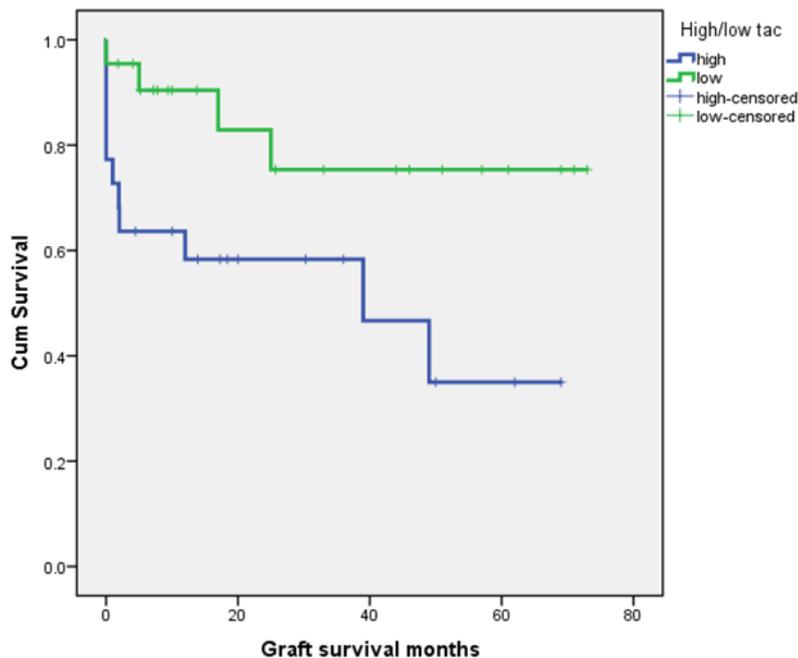
We retrospectively reviewed patients undergoing pancreas transplantation between 2009 and 2014 and calculated the %CoV using their inpatient Tac levels (Borra 2010; mean Tac trough level/standard deviation Tac trough level) x 100). Patients were then separated into 2 groups HIGH and LOW variability depending on their relationship to the median and outcomes were compared.

Results

During the time period 45 patients underwent pancreas transplantation (1 excluded graft loss within 24 hours). Tac %CoV ranged between 19.02% and 114.9% with a mean of 46.95% (median value of 45%). Patients with a value >45% (HIGH) had a 1 yr survival of 58.3% vs. 83% (p=0.026).

Discussion

Tac%CoV is much greater in pancreas transplant recipients when compared with kidney transplant recipients (Borra; Mean 24.2% in HIGH group and Mean 14.2% in LOW group). Even in the modern era with Campath induction, it is possible that more grafts are being lost to rejection related complications than we had previously realised.



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Virtual crossmatching for pancreas transplantation reduces total ischaemic time and is immunologically safe

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Introduction

The pre-transplant crossmatch test is used to predict the likelihood of hyperacute rejection resulting from pre-formed donor directed antibodies. This is achieved through incubation of donor lymphocytes and recipient sera and performance of complement dependent cytotoxicity (CDC) or Flow Cytometry. Luminex assays use synthetic microspheres coated with HLA antigens to capture antibodies present in a serum sample, offering enhanced specificity and sensitivity to traditional methods. Human Leukocyte Antigen (HLA) specificities that would be unacceptable can be avoided. Using Luminex-based antibody screening, it is acceptable to predict that a patient who has no HLA specific antibodies would be crossmatch negative, and could safely be transplanted without the need for a laboratory crossmatch, providing that the recipient has not experienced any potential sensitising events since their last serum sample. This is the basis of the Virtual Crossmatch (VXM). VXM can be extended to include sensitised patients with clearly defined HLA antibody profiles. Using the Single Antigen Bead test, a complete antibody profile can be clearly recorded and regularly updated for each patient. When a donor offer is received, the donor HLA type can be compared with the HLA antibody profile of the patient. This carries much greater immunological risk, relying upon robust HLA typing of the donor and precise recording of potentially sensitising events. If a patient is transplanted on the basis of a VXM, the laboratory crossmatches are performed as soon as possible after receipt of crossmatch material. VXM can be used to eliminate the 4-6 hour delay caused by a pre-transplant crossmatch and, thereby, reduce total ischaemic time (TIT).

Methods

A retrospective analysis of all solid-organ pancreas transplants performed between 1st January 2009 and 31st December 2014 was undertaken. Data on crossmatch type, TIT and donor hospital distance were collated and analysed. For patients who had a VXM, retrospective CDC crossmatches were performed on all patients, and Flow Cytometry crossmatches were also performed on sensitised patients with a reaction frequency of >50%.

Results

159 pancreas transplants were performed in the specified time period. 97 (61%) patients were transplanted on the sole basis of a negative VXM result. A pre-transplant crossmatch (CDC/Flow) was performed in the remaining 62 (39%) cases. Median TIT in the VXM group was 620.5minutes versus 888 minutes in the pre-transplant crossmatch group ($p < 0.0001$). There was no significant difference in donor hospital distance. 100% of the VXM group had subsequent negative retrospective CDC/Flow crossmatch results. There was a significant increase in the use of VXM for pancreas transplant during the study period ($p < 0.0001$).

Discussion

Since 2009 our unit has significantly increased the use of VXM. In our experience, VXM is immunologically safe and significantly reduces TIT resulting in improved outcomes following pancreas transplantation. It is considered that the increased risk of performing a VXM in a sensitised patient is far outweighed by the benefit of reducing the TIT.

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Bladder drained pancreas transplants and urinary anti-microbial peptides

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Introduction

Bladder drainage (BD) of pancreas transplants has historically been favoured to monitor graft function. However, urological complications (UCs) such as urinary tract infection and chemical urethritis often necessitate conversion to enteric drainage (ED). Innate defences, including antimicrobial peptides (AMPs), are essential in defending the urinary tract against infection.

Aim: To investigate the effect of pancreatic enzymes on the AMPs human-beta-defensin 2 (HBD2) and lipocalin-2 (LCN2).

Methods

HBD2 and LCN2 urine concentrations in 3 patient groups [pancreas transplants with BD (n=14), ED (n=12) and renal transplant controls (n=9)] were measured by ELISA and correlated with data on incidence of UC's obtained from retrospective analysis of clinical notes. RT4 bladder epithelial cells were challenged with uropathogenic Escherichia coli or flagellin in presence/absence of pancreatic enzymes and HBD2 and LCN2 gene expression measured by qPCR. AMP functionality was assessed using time-kill antimicrobial assays.

Results

Overall BD pancreas transplant patients had more UCs (79%) than ED (33%) or controls (11%) (p<0.05). No significant difference was observed in urinary HBD2 concentrations between the 3 groups (BD vs. ED vs. controls, ANOVA p=0.6162) or for LCN2 urinary concentration (BD vs. ED vs. controls, ANOVA p=0.7807). Pancreatic enzymes did not affect HBD2 or LCN2 gene expression in RT4 bladder cells nor did they have a statistically significant impact upon functionality.

Discussion

We conclude that the higher incidence of UCs seen in BD pancreas transplant is not due to the influence of pancreatic exocrine secretions on bladder AMP concentration, expression or functionality. Other mechanisms such as loss of epithelial biolayer integrity or neurological bladder dysfunction may play a more important role.

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The value of early protocol computer tomography and endovascular intervention in pancreas pransplant

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Introduction

Early vascular complications following pancreatic transplantation are not rare (3-8%), and represent a non-immunological cause of graft failure. The most common vascular complication is graft thrombosis, either venous or arterial. If occlusion is complete it is difficult to treat and rates of graft failure are high. Typically scans are requested in response to clinical change. We instituted a change in protocol to request scans to pre-emptively identify patients with thrombotic complications

Methods

In early 2013, following a review of our pancreas transplant protocol, we now routinely perform CT angiography at days 3-5 and day 10 following pancreas transplantation. A retrospective analysis of all pancreas transplants performed at our institution from January 2013 to October 2015 was undertaken. Patient medical records, a computer database and hospital computer electronic patient records were studied to identify cases with pancreatic graft thrombosis.

Results

17 patients have now received pancreas transplant with the new protocol. 7 (41%) of the early protocol scans identified asymptomatic vascular complications. 4 (23%) of the 7 patients had venous complications and successful endovascular salvage using combination thrombolysis and stents was possible in all 4 patients. A further 3 (18%) patients were noted to have arterial thrombosis of either the donor SMA or splenic artery. These grafts remain perfectly functional (follow-up 3, 6 and 11 months) perfused by a single vessel and under close radiological/ clinical follow-up. Since the change in our protocol we have not had a single graft loss due to a non-immunogenic cause. Moreover, all 7 cases with identified thrombosis have a fully functional graft.

Discussion

Implementation of early protocol CT scanning identifies a large number of patients with subclinical venous and arterial graft thromboses that are potentially amenable to endovascular techniques. However, we are unclear if intervention has altered the clinical course post transplant.

P139

Abdominal wall reconstruction for large ventral herniae after pancreas transplantation: a single centre experience

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Introduction

Patients undergoing pancreas transplantation are at an increased risk of developing ventral herniae due to previous brittle diabetes, immunosuppression and potential immediate post transplant wound complications. The ventral herniae in these patients are often associated with significant domain loss which may not be amenable to repair by conventional hernia repair techniques. Such ventral herniae not only affect the quality of life in these patients but also potentially threaten graft survival. Abdominal wall reconstruction (AWR) is a major undertaking and has been reported to have a high morbidity risk (upto 50%) even in non-transplant patients. The goal of this study was to review our experience and outcomes in patients that underwent AWR post pancreas transplantation.

Methods

We performed a retrospective analysis of our database to identify patients that underwent AWR post pancreas transplantation. Data collected included duration of diabetes pre-transplant, body-mass index (BMI), interval between pancreas transplantation and AWR, prior incisional hernia repairs post transplant, hernia grade as per the ventral hernia working group (VHWG) grading system, size of the defect, bio-prosthetic material and technique used for AWR, complications, length of stay, graft function and recurrence.

Results

Six (6) (4 male and 2 female) patients underwent AWR after simultaneous pancreas and kidney transplantation. The mean age of the patients was 40.5 (31-54) years and the mean BMI was 25(22-29) kg/m². Duration of diabetes prior to transplantation was 23.6 (17-36) years and the interval between pancreas transplantation and AWR was 2.2 (1.19- 3.52) years. 33% (2/6) patients were grade 3 herniae and 67% (4/6) were grade 2. 33%(2/6) had a recurrent hernia following previous incisional hernia repair post transplantation prior to AWR following early occurrence of an incisional hernia. One of these patients had an onlay polypropylene mesh repair while the other had a primary sutured repair. Mean size of the hernia defect was 17 (15-25) cm². A non-cross-linked porcine acellular dermal matrix based bio-prosthetic mesh was used in 50% (3/6) of the cases while a non-cross-linked non-dermis based bio-prosthetic mesh was used in the other half of the patients. The mesh was placed in the retro rectus space using the suspension technique in 67% (4/6) cases. In the remaining two cases the mesh was also sublay but intra-peritoneal as there was no healthy peritoneum or hernia sac to close the peritoneal space. Non-cross-linked porcine acellular dermal matrix based bio-prosthetic mesh was used for intra-peritoneal placement. All repairs were reinforced with a polypropylene onlay mesh. Anterior component separation was also performed bilaterally in 33%(2/6) and unilaterally in 16.6%(1/6) patients. Mean length of hospital stay was 6 (5-8) days. Dual graft function remained preserved and none of the patients had any complications post AWR. At a mean follow up of 13.5(4-23) months, no patients have had a recurrence, although one patient has developed a de novo hernia.

Discussion

Our small case series appears to suggest that AWR using non-cross linked bio-prosthetic meshes is feasible and safe with good results and has no impact on graft function. A longer duration of follow up and a bigger sample size is required for definitive interpretation. Given the high morbidity risk with AWR, these cases are best performed at specialist units with experience in abdominal wall reconstruction.

P140

Symptomatic orthostatic hypotension following simultaneous pancreas and kidney (SPK) transplantation

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Introduction

SPK transplantation restores insulin secretion & treats end stage renal failure (ESRF)-associated with diabetic nephropathy. However, many patients also have significant neuropathy, particularly autonomic neuropathy (AN), manifest as orthostatic hypotension (OH) and gastroparesis (GP). SPK transplantation may result in improvement in peripheral neuropathy, but the impact on AN is less clear. Indeed, studies suggest that early symptomatic OH may be an SPK-specific complication occurring with minimal AN, due to hyperinsulinaemia.

Methods

We performed a single centre, retrospective review of n=143 SPK recipients transplanted between Jan. 2008 and Sept. 2015. With regards to symptomatic OH & GP, we sought to ascertain 1. The frequency pre- and post- transplant, 2. Treatments and their efficacy, 3. Risk factors. We hypothesised that restoration of renal function/normovolaemia may unmask OH previously ameliorated by the intravascular volume overload associated with ESRF.

Results

Symptomatic AN was reported in 31% of patients during post-transplant follow-up, typically occurring within 3 months (median presentation 69 days post-transplant). OH occurred in 89% of affected subjects, and GP in 15%. 25% of patients with symptomatic OH had no previous history of AN prior to transplantation. A higher proportion of patients who developed symptomatic OH had received haemodialysis pre-transplant, compared with those who did not have OH (42% versus 26% respectively, $p=0.02$). There was a trend towards better renal transplant function in patients with OH compared to those without (3 month creatinine 97 μ mol/L versus 116 μ mol/L respectively). More than half of those affected (55%) received treatment with fludrocortisone or midodrine due to severity of symptoms. At 6 post-transplant, symptomatic PH had resolved in 85% of those affected.

Discussion

Our data suggest that symptomatic OH is a common problem in the early post-transplant period following SPK transplantation and may occur in patients with no obvious OH prior to transplantation.

P141

Biomarkers in the peri-operative period following simultaneous pancreas and kidney transplantation

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Introduction

Patients undergoing simultaneous pancreas and kidney transplant (SPKT) suffer with a significant clinical inflammatory response. However, neither the inflammatory marker (IM) nor the diabetes marker (DM) profiles are defined, despite the potential utility these may have in prognosis prediction and management of peri-operative care, post-SPKT. This study aimed to determine the expression of these biomarkers following SPKT and establish a correlation to clinical outcome.

Methods

The temporal patterns of pro- and anti-inflammatory cytokines (interleukin (IL)-6, -10 and TNF- α), IM's (white cell count (WCC) and CRP) and DM's (insulin, C-peptide, glucagon and resistin) were serially measured at 8 time-points in the first 72 hours post-SPKT. Each marker was measured using Bioplex multi-bead array based system and the results correlated to clinical outcome measures.

Results

46 patients were recruited to the study.

Levels of C-peptide, insulin and glucagon were significantly negatively related to prolonged CIT within the first 72 hours post-pancreas perfusion ($p < 0.05$, linear regression model).

In addition, 48-hour levels of CRP (mean 132.14mg/L (SD 84.73)) correlated significantly with the post-operative morbidity survey on days 5, 7 and 10, total number of complications and the time taken for patients to mobilise post-operatively ($p = 0.001, 0.019, 0.015, 0.007$ and 0.005 respectively, Spearman Correlation).

Finally, levels of pro-inflammatory markers, TNF- α and IL-6 peaked at 30 minutes post-pancreas perfusion, compared to anti-inflammatory marker, IL-10, which peaked at 6 hours post-perfusion ($p < 0.05$, ANOVA). The temporal evolutions of amylase and WCC were also delineated, but did not correlate to any clinically relevant outcome.

Discussion

It is acknowledged that increased CIT correlates to poorer clinical outcomes following pancreas transplantation. For the first time, to our knowledge, we find that increased CIT also correlates to poorer pancreatic endocrine function immediately post-SPKT. In addition, we show that 48-hour CRP levels provide an early, easily measurable predictor of inpatient morbidity. Finally, the pattern of activity of IM's defined in this study provide evidence for the potential use of targeted anti-inflammatory therapies in the peri-operative period.

P142

Comparative outcomes of induction agents in simultaneous pancreas and kidney transplantation

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Introduction

Alemtuzumab is a humanized monoclonal antibody directed to CD52. Its use in pancreas transplantation is attractive as it facilitates steroid avoiding maintenance immunosuppression. However, it is associated with profound and prolonged lymphocyte depletion. There is a paucity of data on long-term patient and pancreas allograft survival, particularly when compared to the interleukin-2 antagonist, Basiliximab. We aim to compare our unit outcomes for both agents.

Methods

We undertook a retrospective, single centre, non-randomised, sequential study of patients receiving a pancreas transplant between June 2001 and June 2014. Patients receiving their second transplant were analysed separately.

Results

270 primary transplants were performed of which 61% received basiliximab and 39% alemtuzumab induction. There was no significant difference in age or gender between groups. More patients in the alemtuzumab group had received organs from a non-heartbeating donor ($p=0.042$). Comparing basiliximab to alemtuzumab, there was no significant difference in graft survival at one year (74.1% vs. 83.7%, $p=0.0791$), three years (69.6% vs. 79.7%, $p=0.0649$) or five years (60.9% vs. 71.8%, $p=0.1339$). Patients receiving alemtuzumab had significantly better one year survival ($p=0.017$), however this difference did not persist at three years $p=0.051$ or five years $p=0.155$. Regarding patients receiving a second transplant, there were no significant differences between both agents for allograft or patient survival.

Discussion

Alemtuzumab and basiliximab induction are equivalent for mid and long-term pancreas allograft survival. Alemtuzumab is associated with improved one year patient survival, however, a prospective randomised controlled trial is required to establish which agent is superior.

P143

Review of UK-wide practice of pancreas transplantation: donor selection, backbench preparation and implantation technique

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Introduction

Since the first pancreas transplant, refinements in surgical technique, organ preservation and availability of novel immunosuppressive therapies have improved patient and graft-survival rates in long term. However, existence of variability of surgical technique in pancreas transplantation might explain difference in outcomes between centers.

Methods

The current UK-wide practice of pancreas transplantation was reviewed on the basis of an online survey to assess current opinions about donor selection, back-bench preparation and implantation technique. The survey was sent to consultant pancreas transplant surgeons practicing at 8 transplant centers in the UK.

Results

27/31 (88%) consultants completed the survey. 84% (21/25) would accept pancreas offers (DCD/DBD) with <16 hrs of predicted CIT. 72% (18/25) agreed to 60 years as upper limit of donor age. 63% (17/27) accept donor BMI of 30 as upper limit. 55% (15/27) surgeons did not have a uniform pancreas benching technique; 15/23 used haemostatic devices for pancreas benching. 74% (17/23) used continuous sutures for Y-graft arterial reconstruction. 85% (22/25) bury the duodenal staple line. 95% (25/27) surgeons used midline incision for pancreas transplant and 96% preferred intra-peritoneal placement. 54% (14/26) placed pancreas head-up and 67% (16/24) placed kidney intraperitoneally. IVC was used for portal venous drainage by 85% (22/26) surgeons and 81% (21/26) used common iliac artery for inflow. Jejunum and ileum was used for exocrine drainage by 43% and 46% surgeons respectively with 92% (22/24) using hand sewn double layer continuous anastomosis technique.

Discussion

This first ever UK survey was conducted to formally assess the variability in pancreas transplantation practice both between and within transplant centres. Non-uniformity in practice may explain the varied outcomes following pancreas transplantation.

P144

Bladder-drained pancreas transplants in the modern era

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Introduction

There has been ongoing debate over the optimal method of exocrine drainage from pancreas transplants for many years, with continued lack of consensus. There are clear advantages and disadvantages to each. Of particular note, bladder-drained pancreas transplants have the advantage of measuring urinary amylase:creatinine ratio as an early marker of rejection or vascular compromise. Conversely, bladder-drainage has its own inherent disadvantages, predominantly long-term urinary complications and bicarbonate losses.

Methods

We performed a retrospective analysis of 51 consecutive pancreas transplants in a single centre over a 7-year period (2008-2015). We analysed short-term outcomes and rates of complications.

Results

There were 19 enteric-drained (ED), 32 bladder-drained (BD). Median length of stay was 22 days ED vs 26 days BD ($p=0.24$, M-W u). Mean relaparotomy rate was 0.53 (0-3) ED, 0.78 (0-4) BD ($p=0.39$, t-test), the most common reason for relaparotomy was bleeding in both groups. 2 patients from BD group have had enteric conversion due to intolerable urinary symptoms, time-lapse to conversion were 6 months and 13 months. A further 2 BD patients have known urinary symptoms, but do not wish to have enteric conversion. There have been 4 anastomotic leaks (2 ED, 2 BD), and a further patient who had a leak from the bladder anastomosis site following graft pancreatectomy (controlled by catheterisation). We found no significant difference in graft survival (log rank=0.27) or patient survival (log rank=0.10) between the two groups. Although the median graft survival was longer in BD group (1179 vs 761 days).

Discussion

Our experience demonstrates that bladder-drainage of the exocrine pancreas is a safe option, with the advantage of the ability to non-invasively monitor for evidence of graft rejection or vascular compromise. This comes at the cost of potential urinary complications, at which point enteric conversion can be considered. Our data showed comparable graft and patient survival between the two groups.

P145

Contrast enhanced ultrasonography in simultaneous pancreas and kidney transplantation

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Introduction

Vascular complications following simultaneous pancreas and kidney transplantation (SPKT) remain the most common causes of peri-operative graft loss. Currently, investigative options are expensive, often cumbersome, involve ionising radiation and potentially nephrotoxic contrast agents and therefore cannot be used for screening.

Contrast enhanced ultrasound (CEUS) combines conventional B-mode ultrasound with microbubble contrast technology, providing a safe, cheap, reiterative and bed-side imaging modality to assess potential complications following SPKT. This study aimed to evaluate the feasibility of conducting CEUS in the peri-operative period following SPKT and assesses the potential benefits of the technique in this cohort of patients.

Methods

CEUS was carried out on the Intensive Care Unit by a dedicated transplant radiology team within 72 hours post-SPKT. SonoVue was the contrast agent of choice.

Results

12 SPKT recipients were recruited to the study (10 male (83.3%), mean age 39.33 (SD 8.917) and mean BMI 25.99 (SD 3.14)). Primarily, CEUS was found to aid in the identification of pancreatic allograft vasculature and morphology when compared to standard B-mode and duplex US.

In addition, mean time from injection of, to visualisation of contrast within pancreatic parenchyma was 29.68s (SD 8.68s) and significantly correlated to serum amylase (145.5mmol/l (IQR 99.75- 309.5), $p= 0.019$ and $r= 0.799$, Spearman Correlation) on the day of imaging. There were no adverse effects of using Sonovue contrast agent.

Conclusions

CEUS is a feasible and potentially useful adjunct in the peri-operative assessment of allograft perfusion and morphology following SPKT and may negate the need for CT angiography. It appears to have utility in identifying acute inflammatory processes within the allograft pancreas.

P146

Assessment of the risks and benefits associated with prophylactic cholecystectomy and appendicectomy in simultaneous pancreas-kidney transplant recipients

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Introduction

In our unit, the transplant pancreas is placed intraperitoneally behind the right colon, in close proximity to the appendix. At the time of transplantation, patients undergo prophylactic appendicectomy to avoid confusion post transplantation. Likewise, following two cases of early cholecystitis post transplant, patients are screened for the presence of gallstones and undergo concurrent cholecystectomy if present. We undertook a retrospective audit to assess the benefits and risk of current practice.

Methods

A retrospective review of all patients who underwent SPK transplantation between 2001 and 2015 was performed. Deceased patients were not included.

Results

207 patients underwent SPK transplantation in the study period. Of these, 22 had undergone previous appendicectomy and 6 cholecystectomy. Of the remainder, 161 patients underwent appendectomy during SPK transplant, none of which resulted in intra-operative or post-operative complications. One patient was found to have an incidental 6mm carcinoid tumour extending into the mesoappendiceal fat, which was successfully treated with subsequent caecectomy.

31 patients were identified to have gallbladder calculi and/or polyps on ultrasound prior to surgery. Of these, 24 underwent cholecystectomy during SPK transplantation with no operative complications. Six gallbladders showed histological signs of chronic cholecystitis. Of the patients who did not undergo prophylactic cholecystectomy, 2 developed cholecystitis following transplantation and subsequently underwent cholecystectomy.

Discussion

Incidental appendicectomy and cholecystectomy at the time of SPK transplantation appears to be safe and beneficial.

P147

Dialysis exposure significantly worsens outcomes following combined kidney and pancreas transplantation

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Introduction

It is accepted that pre-emptive transplantation is beneficial for patients awaiting a kidney transplant. We examined the benefit of pre-emptive transplantation in our pancreas transplant programme.

Methods

Data on all 200 consecutive combined pancreas & kidney transplants performed between 13/01/2001 and 8/4/2015 were analysed with dialysis history prior to transplantation.

Results

Of the 200 transplants, 3 had no recorded data on dialysis exposure. Of the remaining 197 patients, 49 (25%) were transplanted before starting dialysis, 63 had been on dialysis less than one year, and 85 had been on dialysis for more than a year. Patient survival was non significantly poorer in those who had been on dialysis over a year (p=0.19). Pancreas transplant survival (not censored for death) was poorer in patients who had any exposure to dialysis (p=0.04, logrank) while kidney transplant survival was also non-significantly better in patients without prior dialysis exposure (p=0.3).

| | Pre-dialysis | < 12 months dialysis | > 12 months dialysis |
|---|--------------|----------------------|----------------------|
| Actuarial Patient survival | | | |
| 1 year | 100% | 100% | 97.6% |
| 5 year | 96.8% | 97.1% | 90.6% |
| 10 year | 96.8% | 97.1% | 83.7% |
| Actuarial Pancreas transplant survival | | | |
| 1 year | 95.7% | 91.9% | 88.4% |
| 5 year | 95.7% | 79.5% | 77.7% |
| 10 year | 95.7% | 74.8% | 60.8% |
| Actuarial Kidney Graft Survival | | | |
| 1 year | 100% | 96.7% | 95.4% |
| 5 year | 92.4% | 87.7% | 83.8% |
| 10 year | 85.3% | 49.3% | 53.3% |

Conclusion

Pre-emptive combined kidney and pancreas transplantation is associated with superior pancreas transplant survival.

P148

Pre transplant anti-islet antibodies do not predict early graft failure following simultaneous pancreas-kidney transplantation

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Introduction

Islet cell antibodies (ICA) are found in approximately 70% of patients with type 1 diabetes mellitus (T1DM). Their presence suggests β -cell destruction, particularly at the onset of disease. Post transplant appearance of ICA has been associated with "auto-immune" recurrence of diabetes. It is unclear whether the presence of ICA prior to transplantation has an adverse effect on graft survival.

Methods

A retrospective audit of all patients undergoing SPK transplantation between 2001-2015 was performed. Graft failure was defined as a return to insulin dependence. Graft failure due to thrombosis was disregarded, but a separate analysis showed it was not associated with ICA. Data were analyzed for significance levels using Fisher's Exact Test.

Results

A total of 213 patients underwent pancreas transplantation between 2001 and 2015. Of the 205 patients for which ICA results at the time of listing were available, 10 tested positive for ICA. Two of these developed non-thrombotic graft failure, compared to 17 of the 195 patients who tested negative for ICA and developed graft failure ($p=0.25$, Fisher's Exact Test).

Discussion

Recurrent T1DM is an uncommon but recognized occurrence following pancreas transplantation. By the time patients are listed for pancreas transplantation most are seronegative for ICA. The presence of ICA where at the time of listing for transplantation does not appear to predict graft failure.

Preventing Mycotic Haemorrhage after failed pancreas transplants: a novel technique

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Introduction

Arterial mycotic aneurysm formation is a rare but potentially lethal complication of pancreatic transplantation. Aneurysm rupture results in catastrophic haemorrhage with a high mortality risk. Endovascular stents have been utilised to achieve control of established mycotic aneurysms, however, there are no reports of their use pre-emptively to prevent pseudoaneurysm formation resulting from allograft pancreatectomy within a contaminated operative field.

Methods

We report on our unit's experience of prophylactic endovascular stenting using Atrium iCAST balloon expandable stents following failed pancreas transplant.

Results

Case 1: a 38 year old male underwent simultaneous kidney-pancreas transplantation (SPKT) from a 55 year old brain dead donor (DBD). On day 19, he developed a faeculent drain output and underwent emergency laparotomy at which a perforation of the donor duodenum was noted along with significant pancreatitis. He received a prophylactic Atrium stent to the right common iliac artery (CIA) on day 32, successfully excluding the donor arterial stump. The patient remains well after 24 months with no vascular complications.

Case 2: a 42 year old female underwent SPKT from a 43 year old DBD. On day 19 she underwent a transplant pancreatectomy, closure of jejunostomy and washout. A prophylactic Atrium stent was sited on day 21, effectively excluding the donor arterial stump. No vascular complications have occurred in the following 12 months, in spite of subsequent severe infective abdominal complications with the need for a laparostomy and drainage of recurrent abscesses at the site of the previous pancreas allograft.

Case 3: a 47 year old male underwent SPKT from a 39 year old DBD. On day 9 his condition deteriorated and an abdominal CT scan showed pneumoperitoneum requiring laparotomy and lavage on day 10. Re-exploration, on day 11, revealed an enteral anastomotic leak which was repaired with an omental patch and protected with proximal diversion ileostomy. After further deterioration, he underwent transplant pancreatectomy on day 19 following prophylactic Atrium stent insertion to the CIA. Unfortunately, the patient developed fatal fungal sepsis 3 months later. No vascular complications were reported prior to death.

Discussion

Allograft pancreatectomy within an infective field represents a significant surgical challenge. Prophylactic endovascular stenting before or shortly after allograft pancreatectomy in an infected field or with severe pancreatitis may reduce the risk of subsequent vascular complications arising from the donor arterial stump. This potentially minimally invasive and safe procedure could be life-saving and also prevent the need for emergency vascular procedures such as repairs or complex bypasses to prevent limb loss.

P150

A history of smoking has no effect on the outcome of pancreas transplantation: a single centre study

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Introduction

The long term benefits of combined pancreas and kidney (SPK) transplantation compared to kidney transplant alone are largely attributable to a reduction in cardiovascular disease. For this reason, and because of its procoagulant effects, all candidates for SPK transplantation at our centre are required to stop smoking before they can be listed. This study looks at the effects of their previous smoking history on outcomes post transplantation.

Methods

Data on all 200 consecutive combined pancreas & kidney transplants performed between 13/01/2001 and 8/4/2015 were analysed with respect to smoking history, diabetes history, and graft outcomes

Results

102 patients had never smoked, and 92 were ex-smokers, with no smoking history recorded for 6 patients. At the time of transplant smokers had had diabetes for a median 5 years less than non-smokers (24 vs 29 years, $p=0.05$ logrank). There was no difference in pancreas transplant survival (not censored for death) between the smokers and non-smokers, although the survival of those 6 patients with an unrecorded smoking history was significantly poorer ($p=0.02$). The actuarial 10 year pancreas transplant survival was 76.9% in the non-smokers and 71.2% in the smokers.

Conclusion

Smoking hastens the need for transplantation in patients with diabetes, but a past history of smoking before transplantation does not affect pancreas transplant outcomes.

P151

Successful simultaneous pancreas-kidney transplant without need for portal vein extension in recipients with transposition of inferior vena cava: a report on two cases

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Introduction

Left sided inferior vena cava (IVC) or Transposition of IVC (TIVC) is a variant course of IVC. Porto-systemic anastomosis in Simultaneous Pancreas and Kidney transplant (SPKT) in TIVC is surgically challenging due to frequent availability of short portal vein length with pancreas graft. TIVC is an on-table diagnosis as the recipient vessels are not radiologically assessed pre listing. Extension of portal vein may pose increased risk of venous thrombosis. No literature evidence exists with regards to SPK transplant with TIVC. We present 2 cases of successful SPKTs with this vascular variant.

Methods

Case 1: 34 year male underwent a DBD SPK transplant. TIVC was found. The pancreas was positioned head up on right side. The portal vein was 1.5 cm in length and was anastomosed to IVC, end to side, by parachute technique. The arterial Y-graft was anastomosed to left common iliac artery followed by duodeno-jenunostomy. The rewarm ischemia time was 34 min and cold ischemia time <12 hr. The patient made satisfactory recovery. The blood sugar is maintained between 5-6 mmol/l and serum creatinine has gradually stabilized around 160 µmol/l.

Case 2: 35 year female underwent a DCD SPK transplant. TIVC was found. The pancreas was positioned head up on right side. The portal vein was 2.0 cm in length and was anastomosed to left common iliac vein by 4-quadrant technique. The arterial Y graft was anastomosed to left common iliac artery followed by duodeno-jenunostomy. The vascular anastomosis time was 32 min and cold ischemia time was <12 hr. The choice of left common iliac artery for inflow was made in both cases as the graft after venous anastomosis sat on left of right common iliac artery.

Results

Post-operative recovery was unremarkable. The blood sugar is maintained between 4-5 mmol/l and serum creatinine has stabilized around 120 µmol/l. The kidney was transplanted in left iliac fossa intraperitoneally in both the cases and both patients were discharged 2 weeks post transplant.

Discussion

This report suggests that SPK transplant can be safely performed without portal vein extension in recipients with TIVC and the results are at par with normal venous anatomy transplants.

P152

Experience with Arterio-Enteric Fistulas and Pseudo-Aneurysms following pancreas or simultaneous pancreas-kidney transplantation

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Introduction

Aorto-enteric fistulas (AEF) and pseudo-aneurysms (PA) are rare but life-threatening vascular complications with a significant risk of graft loss. We share our unit's experience with these conditions and our learning curve in recognising, investigating and managing these complications.

Methods

We performed a retrospective analysis of all patients who developed AEFs and PAs in the 12-year period of performing simultaneous pancreas-kidney (SPK) or pancreas transplant alone in our unit.

Results

In total 16 patients (2% of 784 SPK and Pancreas transplant alone procedures) developed AEF or PA after transplantation (6 AEFs, 7 PAs and 3 cases of both PA and AEF). Acute intermittent gastrointestinal bleeding (56%, n = 9) was the most common presenting symptom; less common were abdominal pain (25%, n=4), significant haemoglobin drop (6%, n = 1), deranged blood glucose (6%, n=1) and increased serum creatinine (12%, n=2). Time to presentation ranged from 19 days to 6 years, with median time of 6 months.

Computed tomography angiography (CTA) was the investigative modality of choice (detected 75% of the lesions) whilst the remaining were found during emergency laparotomies and in one case by magnetic resonance angiography (MRA) that was later confirmed on CTA. Three grafts were salvaged by endovascular interventions – using coil embolisation or covered stents to control the source of bleeding whilst preserving graft perfusion. We also observed a high incidence of *Candida Albicans* (31%) in the organ perfusion fluid in these cases.

Discussion

Our described experience provides the largest series to date about AEFs and PAs after SPK and pancreas transplant alone procedures. AEFs or PA are to be considered in the differential diagnosis of patients with previous pancreas transplantation presenting with acute or intermittent gastrointestinal bleeding or unexplained haemoglobin drop. CTA appears to be the best investigative modality. Although clinical instability of the patient may influence the treatment option towards surgery, it is important to obtain early involvement of interventional radiology to establish inflow control for both PAs and AEFs as this is key in reducing morbidity in these cases.

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Ultrastructural glomerular features in biopsies from patients with De Novo donor specific antibody and in surveillance biopsies

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Introduction

Patients with *de novo* donor specific anti-HLA antibody (*de novo* DSA) are at increased risk of acute and chronic antibody-mediated rejection and graft loss. Identifying early detrimental effects of the antibody on the graft endothelium may help with diagnosis. Glomerular endothelium can show ultrastructural alterations such as cytoplasmic swelling and crenellation, loss of fenestrations, subendothelial rarefaction and new basement membrane formation. The aim of this study is to compare biopsies from patients with *de novo* DSA to surveillance biopsies from patients without DSA, to see whether some of these features are likely related to the effect of DSA on endothelium.

Methods

We performed ultrastructural examination of glomeruli in 40 biopsies: 15 1-year surveillance biopsies from DSA-negative patients, and 25 biopsies from patients with *de novo* DSA. Parameters recorded were: endothelial swelling, crenellation, and loss of fenestration, subendothelial rarefaction, new lamina densa formation and foot process effacement. Unpaired t tests (Mann-Whitney) were applied using GraphPad Prism 6.

Results

The surveillance biopsies showed no evidence of rejection and were C4d negative. Eleven of the 25 *de novo* DSA biopsies showed no microcirculation injury (MI = glomerulitis+ peritubular capillarities scores)(MI = 0 or 1); 14 had an MI score of ≥ 2 . Four of 25 had focal or diffuse C4d. In 36/40 biopsies, 30 glomerular loops were analysed, whereas 15, 15, 25 and 28 were available in the remaining 4 cases. There was a statistically significant difference between *de novo* DSA biopsies and surveillance biopsies for: mean endothelial swelling per loop ($p=0.03$), mean endothelial crenellation per loop ($p=0.02$), mean loss of endothelial fenestration per loop ($p=0.0001$), % of loops with new basement membrane ($p=0.02$), % of loops with double contours ($p=0.006$), and % of loops with extensive foot process effacement ($p=0.02$). There was no significant difference in mean subendothelial rarefaction per loop.

Discussion

Many glomerular endothelial cell and basement membrane features are significantly different between biopsies from patients with *de novo* DSA and surveillance biopsies. Further investigations will be carried out on a wider range of biopsies, and to evaluate the diagnostic utility of these features.

Impact of macrophage depletion on the development of chronic renal allograft damage

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Introduction

The proportion of renal allografts lost annually as a consequence of chronic allograft damage (CAD) has plateaued at 4%. An improved understanding of the various processes, including chronic rejection, that contribute to CAD is required to identify novel targets for therapies to prevent graft attrition. With roles proposed for macrophages in several of these pathways, this study aimed to define their importance in CAD by evaluating the effect of early macrophage depletion on the activities of intragraft cell populations in a murine model of chronic renal allograft damage.

Methods

Transplants were performed using BM12 (H-2^{bm12}) donors and C57BL/6 (H-2^b) recipients. Recipients were inoculated with a macrophage-depleting agent, liposomal clodronate (LC), or liposomal PBS (LPBS), at days 4, 7 and 10 post-transplant, and culled at 2 or 4 weeks. Transplants between C57BL/6 mice provided the isograft control group, culled at 4 weeks. Kidney sections were analysed by immunofluorescent TUNEL staining and immunohistochemical staining for markers of proliferation (Ki-67), T cells (CD3), regulatory T cells (Foxp3), B cells (B220), macrophages (F4/80).

Results

Intragraft macrophage numbers were significantly reduced at 2 weeks, with relative preservation of renal tubules, in association with LC administration. Rebound allograft infiltration by macrophages indicated recovery of the population at 4 weeks, with a loss of the early protective effect. Analysis of TUNEL staining demonstrated an association between macrophage depletion and a non-significant reduction in the proportion of apoptotic tubules at 2 weeks. Apoptosis was lower in 4 week versus 2 week LPBS-treated allografts ($P=0.0159$), with no observable differences between the 2- and 4- week LC-treated groups. CD3 staining analysis showed no impact of macrophage depletion on the extent of tubulitis in the renal cortex at 2 weeks. Furthermore, the extent of tubulitis was comparable between the 2- and 4-week LC-treated allografts, whereas it was lower in 4 week control allografts compared to their 2 week counterparts ($P=0.0317$). Similarly, analysis of the tubular proliferative response to injury (Ki-67 staining) at 2 weeks found macrophage depletion did not affect the percentage of tubules containing proliferating cells, in contrast to 4 weeks where only LC-treated allografts showed significantly higher tubular proliferation compared to isografts ($P=0.0190$). Macrophage depletion did not affect the total area covered by tertiary lymphoid organs (TLOs), assessed by staining for B cells, though a non-significant trend to delayed TLO organisation was observed. While the Foxp3⁺ T cell population had expanded in LPBS-treated allografts at 4 weeks compared to 2 weeks ($P=0.0079$), it remained relatively unchanged in 4 week LC-treated allografts compared to their 2 week counterparts. Finally, staining for Ki-67 and F4/80 showed comparable macrophage proliferation in the 2-week allograft groups, however at 4 weeks proliferation was higher in LPBS-treated allografts compared to LC-treated allografts ($P=0.0043$).

Discussion

These results indicate that macrophages do contribute to tubule loss in chronic allograft damage. However, the persistence of markers of graft injury in the absence of macrophages supports the existence of additional compensatory effector mechanisms. The impaired development of regulatory cell populations and loss of any early protection by 4 weeks post-transplant suggests early macrophage depletion may be more deleterious than beneficial. Further investigations are required to assess the long-term impact of early depletion, and of depletion at alternative time-points.

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Immunological risk of husband to wife renal transplants in the absence of DSA detected by luminex

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Introduction

It is known that patients with low level preformed donor specific antibodies [DSA] in the context of a negative FCXM/CDC cross match are at high risk of antibody mediated rejection [AMR] and graft loss. The immunological risk of females receiving a renal transplant from their spouse in the absence of preformed DSA detected by luminex has not been formally quantified. The aim of this study is to determine the additional risk posed by pregnancy on spousal transplants in the absence of preformed DSA.

Methods

We retrospectively analysed 93 wife to husband [WH] and 39 husband to wife [HW] transplants at our centre which occurred in the absence of preformed DSA on available current and historic sera. All patients received monoclonal antibody induction with a tacrolimus based immunotherapy protocol.

Results

The females of the HW pairs were younger [46.7±11.5v53.3±10.5 yrs, p=0.002] and more likely to be sensitised [35.9%v16.1%, p=0.02] but the median HLA mismatch was comparable [5(IQR:4-5)v5(IQR:3-5), p=0.71]. There was no difference in ethnicity, number of regrafts or pre-emptive transplants between the groups. Allograft outcomes in the first year and up to year 6 are shown below. There was a significantly higher risk of alloimmune injury in the HW group in the first year post-transplant.

| Event free survival [%] | HW Yr 1 | WH Yr 1 | p value | HW Yr 6 | WH Yr 6 | p value |
|-------------------------|---------|---------|---------|---------|---------|---------|
| Graft loss | 94.9% | 96.8% | 0.60 | 85.7 | 80.1 | 0.83 |
| Rejection | 78.7% | 82.4% | 0.60 | 69.3 | 67.6 | 0.82 |
| AMR | 86.7% | 96.7% | 0.03 | 83.5 | 90.1 | 0.22 |
| TG | 94.1% | 100% | 0.02 | 90.5 | 91.6 | 0.65 |
| DSA | 76.0% | 86.7% | 0.11 | 67.5 | 77.2 | 0.27 |

Discussion

This study shows that despite an absence of luminex positive DSA pre-transplant, male to female spousal transplants have a higher risk of early alloimmune injury, which is likely secondary to a memory response. Such patients should be considered as high immunological risk.

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Careful deselection of low risk unacceptable antigens can facilitate renal transplantation in highly sensitised patients with excessive time on the waiting list

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Introduction

Highly sensitised patients wait considerably longer for deceased donor transplantation. Modern histocompatibility testing techniques make it possible to monitor the HLA antibody profile of highly sensitised patients. This creates the opportunity to attempt transplantation against previously sensitising mismatched HLA antigens with a low risk of early, severe rejection. We report our early experience of deselecting low risk unacceptable antigens in highly sensitised patients.

Methods

Of 294 patients on the local waiting list, 68 had a calculated reaction frequency (cRF) >95% and 18 had been waiting > 6 years. 17 patients were identified in whom it was possible to de-list previously declared unacceptable antigens by the consultant clinical scientist who carefully reviewed each patient and where antigens were felt to be low risk such as historic weakly positive, or a low mean fluorescence intensity (MFI) <3000 by Luminex, these were deselected as 'unacceptable' for transplantation from the Organ Donation and Transplantation database. All patients who then went on to be transplanted had clinical data such as donor/recipient demographics, renal function, rejection and transplant and patient survival recorded.

Results

There were 11 female and 6 male patients in whom it was possible to deselect unacceptable antigens and 10 patients (76.9%) had a reduction in their CRF as a result. 13 of the cohort subsequently received a transplant between 03 Sep 14 and 19 Oct 2015. Of those receiving a transplant, mean age was 52±11.93 years, 8 had received ≥1 transplant previously and mean waiting list time for this transplant was 10.4±5.4 years. There were 10 DBD, 2 DCD and one live non-directed donor with a mean donor age of 49.92±13.94 years. The HLA mismatch levels were 1 at level 1 (000); 4 at level 2 (ODR and 0/1B) and 8 at level 3 (ODR and 2B) or (1DR and 0/1B). All patients had a negative T and B cell complement dependent cytotoxic crossmatch though 2 patients had positive flow cytometry T cell and B cell crossmatch. 7 patients received a transplant as a result of antibody deselection, transplanted against previously unacceptable antigens, and for 6 deselection made no difference in their offer. Mean cold ischaemia time was 17:09h. All but 2 patients were given rabbit anti-thymocyte globulin induction and all patients received prednisolone, tacrolimus and mycophenolate mofetil maintenance immunosuppression. Of the patients who have not received a transplant yet, 2 have been suspended from the list temporarily and 2 patients are still awaiting transplant. 6 patients (46.2%) had delayed graft function. 3 patients (23.1%) had acute rejection following transplantation, one cell mediated and 2 antibody mediated. One patient died of unrelated causes and maintained transplant function. No transplants have failed. Serum creatinines at day 7, 14, 1 month, 2 months, 3 months and 6 months were 301±229.37, 156±298.84, 145.5±219.46, 162±55.81, 143±45.91, 125±53.25 µg/L respectively.

Discussion

Highly sensitised patients can benefit from deselection of low risk unacceptable antigens to reduce the cRF and facilitate a transplant. This small study has found such patients to have good early transplant function with a low risk of acute rejection. Longer follow up is required to determine if these higher immunological risk transplants will continue to have adequate function and transplant survival.

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Renal ischaemia and reperfusion: the mitochondrial perspective

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Introduction

Due to the deficit of donor kidneys, there is an effort to utilise suboptimal organs for transplantation. These organs frequently experience warm ischaemia and are vulnerable to ischaemia- reperfusion injury (IRI) which causes delayed graft function and graft loss. Mitochondria have been implicated in this process through the production of reactive oxygen species (ROS) and isoflurane has been shown to have a protective effect through unknown mitochondrial mechanisms. Therefore mitochondria may be an important target and isoflurane a potential therapy to ameliorate IRI and increase graft survival. This research aimed to determine whether renal ischaemia - reperfusion injury affects the expression and function of mitochondrial electron transport chain (ETC) protein complexes, and to determine the effect of isoflurane pre-conditioning.

Methods

A murine surgical model was used to induce renal ischaemia and reperfusion through renal pedicle clamping. A variety of ischaemic and reperfusion times were used to identify mitochondrial changes. Isoflurane pre-treatment in a group of mice allowed analysis of its effect. After harvest, the kidneys were snap frozen and processed for mitochondrial analysis using Western Blot, Blue Native PAGE and in gel activity analysis.

Results

Ischaemia impacted the expression of mitochondrial ETC protein expression, increasing Complex III, IV and V levels. Ischaemia also affected function, decreasing Complex II activity. These changes were more pronounced with longer ischaemia and persisted in early reperfusion. Pre-treatment with isoflurane prevented these mitochondrial changes.

Discussion

The increase in Complex III levels and the reduction of Complex II activity indicate mitochondrial involvement in IRI and could contribute to cellular damage through ROS production on reperfusion. Isoflurane prevented these mitochondrial changes and therefore has potential to be a therapeutic agent for the prevention and treatment of IRI in transplantation.

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mTOR inhibitors & ischemia-reperfusion injury: role of endothelin-1

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Introduction

mTOR inhibitors are immunosuppressive agents used in maintenance immuno-suppression. De Novo early use of Everolimus and Sirolimus has increased in recent times. We have previously shown that mTOR inhibitors significantly influence the transmigration of immune cells after ischemia/reperfusion injury (I/R), which could explain a reduction of graft infiltration after early immunosuppressive treatment with these drugs. The aim of our study was to investigate the underlying mechanisms by which Everolimus and Sirolimus are able to reduce I/R.

Methods

An I/R model with human microvascular EC and human circulating immune cells (PBMC) was designed to evaluate the Endothelin-1 secretion of EC as well as the reactive oxygen species (ROS) production. ECs were either in naïve condition or activated with IFN- γ /TNF- α for 24h. After cell activation EC were placed under hypoxic conditions (<2% O₂) for 2h and were further treated before re-oxygenation with Everolimus (10ng/ml Certican® Novartis, Basel, Switzerland) or Sirolimus (10ng/ml Rapamune, Pfizer, NY, USA) for 2 and 24h. Untreated cells served as control and hypoxic cells served as positive control.

Results

The exposure of EC to I/R caused a significant increase of ROS levels. Treatment of naïve EC with Everolimus and Sirolimus for 2h could prevent the up-regulation of ROS production compared to the 24h EC treatment (naïve-EC Everolimus: 2h 1.75±0.07 FI vs. 24h 2.11±0.14 FI; naïve-EC Sirolimus: 2h 1.47±0.06 FI vs. 24h 1.88±0.09 FI). Prolonged Everolimus and Sirolimus treatment significantly reduced endothelin-1 secretion of activated EC (act-EC/act-PBMC Everolimus: 2h 26.0±1.0 pg/ml vs. 24h 16.2±0.6 pg/ml; act-EC/act-PBMC Sirolimus: 2h 25.9±0.8 pg/ml vs. 24h 16.0±1.2 pg/ml; act-EC/naïve-PBMC Everolimus: 2h 22.2±0.4 pg/ml vs. 24h 11.7±0.8 pg/ml; act-EC/naïve-PBMC Sirolimus: 2h 24.5±0.6 pg/ml vs. 24h 13.7±0.4 pg/ml).

Discussion

mTOR inhibitors are able to reduce the metabolic damage after I/R through reduction of ROS. It seems that the protective effect diminishes within short time and the application should already be started previous to severe inflammation. Everolimus and Sirolimus are also able to reduce Endothelin-1 production. In case of inflammation long time treatment with both immunosuppressive agents can positively affect Endothelin-1 levels, preventing endothelial inflammation

Assessment of candidate biomarkers for chronic rejection in post-transplant renal patients

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Background

Transplantation is the only treatment option for end stage kidney disease. However, post transplantation deterioration of graft kidney remains a common issue. This deterioration of graft function is compounded by current clinical measures of renal function allowing significant fibrosis to develop within the transplanted kidney without an obvious change in function.

We believe that the identification of molecular biomarkers will provide a quantitative phenotype allowing accurate, non-invasive and early diagnosis of chronic rejection. We investigate whether multiplexing of previously reported candidate biomarkers are better predictors of declining renal function than currently used clinical tests.

Methods

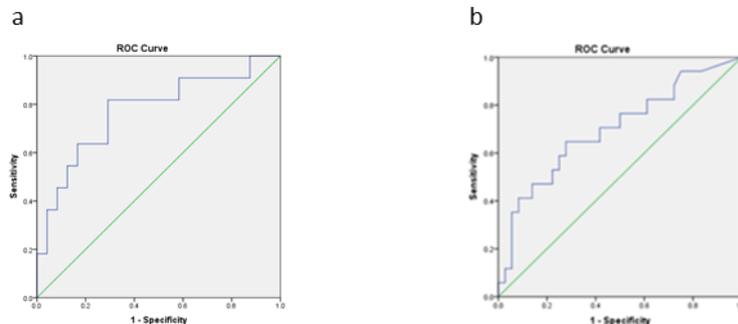
We have recruited a group of renal patients attending transplant clinics at Renal Services, the Freeman Hospital who are between 2 and 10 years post-transplant. The study cohort was stratified into groups with declining or stable renal function as assessed by their change in eGFR over the year prior to recruitment. Samples (serum, plasma EDTA, Plasma lithium heparin and urine) were collected, processed and then stored for use.

We examined a panel of previously published candidate biomarkers. The candidate biomarkers included regulators of complement, chemokines and regulators of fibrosis involved in function-limiting graft remodelling.

Results

The candidate biomarkers were assessed by Student's t-test and ROC curve analysis. A number of candidate biomarkers had significant p values, urinary protein: creatinine (0.016), PIIINP urine: creatinine (0.033), e-cadherin urine: creatinine (0.040).

ROC univariate analysis was carried out for the candidate biomarkers as illustrated in (a), Urinary PIIINP: Creatinine, Urinary e Cadherin: creatinine. ROC multivariate analysis was also carried out to examine if combining biomarkers improved the accuracy of the test (b) AUC was 0.715 for Urinary Protein: Creatinine, Urinary PIIINP: Creatinine, Urinary e Cadherin: creatinine, Urinary CCL2: creatinine.

**Conclusions**

A number of candidate biomarkers are associated with declining function in our cohort. However, on their own or in combination these molecules provide no more information than existing tests such as total urinary protein corrected for creatinine.

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The QUOD Biobank – A national bioresource aiming to identify relevant markers predicting organ transplantability and enhancing utilisation

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Introduction

In recent years the transplant community faced challenges regarding the extended quality of organs available for transplantation, leading to uncertainty regarding outcomes. In addition, there is a need for a more accurate donor and organ characterisation supporting clinical decision making at time of offering and preventing unnecessary discard of life saving organs. QUOD (Quality in Organ Donation) is a National Consortium developed in collaboration and funded by NHSBT. It aims to improve the quality of organs, develop better assessment criteria and prepare targeted intervention prior to transplantation, by providing biological samples from deceased organ donors to the transplant research community. To update and alert the UK transplant community we would like to present the potential of this resource to the attendees of the annual BTS Congress.

Methods

QUOD was established to create a UK national bioresource of samples with associated clinical data from organs from consented organ donors. It is a unique programme targeting DBD and DCD organ donors cared for in 62 hospitals across the UK. Over 500 individuals are involved nationally in the consenting, collection and processing procedures including 16 Histocompatibility and Immunogenetics clinical laboratories, all UK clinical organ retrieval teams and the SNODs (Specialist Nurses in Organ Donation), who obtain specific QUOD consent from donors' relatives.

Results

The rate of programme activities has now reached a steady state, in which between 9 and 22 new donors (14 on average) are being added each week. Current design of sample collection allows acquisition of approximately 15 samples from each donor on average, including several types of tissues (blood, urine, liver, kidney, spleen, ureter), several solutions or states for storage and assaying, and several time points (blood and urine). Since the start of the programme, over 16,000 samples were deposited in the QUOD biobank, contributed by more than 900 individual donors. Sample aliquoting and sectioning techniques were further integrated into QUOD biorepository processes, increasing the maximum capacity for separately available biospecimens to 110,000 biobank items (aliquots and tissue sections).

Discussion

These developments in programme scale, sample processing, and rich biobank content enable a wide range of scientific questions for new experimental enquiries. Major progress was achieved in connecting interests of research groups to the resources made available by the QUOD initiative. A total of 16 research applications has now been received and will be described as examples of research that can take place using this unique resource.

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Induction of immunosuppression with ATGs ameliorates microcirculation and reduces Leukocyte Adherence after ischemia-reperfusion-injury

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Introduction

The failure of translating results obtained in animal models into humans is a pivotal problem of research in transplantation. The aim of our study was to test the possible use of the human placenta in order to study the modulation of leukocyte-endothelial reactions through immunosuppression with rabbit ATGs after ischemia-reperfusion in a human model by means of intravital microscopy.

Methods

Human placentas (n=12) from elective caesarean deliveries were used after informed consent and IRB approval. All placentas were immediately connected to a monitored double perfusion system consisting of a two roller-pumps, reservoir, oxygenator, hemo-filter and bubble-trap. The placentas were reperfused with compatible human blood for 240 min after 60 minutes ischemia (perfusion with Ringer Lactate) after treatment with ATG (1mg/kg; Thymoglobuline, Sanofi, USA). Pressure, flow, and AVDO₂ were investigated. Biopsies were obtained after the experiments. Tissue expression of inflammation (IL-6, TNF- α) and adhesion-molecules (ICAM-1, PECAM, CD62E) was investigated by immunohistochemistry. Intravital Microscopy was performed to analyze adherence and infiltration of leukocytes.

Results

Our human placenta model could be validated for the study of inflammatory and vascular-endothelial reactions. The hemodynamic measurements were consistent within the single experiments and the AVDO₂ showed a continuous vitality of the perfused tissues. The blood cells counts were stable thorough the reperfusion, even in presence of ATG. Morphological and immunohistochemical analyses confirmed a normal configuration of placental tissue and its endothelium after 4 hours of reperfusion. Intravital microscopy was feasible and allowed quantification of adherent leukocytes, showing a reduction of the leukocyte adherence after Thymoglobulin treatment, and a better microcirculation.

Discussion

The isolated human placenta allows the study of functional human endothelium in a vascular structure. Our preliminary results show that this model is an adequate tool for the study of leukocyte-endothelial reactions after ischemia-reperfusion injury. Our results confirm in a human model the improvement of the microcirculation after induction of immunosuppression with ATGs.

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Detection of C1q binding IgG HLA-specific antibodies using C1qScreen is highly predictable based on antibody level and accounting for prozone effect and presence of denatured HLA

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Introduction

It has been argued that the C1qScreenTM is a reliable tool to distinguish complement binding from non-complement binding HLA-specific antibodies and is used to identify organ transplant recipients at high risk of antibody mediated rejection. It has been suggested, however, that the assay does not reliably differentiate complement fixing and non-complement fixing IgG isotypes, but instead C1q binding is influenced by single-antigen-bead (SAB) antigen levels, high-level IgG binding, prozone effect and interference by denatured antigen on SAB (dnSAB).

Methods

Untreated, EDTA treated (to obviate the prozone) and diluted (1:20) sera obtained from 25 highly-sensitised patients were tested using Luminex single-antigen HLA-class I antibody detection beads and using C1qScreenTM. SAB HLA-class I antigen levels and dnSAB were determined using W6/32 and HC10 monoclonal antibodies respectively.

Results

Using EDTA treated sera, for low-level (<10%) dnSAB, IgG-SAB-MFI was highly predictive of a positive C1q result (C1q-SAB-MFI >400), with an ROC-AUC of 0.96. The correlation between IgG-SAB-MFI and C1q-SAB-MFI was consistently lower using untreated serum and with increasing dnSAB levels. The highest specificity (94%, 95%CI: 90-96%) and sensitivity (94%, 95%CI: 89-97%) for predicting C1q-positivity (C1q-SAB-MFI >400), was observed at IgG-SAB-MFI >9000.

Conclusion

After correction for prozone using EDTA treated sera and taking account of dnSAB, results obtained using C1qScreenTM are highly correlated with results using the conventional IgG HLA-class I SAB assay. Correlations between C1qScreenTM and kidney allograft outcome are likely secondary to the presence of high-level IgG donor HLA-specific antibody. The high cost of performing a C1qScreenTM adds little clinical value.

Presence of day-14 post transplantation of donor specific IgM antibody predicts poor graft survival in HLA-incompatible renal transplantation

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Introduction

IgG antibodies against donor human leucocyte antigens (HLA) are monitored in the post-transplant period due to its established role in predicting rejection and renal allograft survival. Role of IgM donor HLA specific antibodies (DSA) is not fully understood, especially in highly sensitised patients undergoing direct transplantation. We designed this study to determine if additional post-transplant monitoring of IgM DSA predicts rejection episodes or graft failure.

Methods

Samples from 92 patients who had undergone HLA-antibody incompatible transplants were tested at 3 time points post-transplantation – days 7, 14 and 30 using Luminex microbead assay with EDTA containing wash buffer (LAB screen SAB, One Lambda, CA, USA). IgM was defined positive if the MFI values were greater than 2000. Presence of post-transplant IgM was correlated with early antibody mediated rejection (within day 30 post transplantation) episodes and graft failure. Statistical analyses were performed using SPSS IBM software (Fischer exact 2 tailed test at 5% significance level and Kaplan Meier survival analysis).

Results

Overall, post-transplantation IgM DSAs levels to the peaked at day 14 similar to IgG DSA levels (Figure 1, on the right). IgM DSA was positive in 32 patients (35%) of which 17 patients had an episode of antibody mediated rejection. IgM DSA was negative in 29 patients who had rejection. Presence of IgM DSA was not associated with rejection (P=0.83). However, post-transplant IgM is associated with predicting graft survival (p=0.37); particularly day 14 post-transplantation (p=0.008) (Figure 1). Day 30 IgM did not predict graft survival (p=0.46).

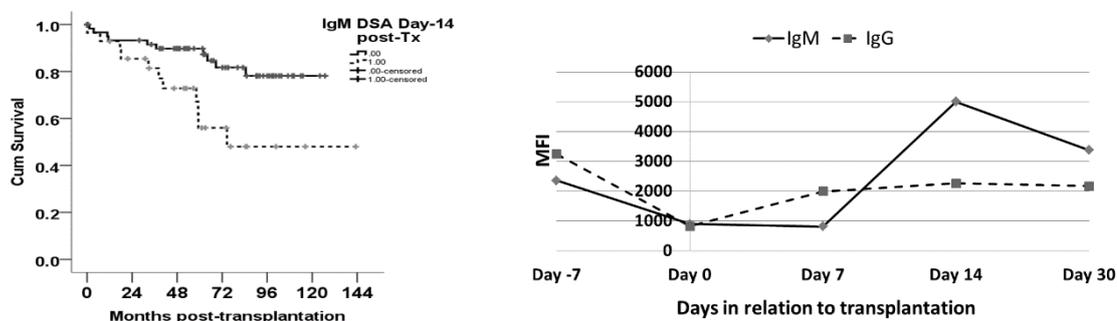


Figure 1: Day 14 post-transplant IgM DSA predicts death censored graft survival (Left) and post-transplantation dynamic of IgM DSA follows IgG DSA (right).

Discussion

This study shows additional value of post-transplantation IgM DSA measurement over and above IgG in prediction of death censored graft survival. The IgM monitoring did not predict episodes of antibody mediated rejection and the median trend of IgM levels was similar to IgG DSAs. This finding needs to be validated in multi-variate analysis and larger cohort in a multi-centre study.

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Targeted sequencing in kidney transplant recipients with post-transplant FSGS

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Background

FSGS after kidney transplantation is associated with poor graft survival. It has been previously reported that in familial forms of FSGS, the likelihood of recurrent disease after kidney transplantation is very low. We aimed to investigate the distribution of gene mutations in kidney transplant recipients with post-transplant FSGS by targeted sequencing.

Methods

20 adult kidney transplant recipients (16 male, mean age at recurrence diagnosis 49 years, range 25-70) who developed post-transplant FSGS were studied in a single renal unit in England. DNA was extracted from whole blood or saliva using standard protocols. An Illumina TruSeq Custom Amplicon Targeted Next Generation sequencing (NGS) panel was designed covering 21 genes for FSGS. NGS sequencing was performed on the MiSeq v3 system. Data were analysed using our standard Mendelian disease pipeline and all variants were confirmed by Sanger sequencing.

Results

3 rare, non-synonymous coding variants were identified, affecting 2 individuals. 2 variants were heterozygous dominant, and 1 X-linked recessive. The variants were identified in ITGB4 (2), and NFX5 (1). Only one variant (ITGB4) was predicted to be pathogenic by SIFT and/or Polyphen2.

Conclusions

We have shown a low frequency of potentially pathogenic variants in our kidney transplant recipients with post-transplant FSGS. Although it will not directly influence the treatment of the patients, this knowledge should be reassuring for patients with genetic forms of FSGS. Furthermore, it may enhance the likelihood of living donor transplantation in patients with familial or genetic FSGS, because a potential donor can be assured that the risk of graft failure due to recurrence is low.

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Modulation of the local and systemic Relaxin-System in patients with end-stage chronic heart failure

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Introduction

Relaxins are vasoactive peptide hormones with diagnostic and therapeutic relevance in patients with chronic heart failure (CHF). Clinical trials on acute heart failure patients have shown that Serelaxin treatment, a recombinant human relaxin-2, is safe, well tolerated and improves clinical outcome. Our aim was to investigate the local and systemic expression profiles of Relaxin-2 and Relaxin-3 and related molecules (iNOS, and MMP-9) in patients with end-stage CHF.

Methods

Patients suffering from CHF undergoing heart transplantation or LVAD implantation were included into the chronic heart failure group (CHF; n=7) and healthy myocardial tissue and blood samples from surgery patients with EF>65% served as controls (ctr; n=5). We analyzed the local and systemic expression of relaxin-2 and -3, MMP-9 and iNOS after informed consent. Myocardial tissue samples and blood samples of the patients were analyzed via immunohistochemical staining and ELISA analysis, respectively. Results are expressed as mean±SEM, whereas p<0.05 was considered as statistically significant.

Results

A significant higher protein expression level of relaxin-2 was detected in the CHF myocardial tissue compared to the control group (ctr 26.49±1.37% vs. CHF 31.35±0.61%). Consistently, MMP-9 as well as iNOS were significantly higher expressed in the CHF group compared to controls (MMP-9: ctr 54.65±0.78 vs. CHF 66.37±1.70%, iNOS: ctr 45.81±1.47% vs. CHF 50.62±1.57%). The circulating levels of Relaxin-2 did not differ significantly between both groups. However, lower myocardial Relaxin-3 levels in the CHF group compared to controls was observed.

Discussion

Our study shows a modulated expression profile of relaxin-2 and relaxin-3 in patients suffering from end-stage CHF. Additionally, MMP-9, postulated to mediate its extracellular matrix turnover via relaxin-2 signaling, and iNOS, are differently expressed in our patients collective. Modulation of Relaxin-2 may be considered as a therapeutic alternative in patients with CHF.

P166

The incidence of IgM HLA specific antibody class switching in a renal transplant population – and the potential impact on graft outcome

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Introduction

We have previously reported the incidence and persistence of IgM HLA specific antibodies (Abs) in our renal transplant population. This study used sequential testing to determine the incidence of class switching to IgG and whether this constituted a risk to transplant outcome.

Methods

4872 sera from 3072 patients were tested between 01/06/2011 and 30/09/2014 using a Luminex based IgM Ab detection assay. Patients with IgM Abs that went on to class switch to IgG were reviewed to determine if antibody was donor directed (DSA) and associated with antibody mediated rejection (AMR).

Results

IgM Abs were defined in 270 sera from 239 patients (7.7%). Within this cohort, 17 patients (7.1%) class switched to IgG. 8 patients had IgM Abs that switched post transplant. In 4 of these cases the IgM Abs were DSA. The first patient developed a de novo IgM DSA post transplant that switched to IgG was treated for AMR but the graft failed. A second patient developed IgM DSA post nephrectomy that eventually switched to IgG. The remaining 2 patients had pre transplant IgM DSA with positive prospective CDC crossmatches; the IgM Abs went on to class switch post transplant leading to persistent AMR and graft loss in one case.

Discussion

BTS BSHI antibody detection guidelines state that patients with an IgM DSA strong enough to cause a positive CDC crossmatch can proceed to transplant with a standard level of risk. Our data shows that IgM DSA can switch to IgG post transplant, in some cases resulting in AMR.

P167

Modulation of Neuregulin-1 and its receptor ErbB4 in patients undergoing heart transplantation

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Introduction

Neuregulin-1 (NRG-1) is a paracrine growth factor released by endothelial cells, which has shown cardioprotective effects in animal models of heart failure. ErbB4 is a member of the ErbB family that serve as receptor for NRG-1. Administration of NRG-1 has been shown to improve LV function in chronic heart failure (CHF) experimental models. Our aim was to determine whether CHF is associated with changes in expression and distribution of NRG-1 and its receptor erbB4 in human myocardium.

Methods

Expression of Neuregulin-1 and its receptor ErbB4 was assessed by means of real-time PCR on left ventricle and atrial myocardium of patients with CHF undergoing heart transplantation (n=12). All patients gave informed consent. Biopsies (n= 40) of the explanted hearts were obtained and divided according to the anatomical origin (Left Ventricle, Atrium). A control group consisting of left ventricle (n=5) and right atrium (n=5) muscle biopsies from patients with good ejection fraction (EF > 65%) was designed.

Results

Expression of ErbB4 was significantly down regulated in the left ventricle of patients in comparison to the control group and up regulated in atrium (CHF vs. healthy ventricle: 8.66E-05 vs. 3.35E-04; CHF vs. healthy atrium: 1.20E-04 vs. 6.20E-05). Expression of Neuregulin-1 was significantly up regulated in the left ventricle and in both left and right atrium of patients in comparison to the control group (CHF vs. healthy ventricle: 2.4E-04 vs. 2.45E-05; CHF vs. healthy atrium: 5.34E-04 vs. 2.83E-04).

Discussion

Neuregulin-1 and its receptor ErbB4 show different expression patterns in patients with end-stage CHF and in patients with conserved EF. Reduced heart function originated a higher expression of Neuregulin-1 in cardiomyocytes and a decrease on the expression of ErbB4. Our results confirm the modulation of the NRG-1/ErbB4 signalling in human heart failure.

P168

Modulation of Nesfatin, Visfatin and Resistin in patients undergoing heart transplantation

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Introduction

There is growing interest in adipokines and their role in the pathogenesis of end-stage chronic heart failure (CHF). Adipokines are adipose-derived hormones, which play a role in food intake, body weight and in the pathogenesis of the metabolic syndrome and insulin resistance. Our aim was to determine whether CHF is associated with changes in expression and distribution of three adipokines (nesfatin, visfatin and resistin) in human myocardium of patients in end-stage CHF.

Methods

Expression of Visfatin, Nesfatin and Resistin was assessed by means of real-time PCR and immunohistochemistry on left ventricle and atrial myocardium of patients with end-stage CHF undergoing heart transplantation (n=12) after informed consent. Biopsies (n=40) of the explanted hearts were obtained and divided according to the anatomical origin (Left Ventricle, Atrium). A control group consisting of myocardial biopsies from patients with ejection fraction >65% was designed. Serum concentrations of Nesfatin, Visfatin and Resistin of patients with CHF were measured by ELISA.

Results

Expression of Nesfatin was significantly up regulated in both atrium and left ventricle of CHF patients. Serum expression of Nesfatin was slightly higher than healthy controls. Expression of Visfatin was significantly up regulated in the left ventricle and in both left and right atrium of patients in comparison to the control group. Although systemic Resistin was significantly higher in serum of CHF patients, there were no local differences in myocardium.

Discussion

Our results indicate a modulatory role of Nesfatin, Visfatin in the local signaling of chronic heart failure. These data may open up new perspectives for these adipokines in the diagnostic and prognostic evaluation of end-stage CHF.

Clinical relevance of pre-formed IgM HLA- donor specific antibodies (DSA) in HLA-incompatible kidney transplantation

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Introduction

Pre-transplant IgG antibody screening is common practice due to its established role with kidney transplant failure; the role of pre-formed IgM human leukocyte antigen (HLA) specific antibodies has not been thoroughly explored. We aimed to explore whether additional testing for pre-formed IgM HLA-specific donor-specific antibody (DSA) is useful for prediction of rejection and graft survival in a large cohort of patients undergoing HLA antibody incompatible transplantation.

Methods

Samples from 92 patients who had undergone HLA-antibody incompatible transplants were tested at pre-conditioning or pre-transplant for cases that did not require antibody removal therapy using Luminex microbead assay with EDTA containing wash buffer (LAB screen SAB, One Lambda, CA, USA). IgM was defined positive if the MFI values were greater than 2000. Presence of pre-formed IgM DSA was correlated with early antibody mediated rejection (within day 30 post transplantation) episodes and graft failure. Statistical analyses were performed using SPSS IBM software (Fischer exact 2 tailed test and Kaplan Meier survival analysis).

Results

Early antibody mediated rejection (within 30 days) was seen in forty-seven out of the ninety-two cases, of which 17 were positive for IgM DSA. Statistical analysis by Fisher's Exact Test (two-tailed) at 5% significance level showed no significant association of episodes of early rejection with pre-formed IgM HLA-specific DSA, $P = 0.83$. Statistical analysis of death censored graft survival in all eighty-six cases showed no significant association with pre-formed IgM HLA-specific DSA, $P=0.44$ (see Figure below).

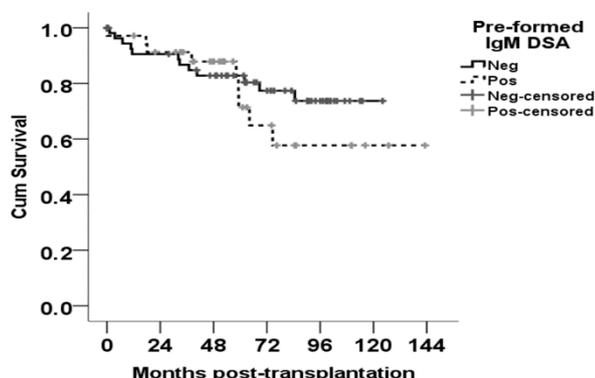


Figure 1: Pre-transplant IgM DSA does not predict death censored graft survival.

Discussion

Additional testing for pre-formed IgM HLA DSA is not useful for prediction of rejection or graft survival in a cohort of HLA-incompatible kidney transplantation. This finding needs to be validated in multi-variate analysis accounting for other baseline characteristics and for larger cohort in a multi-centre study.

P170

Lessons learned on transplant ureter stenosis from two years of reimplantation

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Introduction

Transplant ureter stenosis occurs in up to 5% of renal transplants. Intervention is invariably required to salvage the graft, with a variety of surgical and endo-urological techniques employed to restore patency. We present our experience of the management of ureteric stenosis over a two year period.

Methods

Outcomes of intervention in a prospectively monitored cohort of patients with transplant ureteric stenosis are reported. Both donor and recipient demographics were recorded with specific emphasis on time to stenosis occurrence, time on dialysis (as a surrogate measure of prior bladder inactivity), age, BMI, episodes of rejection and BKV infection. A subgroup of patients with early recurrence was identified and subgroup analysis was performed comparing demographics to all patients transplanted in 2013 and 2014. Interventions employed were resection of the affected segment and reimplantation or endo-urological plasty of the stenosis. Outcome was measured by serum creatinine vs baseline post stent removal.

Results

26 patients were identified. 16 underwent primary stenosis resection and reimplantation. 7 underwent stenosis plasty and stent insertion. 3 patients were unsuitable for surgery or intervention due to comorbidities. Demographics demonstrated a bimodal presentation of ureteric stenosis, with the peak occurrences being early (within 1 year of transplant (n=14)) and late (a decade after transplant (n=6)). 16 were DBD, 7 LD and 3 DCD.

Early recurrence occurred at a rate of 5.9% (15 of 252 total Tx). Mean BMI was significantly higher 31.6 vs 26.2 ($p < 0.05$ t-test). There was no significant difference in age (55 vs 55), time on dialysis (4.7 vs 4.1), cold ischaemic time (9.1 vs 12.9), or anastomosis time (33.9 vs 31.2). Of 16 reimplantations, 3 had early recurrence requiring further reimplantation. All patients had a creatinine within 10% of baseline 3 months post procedure. 3 stenosis plasty had similar success with no recurrence following the procedure, however 4 required ongoing stent changes on a 3 monthly basis and are being considered for further intervention.

Discussion

We demonstrate good outcomes from ureteric reimplantation for ureteric stenosis. Despite 18% recurring early after the procedure, serum creatinine was restored in the all. Endourological plasty can be considered in selected cases as a temporising measure. Further data is needed on long term outcomes.

P171

Is renal transplant a treatment of choice for patients with obesity? An analysis to compare transplant outcomes according to BMI (Body Mass Index)

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Introduction

According to the World Health Organization, worldwide obesity has doubled since 1980. In 2014, there were 1.9 billion 'overweight' and 600 million 'obese' adults. This changing human health dynamic is impacting planning and management of disease. Historically for renal transplants, recipient BMI $\geq 30\text{kg/m}^2$ (obese) was considered to be associated with increased risk of perioperative morbidity and mortality in addition to poor graft survival. In this study, we intend to analyse our renal transplant recipient population in terms of perioperative complications (90 days) and graft survival (3 years) in relation to their BMI.

Methods

We performed a retrospective analysis of our renal transplant unit data between 2008 and 2013. We divided patients into three cohorts based on BMI (kg/m^2) [Cohort A <25, B 25-29.99, C ≥ 30]. We recorded and compared their basic demographics, risk factors, peri-operative complications and patient and graft survival. Chi-square analysis was used to assess statistical significance between BMI and each specific type of surgical complication. A one-way ANOVA was applied to assess statistical significance between BMI and number of post-surgical complications per patient. Complications specific to graft performance were then isolated and analysed in the same way.

Results

Study sample size = 610 transplant recipients where complete data (90 days) was available: [Cohort A=294, B=224, C=92, excluded=24]. The sample included 6 'underweight' patients (BMI <18.5) and 6 'moderately obese' patients (BMI: 35-39.99). No patients were 'morbidly obese' (BMI ≥ 40).

- Table 1: BMI vs. Specific Surgical Complication Type (ordered by Total)

| Complication Type | Affects Graft? | Cohort A N=294 | Cohort B N=224 | Cohort C N=92 | TOTAL N=610 |
|----------------------------------|----------------|-------------------|-------------------|------------------|----------------|
| Rejection | | 78 | 58 | 28 | 164 |
| Delayed Graft Function | Y | 52 | 53 | 21 | 126 |
| Urinary Infection | | 52 | 44 | 18 | 114 |
| Wound Infection | | 30 | 30 | 15 | 75 |
| Urinoma/other collection | | 17 | 18 | 15 | 50 |
| Lymphocele | | 10 | 10 | 11 | 31 |
| Primary Graft Failure | Y | 6 | 6 | 1 | 13 |
| Bleeding | | 5 | 6 | 1 | 12 |
| Transplant Renal Artery Stenosis | Y | 6 | 2 | 3 | 11 |
| Ureteric Stenosis/Stricture | | 3 | 5 | 3 | 11 |
| Renal Vein Thrombosis | Y | 3 | 1 | 1 | 5 |
| TOTAL - Complications | | 262 | 233 | 117 | 612 |
| AVERAGE - Complications | | 0.9 | 1.0 | 1.3 | 1.0 |

Chi-square significant values (highlighted): Lymphocele ($p = 0.004$), Other collection ($p = 0.015$)

- Significant one-way ANOVA for BMI vs. Number of Complications per patient: [$F = 3.89$; F Critical = 3.01; $p = 0.021$]. Two-tail t-tests assuming unequal variances (due to unequal cohort sizes) verified the multiple comparisons and proved significant ($p = 0.039$ – Bonferroni corrected) for Cohort A vs. C.

- Three years graft survival (censored data): [Cohort A 92%, B 91%, C 94%].

Discussion

Our results show that obesity is not only associated with increased risk of perioperative complication but also multiple complications in the same individual. Lymphocele and postoperative collections are both associated with obesity but fortunately neither had any impact on graft and patient survival (i.e. long-term outcome). Therefore, we suggest that with careful perioperative planning, informed consenting and multidisciplinary approach, renal transplant should still be considered as a gold standard treatment in obese patients.

P172

Renal transplantation in the context of untreated early prostate cancer: is it always contra-indicated?

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Introduction

European and British guidelines suggest that renal transplantation (RT) should not be performed in patients with untreated malignancy. However due to the indolent nature of low-risk prostate cancer (CaP) active surveillance (AS) is an accepted management strategy and an alternative to radical treatment in non-RT patients. We describe our initial experience with AS in RT patients with CaP.

Methods

Two-centre retrospective cohort study identified patients with planned or performed RT and CaP. A literature review investigated autopsy prevalence of CaP and CaP treatment pre-RT.

Results

3 patients (centre 1) had RT (2 living donor and 1 deceased donor). Recipients were age 69, 65 and 61 and were diagnosed with CaP 21, 26 and 12 months prior to RT. Gleason grade was 3+3 in 3 and 3+4 in 1. Active surveillance was performed in all patients with no significant rise in PSA or change in tumour dynamics at median follow up 49 months. Mean PSA was 5.0 with all <5% tumour volume. One patient died 7 years post-RT of an unrelated cause. The deceased donor RT failed after 6 months requiring dialysis. 2 patients (one at each centre) are awaiting living donor RT on AS.

Conclusions

No patient had progression of CaP on AS post-RT with short-term follow up. Autopsy evidence suggests that in older men low-risk CaP is extremely common. As such a high proportion of unscreened men who receive a RT may have undiagnosed low-risk CaP. If so, standard immunosuppression appears not alter the indolent nature of low-risk CaP. Although recent authors (ESOT 2015) recommend radical treatment for all CaP patients pre-RT, we believe that in carefully selected and counselled patients, RT can be performed on AS. Indeed AS does not preclude radical CaP treatment after RT if needed. Despite being a small cohort and short follow-up, it would appear that RT in this setting is feasible. Further work is needed to audit long term outcomes and further define CaP patients on AS suitable to receive RT without radical CaP therapy.

P173

Is it a big problem? Obesity and kidney transplantation

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Introduction

There is an increasing prevalence of both end stage renal disease and obesity. Transplantation is the optimum form of renal replacement therapy. Concerns about operative risks and graft outcome may limit access to kidney transplantation in obese patients. This study assesses the early outcomes of obese transplant recipients in our centre over a 5 year period.

Methods

All consecutive renal transplant recipients in our centre from 2010 to 2014 were considered. We performed a retrospective analysis of prospectively collected data in the Renal Transplant Database. Length of hospital stay, perioperative complications and graft function were evaluated.

Results

There were 393 renal transplants carried out in this 5 year period. 360 (93%) had a pre-operative BMI recorded and were included in analysis. 212 (59%) were male and mean age at transplantation was 48 years (16-77 years). 179 (49%) were live donor transplants. Mean BMI was 26kg/m² (16-40), 80 (22%) had a BMI of at least 30kg/m².

The patients were considered according to established BMI categories, and the results are detailed in Table 1. A complication was defined as: infection, cardiac event, arrhythmia, ileus, GI bleed, seizure, haematoma, urine leak, wound breakdown, venous thrombosis/pulmonary embolism.

| BMI (kg/m ²) | Number | % Live Donor | Mean day of creat fall | Mean discharge creat | Median length of stay (Days) | % of patients who developed complications |
|--------------------------|--------|--------------|------------------------|----------------------|------------------------------|---|
| <24.9 | 141 | 47 | 2 | 132 | 9 | 34 |
| 25-29.9 | 153 | 47 | 2 | 143 | 9 | 28 |
| 30-34.9 | 54 | 59 | 4 | 216 | 10 | 31 |
| >35 | 12 | 33 | 6 | 225 | 9.5 | 42 |

Discussion

Obese patients had a greater incidence of delayed graft function and a higher discharge creatinine than non-obese renal transplant recipients. However the perioperative complication rate was not significantly different and the length of hospital stay was comparable. Renal transplantation can be successfully performed in obese patients, when the risks of complications are balanced against the inevitable limitation of life expectancy associated with prolonged maintenance dialysis therapy.

P174

A retrospective study of the use of interventional radiology in the management of complications following renal transplantation. A single centre experience

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Introduction

Complications following kidney transplant surgery result in morbidity to patients and carry the risk of graft loss and mortality. Management of these complications includes a multidisciplinary approach. In many cases, complications can be treated non-surgically by interventional radiology, which is minimally invasive and can avoid the need for open surgery. In this study we aimed to investigate the input of interventional radiology in the management of post renal transplant complications and its outcomes.

Methods

We performed a retrospective analysis of renal transplants performed in our centre between January 2008 and December 2013. We recorded all the perioperative complications where a radiological input was possible. This included peri-transplant collection including urinoma, lymphocele, haematoma or any other significant collection; transplant renal artery stenosis (TRAS) and ureteric stenosis or stricture. Radiological intervention included radiological drainage of collections, angioplasty for TRAS and ante-grade stenting of ureteric strictures or stenosis. Treatment of each type of complication was assessed. Paired t-test was used to assess the statistical significance of the measured success rates.

Results

Transplant data of 634 renal transplants performed during the study period were included. A total of 83 episodes of the above complications with 71 successful events were recorded, as shown in table 1.

Table 1: Outcome of IR in treatment of renal transplant complications.

| Complication | Episodes | IR treated | IR success rate | P value |
|--------------------------------|-----------|------------|-----------------|---------|
| Peri-transplant collection | 46 | 42 | 91% | <0.01 |
| TRAS | 19 | 19 | 100% | <0.01 |
| Ureteric stricture or stenosis | 18 | 10 | 56% | 0.52 |
| Total episodes | 83 | 71 | 86% | |

Discussion

We observed significant success with IR in the treatment of post transplant peri-transplant collections and TRAS. In the case of ureteric stricture or stenosis almost half of them were treated with IR with excellent outcomes. This study suggests a multidisciplinary approach towards management of renal transplant complications and encourages the need for development of clinical care pathways to identify, treat and follow up such patients.

Minimally-invasive access and off-pump LVAD implantation - strategies to improve outcomes

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Introduction

Off-pump and minimally invasive LVAD implantation strategies are currently investigated to prevent the negative effects of CPB, render the implantation procedure less traumatic and reduce adhesions in order to facilitate subsequent transplantation. We reviewed the patients implanted with LVAD at our center since minimally invasive off-pump implantation was defined as our intention to treat implantation method. Our secondary aim was to identify factors predicting the need for conversion as well as to assess the consequences of conversion from off-pump to on-pump.

Methods

Of 32 patients (81.3% male, 53.5 ± 11.7 years, INTERMACS class 2.4 ± 1.1) who presented for LVAD implantation (HVAD, Heartware Inc., USA) from January 2013 to August 2015, 24 (75%) were found eligible for off-pump surgery. Off-pump implantation through a minimally invasive access or full sternotomy was intended in 19 (79.1%) and 5 (20.9%) and performed in 12 (63.1%) and 3 (60%) patients, respectively. On-pump implantation through a minimally invasive access and full sternotomy was intended in 1 (3.1%) and 2 (6.3%) and implemented in 7 (21.9%) and 5 (15.6%) patients. CPB was established in 9 (37.5%) of those originally considered eligible for off-pump surgery. Procedure duration, transfusion requirements, bleeding, and mortality were investigated. In order to identify factors predicting the need for conversion and assess the consequences of conversion from off-pump to on-pump, a sub-group analysis was performed.

Results

Off-pump procedures (209 ± 48 min) were significantly shorter than on-pump (239 ± 42 min), with the shortest duration of procedure recorded for off-pump implantation through a full sternotomy (191 ± 14 min). Minimally invasive off-pump implantation was associated with the lowest transfusion requirements during the initial 48 hours including the surgical procedure (3.17 ± 5.0 units of PRBC vs. a maximum of 15.7 ± 15.1 in the full-sternotomy group), the lowest 24h chest tube loss (1347 ± 501 ml vs. a maximum of 3507 ± 3200 ml in the full-sternotomy group). The lowest in-hospital mortality was registered in the full sternotomy off-pump group (0%). The in-hospital mortality rates for off-pump and on-pump implantation, however, were equal (26.7 vs. 25.5%) and did not differ significantly from the overall in-hospital mortality. Comparison between the conversion and non-conversion groups yielded no differences in age, BMI, INTERMACS class (2.1 ± 0.9 vs. 2.9 ± 1.0), LV-EF (16.4 ± 4.6 vs. 16.0 ± 3.5%) and TAPSE (15.1 ± 3.0 vs. 16.9 ± 4.0 mm). Higher need for conversion was found in women, in patients with non-ischemic cardiomyopathy, in patients with valve disease, and in patients receiving destination therapy. Patients who underwent conversion had a higher duration of procedure (249 ± 45 vs. 209 ± 48 min), a higher 24h chest tube loss (2509 ± 1951 vs. 1448 ± 543 ml), a higher transfusion need (6.3 ± 5.9 vs. 3.5 ± 4.8 units of PRBC), and a higher ICU length of stay (35.1 ± 23.8 vs. 17.0 ± 12.7 days). Differences in in-hospital mortality were not significant.

Discussion

Our data suggest that off-pump and minimally invasive LVAD implantation can be implemented with complication and mortality rates that do not exceed those of on-pump implantation. Conversion from off-pump to on-pump is associated with a poorer outcome than off-pump implantation, especially regarding length-of-stay, transfusion and bleeding. Further investigations in larger patient cohorts are warranted in order to establish their superiority over conventional implantation.

P176

Surgical reconstruction for ureteric stricture in kidney transplant recipients

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Background

Urological complications can have a significant effect on the outcome of renal transplantation. The aim of this study was to review the incidence of ureteral obstruction and outcomes after surgical management at our Unit.

Patients and methods

We interrogated a prospectively maintained database and undertook a retrospective analysis of 982 kidney transplants (and kidney-pancreas transplants) performed between January 2010 and April 2015. We also searched the PACS radiology system for all cases of nephrostomy insertion to identify all patients with a transplant ureteric stricture. In all the transplant patients, the uretero-neocystostomy had been protected with a double J stent held in place for a median time of 1.4 months post-operatively (range 0.4-25.9).

Results

After a median follow up of 35.1 months, an obstruction of the transplant collecting system requiring percutaneous nephrostomy (PCN) was recorded in 28 patients (2.9%). More in details: 1.6% of kidney-pancreas transplants, 1.8% of the living donor grafts, 4.8% of the organs from deceased brain donor and 4% of the kidneys from deceased cardiac donors (p=ns). In 12 of the above 27 grafts (44.4%), a regular stent change was therapeutic. In the remaining 16 patients, surgical intervention was then considered, but it was not feasible in 4 cases (25%). One patient had a ureteric reimplantation (8.3%), ten patients underwent Boari flap reconstruction (83%) and one patient had both procedures done (8.3%). Surgery resulted in significant and persistent improvement in renal function: serum creatinine improved from an average of 183 mmol/L pre-operatively to 147 mmol/L at 1 month and 120 mmol/L at 12 months after the operation (p<0.01). Patients undergoing surgical intervention had better improvement in serum creatinine 1 month post procedure, compared to patients who remained with PCN (p<0.05). Graft loss happened in 7 patients (0.7%): 4 of these could not undergo surgery, and three had recurrence of stenosis after the operation. No pre-existing BKV infection was associated with ureteric stricture.

Conclusion

The incidence of ureteric stricture following renal transplant is low, but it still represents a cause of graft loss. Appropriate corrective surgery can diminish the effect of urological complications on graft survival.

Renal transplantation in abnormal bladder: the pros and cons

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Introduction

Renal transplantation in patients with abnormal bladder is a high-risk transplant due to previous surgical intervention required to optimize the bladder function before transplantation and the frequent use of intermittent catheterization after transplantation. This may increase the incidence of urinary tract infection in immunosuppressed patients. In this study we aim to determine the outcome of renal transplantation in patients with abnormal lower urinary tract.

Methods

A retrospective review of the electronic and paper records of patients with pre transplant structural and /or functional bladder abnormality was compared with a control group of patients without bladder abnormality. Both groups received renal transplantation simultaneously during the same period of time (1990-2014). Estimated glomerular filtration rate (eGFR) less than 15 ml/min was considered as graft failure. Statistical data analysis was done by IBM SPSS version 20 with student t-test used for mean and Chi-Square test used for categorical variable. P value \leq .05 was considered significant.

Results

The study group included 30 transplanted kidneys in 25 patients (5 patients received their second graft after failure of the first graft). The most common cause of abnormal bladder was posterior urethral valve in 40% (10 patients) and neuropathic bladder due to spina bifida in 20% (5 patients). The control group include 30 grafts in 30 patients. Patient's characteristics are summarized in the following table.

| Patients characteristics | Study group | Control group | P value |
|---------------------------------------|--------------|---------------|---------|
| Mean age at time of transplantation | 32± 17 years | 47±12 years | .000 |
| Sex (Male: Female) | 18:7 | 20:10 | .39 |
| Type of donor kidney (Live: Deceased) | 8:22 | 7:23 | .76 |
| Number of transplant (First: Second) | 25:5 | 30:0 | .02 |
| Previous urological operations | 18(72%) | 2(.06%) | .000 |
| Need for native nephrectomy | 9(36%) | 4(13%) | .11 |
| Febrile urinary tract infection (UTI) | 90% | 40% | .000 |

There was no statistically significant difference in the graft survival and mean eGFR at one, three and five years between the study and the control groups as shown in the following table.

| Graft survival and eGFR | Study group | Control group | P value |
|----------------------------|---------------|---------------|---------|
| One year Graft survival | 90% | 97% | .30 |
| Mean eGFR at one year | 45 ±27 ml/min | 51±19 ml/min | .33 |
| Three years Graft survival | 88% | 91% | .67 |
| Mean eGFR at three years | 38 ±26 ml/min | 48±22 ml/min | .16 |
| Five years Graft survival | 82% | 87% | .68 |
| Mean eGFR at five years | 33±25 ml/min | 43±25 ml/min | .22 |

Discussion

Despite the earlier age at transplantation, the previous urological operations and the high incidence of UTI after renal transplantation, graft survival and functions after renal transplantation were not significantly different between abnormal and normal bladder patients. We concluded that it is safe to transplant into abnormal bladders once they have been assessed, reconstructed if necessary and are being managed appropriately.

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Influence of smoking exposure on patient outcomes after kidney transplantation

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Introduction

The influence of smoking exposure on post kidney transplant outcomes remains uncertain in the transplantation literature. The aim of this UK-based single-centre analysis was to determine patient specific outcomes in the contemporary era for kidney allograft recipients stratified by any smoking exposure (current or ex-smoker) versus no smoking exposure.

Methods

Data was extracted by the hospital informatics team for all kidney allograft recipients transplanted at our centre between 2007 and 2015. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events.

Results

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up 4.4 years post-transplantation. The median age for the cohort was 47, males (n=681, 59.7%), Caucasian ethnicity (n=822, 72.1%), deceased-donor recipients (n=633, 56.4%), repeat transplants (n=111, 9.7%), diabetes as cause of end-stage kidney disease (n=117, 10.3%) and previous/active smoking exposure (n=274, 24.0%). Overall, 24.0% of the cohort had some documented smoking exposure and were classified as ever smokers for analysis. Males were more likely than females to have smoking exposure (28.8% versus 17.0% respectively, $p<0.001$) but there was no other association with any other baseline demographic. Smoking versus non-smoking exposure was not associated with an increased risk of mortality (8.8% versus 6.6% respectively, $p=0.139$). The most common cause of death in both groups was cardiovascular; there were no statistically significant differences between groups in the proportion of categories of death. In terms of post-transplant events, smoking versus non-smoking exposure increases risk of post-transplant cancer (10.2% versus 4.8% respectively, $p=0.002$), post-transplant diabetes (11.3% versus 7.2% respectively, $p=0.029$) and post-transplant cardiac events (11.3% versus 4.4% respectively, $p<0.001$), however we observed no increased risk of cerebrovascular events (2.2% versus 2.4% respectively, $p=0.823$). However, in a Cox regression model, smoking exposure was not determined to be an independent risk factor for patient survival (hazard ratio 1.4, 95% CI 0.9-2.3, $p=0.172$).

Conclusion

Any smoking exposure is associated with post-transplant morbidity including increased risk of cancer, cardiac events and diabetes, but we observed no increased risk in mortality. As median follow up was only 4.4 years, longer term follow up of a larger cohort is necessary to clearly discriminate smoking risk and also to stratify risk between active versus ex-smokers.

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Does recipient sex status effect outcome in deceased donor kidney transplants?

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Introduction

The influence of recipient gender on transplant outcomes is controversial. However, within animal models data indicates that the tolerance to ischaemic re-perfusion injury could be affected by recipient sex. The aim of this study was to determine if recipient gender impacted on the outcomes for deceased donor renal transplants.

Methods

Retrospective analysis of all adult renal transplantation, over a four year period (2011-2014), was performed. Baseline demographic characteristics and outcomes were compared by sex status for all deceased donor transplants. Outcome measures included serum creatinine at one year and biopsy proven acute rejection (BPAR) rates. The rates of DGF and their outcomes were also analysed.

Results

Three-hundred-and-sixty-one deceased donor transplants were identified; 107 DCD and 254 DBD with females accounting for 43% and 40% of each group respectively. The overall donor and recipient case mix was not significantly different with mean BMI of DCD and DBD being equal for each sex (26.7 vs 26.5). The serum creatinine at one year was statistically lower in female DCD and DBD kidney recipients compared to males and was independent of donor sex (DCD 123.4±11.20 vs. 155± 6.99 and DBD 116.8±7.05 vs. 135.5±5.72, p<0.05). A significantly lower incidence of DGF was seen in the female cohort (DCD 41.2% vs. 58.9% and DBD 42.6% vs 57.4%, p<0.05) but no significant difference were seen for BPAR rates (DCD 10.9% vs. 6% and DBD 10.8% vs. 15%, p>0.05) or one year graft survival (DCD 89% vs. 97% and DBD 87% vs. 91%). Outcomes following DGF showed a significantly lower creatinine for the female DBD recipients only (DCD 125.8±9.94 vs. 137.1±7.26 and DBD 137.1±10.01 vs. 183.3±17.05) with BPAR and one year graft survival showing no sex differences.

Conclusion

Female transplant recipients present an early benefit following transplantation, with lower creatinine and DGF rates. This may be a direct result of sex differences in the ability to withstand the systemic insults of IRI.

Defining future research priorities: results of the UK kidney transplant priority setting partnership

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Introduction

Research agendas in kidney transplantation are often driven by the interests of individual researchers and/or of the pharmaceutical industry. This often overlooks the priorities of patients, carers and clinicians. The Kidney Transplant Priority Setting Partnership (PSP) was established with the aim of involving all stakeholders in identifying and prioritising future research in the field.

Methods

The PSP methodology is as outlined by the James Lind Alliance. (1) A steering group, coordinated by the Centre for Evidence in Transplantation (CET), was convened to include representation from all key professional and patient bodies involved in the care of kidney transplant recipients and living kidney donors. (2) Partner organisations with an interest in Kidney Transplantation were invited to contribute to and help publicise the process. (3) An initial survey collected treatment uncertainties (unanswered research questions) from a mixture of patients, carers and clinicians, which were added to those identified from other surveys conducted by partner organisations. (4) Survey responses were refined to remove duplicate and out-of-scope topics, and the existing literature searched to identify and exclude topics already answered by current evidence. The next steps are: (5) a prioritisation survey to create a long-list and (6) a final workshop to identify the top ten priorities for future research.

Results

The process included over 20 partner organisations representing both patients and clinicians. The initial survey identified 497 uncertainties. 132 were deemed out-of-scope and excluded. The remaining 365 were categorized and grouped into 97 "indicative" uncertainties. Seven of these were considered to be answered by the existing literature. Of the remaining 90, 45 were submitted by more than two respondents and were taken forward to the prioritization survey. The prioritisation survey is underway and has received nearly 200 responses to date.

Conclusions

This project uniquely brings together patients and clinicians to prioritise future research in kidney transplantation. The prioritisation survey will close in December 2015m and the final workshop will be held at the beginning of February 2016, with the results to be presented at the BTS congress

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Critical appraisal of UK clinical practice guidelines in kidney transplantation using the appraisal of guidelines for research and education (AGREE) II tool: a systematic review

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Introduction

Clinical Practice Guidelines (CPGs) in health care have shown to be lacking quality and the appraisal of CPGs in organ transplantation is limited. We systematically reviewed the quality of United Kingdom (UK) CPGs in kidney transplantation using the Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument.

Methods

CPGs in kidney transplantation and donation from 2010 to present were identified through searches of MEDLINE, NHS Evidence Search, National Institute for Health and Care Excellence Evidence Search and the websites of relevant UK societies. Using the AGREE II instrument three appraisers, including one transplant clinician and two methodologists measured the quality of CPGs across six domains and commented on the overall guideline quality and whether they would recommend the guideline for future use. Domain scores were reported as a percentage of the maximum possible score for that domain. Inter-rater reliability was measured using the Intraclass correlation coefficient (ICC).

Results

Searches identified 588 records of which 10 CPGs met our inclusion criteria. These included six CPGs by the British Transplantation Society (BTS), one by the UK Renal Association, and three were a combination of the BTS and/or UK Renal Association, British Society for Histocompatibility and Immunogenetics (BSHI) and the British Committee for Standards in Haematology (BCSH). The mean domain scores were as follows: **Scope and Purpose**, 79% (range 50-93%); **Stakeholder Involvement**, 54% (range 33-70%); **Rigour of Development**, 51% (range 26-67%); **Clarity of Presentation**, 85% (range 72-94%); **Applicability**, 30% (range 18-63%); **Editorial Independence**, 34% (range 0-69%). The domain Clarity of Presentation scored highest across CPGs, closely followed by Scope and Purpose. The poorest scoring domains were Applicability and Editorial Independence. Editorial Independence also had the widest range of scores. Out of the 23 AGREE items, those scoring highest were items 1 (Overall objectives of the guideline are specifically described), 15 (Recommendations are specific and unambiguous) and 17 (Key recommendations are easily identifiable). Items that scored poorest were items 8 (Criteria for selecting the evidence are clearly described), 20 (Potential resource implications of applying the recommendations have been considered), 5 (Views and preferences of the target population have been sought), 7 (Systematic methods were used to search for evidence) and 19 (Guideline provides advice and/or tools on how the recommendations can be put into practice). Just over half CPGs were recommended for future use with modifications (60%), three were recommended for use without modifications (30%) and one was not recommended (10%). The overall CPG quality was scored as 5 out of 7 (Range 3-6). The ICC across the guidelines ranged from 0.42 to 0.81, with the average inter-rater reliability being substantial at 0.60.

Discussion

The overall average quality of UK CPGs was satisfactory, however there was wide variability in how well each of the AGREE domains were addressed. The quality of CPGs needs to be improved, specifically regarding how supporting evidence is identified, and adequate descriptions of how to implement recommendations and resources required.

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Urinary catheter care following renal transplantation: how soon can it safely be removed? Outcomes of a national survey of renal transplant consultants and single centre experience

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Introduction

There is no consensus on duration of urinary catheterisation (UC) following renal transplant (RTx) surgery. Current duration of UC varies throughout UK transplant centres from postoperative day-2 to day-7. This study includes the outcomes of a national survey dispatched to UK renal transplant surgeons regarding postoperative urinary catheter care (POUCC). We also looked at our own POUCC practice (UC removal day-2) and subsequent patient outcomes.

Methods

- 1) An online survey was sent to explore various factors influencing POUCC amongst UK consultant RTx surgeons.
- 2) Retrospective RTx data was collected from 2010-2011, including length of stay, urinary leak, haematuria, urinary obstruction, re-catheterisation and UTI rate within 30 days of RTx.

Results

- 1) Response rate was 51% (n=48) representing 83% of UK RTx centres. 75% of respondents would consider UC removal earlier than current practice of day-5 (with the modal response being day3-4). Rationale for UC is prevention of urinary leak (64%). 28% felt that duration of UC prolonged inpatient stay.
- 2) There were 161 RTx fulfilling our criteria. The male:female was 2:1, with a mean age (+/-SD) of 50.1 years (+/-13.1). Outcomes are tabulated below:

| VARIABLE: | UC removal day-2 (n=117) | UC removed > day-2 (n=44) | SIGNIFICANCE (p-value) |
|-------------------------|---------------------------------|-------------------------------------|-------------------------------|
| Length of Stay (+/-SD) | 4.5 (+/-0.4) days | 8.4 (+/-3.6) days | 0.002 |
| Urinary Leak | 4 | 1 | 0.711 |
| Haematuria | 5 | 1 | 0.559 |
| Re-Catheterisation | 5 | 2 | 0.939 |
| Urinary Tract Infection | 5 | 5 | 0.049 |

Conclusion

There are no internationally agreed criteria regarding POUCC following RTx. National opinion would suggest UC removal should be sooner (26% day-3 and 34% day-4) than current national practice (day-5). Outcomes from our single centre study suggest that day-2 removal post RTx is safe practice, without significant detriment when compared to those undergoing UC removal > day-2. Length of stay is significantly reduced when the UC is removed on day-2.

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Who is not recruited to a trial? Demographics in participants and exclusions in a clinical trial of an investigational medicinal product

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Introduction

Little is known about the reasons for failure to recruit participants to randomised trials, yet low recruitment is a major cause for early trial closure. The PoWAR study is a multicentre, double-blind, randomised, controlled trial of a single dose of prophylactic antibiotic prior to hand-assisted laparoscopic kidney donation, to assess whether this leads to fewer infectious complications including wound, urinary and chest infections. We assessed all those who were screened for the study in order to determine which participants failed recruitment.

Methods

265 kidney donors from one UK transplant centre were screened for the PoWAR study. Demographic data and reasons for failure of recruitment were documented.

Results

265 living kidney donors were screened for the POWAR study at the host site. 57% of these were male (n=151) and 43% of these were female (n=114).

106 (70.2%) male patients were consented and randomised compared to 70 (61.4%) female patients who were consented and randomised ($p=0.06$ chi square test). 29 (19.2%) men declined to take part in the PoWAR study. 10.6% (16 patients) were ineligible for the study, 5% (8 patients) of which were due to an antibiotic allergy. 70 (61.4%) female patients were consented and randomised. 18(15.8%) women declined to take part in the PoWAR study. 22.8% (26 patients) of females were ineligible for the study, 12% (14 patients) of which were due to an antibiotic allergy.

The average male donor age who consented to the study was 44 years old. The average female study donor age was 46.8 years.

Discussion

Although a greater number of male donors were screened, a higher proportion of men went on to enter the study compared with women. A higher number of female patients were excluded due to antibiotic allergy, compared with male patients. The decline rates between genders are very similar, and are relatively low.

Even in a study with a simple design, most trial candidates fail to proceed. This has important implications for study design and assessment of anticipated recruitment rates.

Imaging post renal transplantation

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Introduction

Increasing use of kidneys from less than ideal donors can potentially increase the risk of surgical complications after kidney transplantation, including early graft loss. It is not clear if this trend towards increasing use of extended criteria organs necessitates correspondingly increase use of imaging investigations to facilitate early detection of potential complications. We therefore retrospectively analysed our experience of use of imaging during the index admission for kidney transplantation.

Methods

A retrospective analysis was undertaken of all radiological assessments in the index admission for adult patients who received a single or dual kidney transplant between 1/9/2011 and 01/10/2014 in our centre. Patient age, sex, type of donor organ, number of scans during the admissions, indication, location and time of scans were recorded. Risk of re-operation during the index admission was also recorded. All transplant recipients had a protocol ultrasound scan (USS) within the first 24 hours.

Results

477 single and 23 dual kidney transplants were performed during this period. 130 patients received kidneys from live donors (LD), 253 from donors after circulatory death (DCD) and 117 from donors after brainstem death (DBD). During the index admission, 938 USS and 72 CT scans were performed. On average, each patient had 1.88 USS (1.93 for DCD recipients and 1.66 for DBD recipients) and 0.14 CT (0.15 for DCD and 0.09 for DBD recipients) for scans for the admission. 351 (94.9%) initial USSs were performed either in recovery (233, 63.0%), or on the ward (118, 31.9%). Only 19 (5.1%) were carried out in the radiology department. 88.1% of the initial protocol USS were normal, 7.5% indicated a collection and 4.4% an abnormal flow. There was no difference between donor types.

53/500 (10.60%) patients returned to theatre for re-exploration of the kidney transplant. The main indications for return to theatre were haemorrhage or suspected graft vessel thrombosis. Return to theatre was precipitated by abnormal radiological findings in 47/53 (88%) patients and 3 (5.6%) patients were re-operated on based on clinical grounds only (missing data for 3 patients). Only 2 patients were found not have significant abnormalities upon re-operation. 39.5% of recipients with an abnormal first USS were returned to theatre during the index admission, compared to 10.2% of recipients whose first USS was normal.

Discussion

While most initial USS after a kidney transplant are normal, an abnormal first USS should raise a high index of suspicion for a significant complication and early operative intervention should be considered. We found no indication to suggest a requirement for more intense imaging monitoring in kidneys transplanted from DCD donors.

Application of 3D printing technology in complex paediatric renal transplantation

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Introduction

Significant structural complexities (e.g. vascular anomalies), can render implantation infeasible, particularly in small paediatric patients. Surgical decision-making currently relies on 3D medical imaging. However these images are limited in evaluating clinically relevant structures by their presentation on 2D screens. As a solution we have assessed the feasibility of using 3D printing technology to fabricate physical models in order to portray patient-specific anatomy and disease morphology. We assessed their utility to inform complex paediatric renal transplantation using preliminary questionnaires (score 1-5, 1=not useful, 5= very useful).

Methods

We describe 2 patients referred for living donor transplantation.

Case 1: 6 yr F (18 kg) with blocked IVC and jump PTFE graft (supra-coeliac to aortic bifurcation) for aneurysmal disease. Her model was printed retrospectively.

Case 2: 2 yr M (12 kg) with renal arterial aneurysmal disease and an IMA aneurysm measuring 7x6 mm. His model was printed prospectively to help plan surgery.

Results

Case 1 underwent a successful living donor transplant. 5 surgeons independently confirmed the 3D model would have been very useful in preoperative planning, as a teaching tool, and for consenting the family (score 5 for all).

Case 2 underwent bilateral laparoscopic nephrectomy prior to living donor transplant in the future. The operating surgeon confirmed the pre-operative evaluation of the 3D model provided great reassurance (score 5) with intraoperative geometrical anatomical correlation of the hilar vessel anatomy and spatial relations between the model and the patient (score 5) during surgery.

Conclusions

To our knowledge these are the first reported cases of 3D printing technology for use in complex paediatric transplantation. Our initial experience proves promising with respect to clinical translation, providing the surgical team with full 3D haptic spatial appreciation for making critical clinical decisions.

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The role of generic peri-operative ward surgical checklists in renal transplantation

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Introduction

The ward preparation of patients for unplanned surgery and their out-of-hours post-operative recovery is often led by junior doctors with limited surgical experience. Furthermore, renal transplant patients may often receive ward care by medical rather than surgical staff.

Methods

Pre- and post-operative generic ward-based surgical checklists (GSC) were designed using an "A to H" mnemonic to aid cognitive processing. A validation questionnaire was used to determine the perceived impact of the GSC on patient safety and quality of care, as well convenience to staff. The study recruited consultants, junior doctors, medical students and nursing staff from different tertiary renal transplant units.

Results

Twenty-one staff members were recruited. 90% strongly agreed that the checklist would improve patient safety and quality of care. Similarly, all staff members felt that the checklist covered all the critical or important perioperative steps and would improve patient transit to the operating room. Furthermore, the GSC was thought to be quick (76%) and easy / simple to use (86%). Whilst all study participants supported the implementation of the checklist, only 48% strongly believed its delivery should be in an 'App' format.

Discussion

The GSC developed may be an acceptable, comprehensive and useful method of improving ward care of renal transplant patients, but further work is needed to pilot it. Interestingly, its delivery in the current 'pocket card' format may be preferable to an App, despite recent technological advances.

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Acute operative complications and 1,5,& 10 year outcomes in living donors by type of live donor nephrectomy - U.K. cohort study

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Introduction

Living kidney donation has significantly improved recipient and graft survival world wide. With a move to increase these numbers further, it becomes mandatory to have a better understanding of the short and long term outcomes and risks of kidney donation.

Aim

To investigate occurrence of acute operative complications and 1,5,& 10 year outcomes in living donors by type of nephrectomy.

Methods

National Health Service and Blood and Transplant, U.K (NHSBT), obtains informed consent from all patients undergoing a transplant in the UK for continuing data collection and subsequent analyses. The study protocol was reviewed and passed by the Renal Registry (RR) projects advisory group, UK. From January 1, 2001 until December 31, 2013 inclusive, all live kidney donors were included in the study. No formal sample size estimate was produced for the study; all eligible patients' records were used. December 31, 2014 was considered the study end, meaning that all patients had at least one year of follow-up. Datasets, based on regular returns from individual transplant centres across the UK, were obtained from NHSBT.

Results

A total of 9750 live donor records were available. Nephrectomy type was available for 9602 donors; Open 3132 (33%), Pure laparoscopic - 3886 (38%) and hand assisted laparoscopic- 2802 (29%). We analysed the incidence of operative complications; splenectomy, reoperation required, organ perforation, operative haemorrhage, pneumonia, pneumothorax, pulmonary embolism, wound infection, DVT, other complications and a combined variable for any one or more complication.

Statistically significant differences were noted for the incidence of reoperation (41/2794, P=0.018), organ perforation (44/2802, P=0.032), wound Infection (60/ 2796, P=0.018), other complication (323/2793, P<0.0001), any one or more complications (402/2802 P<0.0001) in the hand assisted laparoscopic group when compared to the other 2 groups. Incidence of operative haemorrhage (64/3122, P<0.0001) and pneumothorax (46/3130, P<0.0001) were higher in open nephrectomies. Pure laparoscopic nephrectomy yielded the least complications.

One, 5 and 10 year outcomes were analysed using logistic regression methods to facilitate adjustment for donor age, gender and operative complications. At one year, there was significantly more wound pain in the open group in comparison to both the laparoscopic groups P=0.001. Incisional and operation related hernia was more in the hand assisted laparoscopic group P=0.048. Other operation related conditions was more in the laparoscopic groups, especially pure, compared to the open group P=0.024. At five years (n= 6011) wound pain remained significant with more wound pain in open nephrectomy group: 9/2814 vs. 0/ 2282 P=0.007. At 10 years (n=1863) there were only 2 donors with wound pain, both in the open group. Also all laparoscopic procedures were "pure", as the hand assisted procedures only started in 2007 in the U.K.

Conclusions

Though there were small numbers of complications overall, significant differences were identified with most complications seen in hand assisted laparoscopic nephrectomies and least in pure laparoscopic operations. Wound pain remained significant in long term outcomes and was mainly related to open nephrectomy.

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The outcomes of 1700 living donor kidney transplants from a single centre

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Introduction

Living donor kidney transplantation (LDKT) is the gold standard treatment for end stage renal disease (ESRD).

Methods

A single-centre retrospective review of available records for living donor transplants spanning the period from 1969 to 2015. Patient demographics and outcomes for donor nephrectomies and the associated transplants were reviewed. The primary outcome assessed is graft survival. Results were stratified over 3 fifteen year time periods.

Results

There were 1700 individual records in the database. Mean donor age was 44.3 (SD 12.17) years with a male to female ratio of 1:1. There were 175 open donor nephrectomies (13.9%) and 1074 laparoscopic assisted (63.2%). The majority of donors were related to the recipient (70.6%) and the left kidney was the organ predominantly used (72%). The mean length of stay after donor nephrectomy was 4.23 days. 20 donors required a re-operation and 10 of the laparoscopic cases were converted to open.

Recipient mean age was 35.8 (SD 17.7) years. The median graft survival was 24.5 years, 74.1% of the recipients had a functioning graft at the time of follow-up, 17.6% had a failed graft and 5.2% had died with a functioning graft. The mean follow-up period was 6.3 years.

From the period 1969-1985 207 LDKT were performed with a 10 year graft survival rate of 70% and mean follow-up of 11 years. From 1986-2000, 224 LDKT were performed with a 10 year graft survival rate of 80% and a mean follow-up of 11.7 years. From 2001-2015, a total of 1269 LDKT were performed with a 10 year graft survival rate of 85% with a mean 4.56 years follow-up. Log rank test of graft survival showed a chi squared statistic of 22.4 ($p < 0.001$).

Discussion

Living donor nephrectomy and transplantation is a safe and effective treatment option with low complication rates for donors and good graft outcomes. The volume of LDKT is increasing and graft survival is improving significantly over time.

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National audit of nephrectomised kidneys for T1a/b tumours and assessment of their suitability for an altruistic transplant program

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Introduction

The national shortage of available kidneys for transplantation in the UK is well documented and has led to increasing numbers of “extended criteria” donor kidneys being utilised to good effect. Our centre has a local program of transplanting kidneys undergoing radical nephrectomy for T1a/b tumours without tumour recurrence over a three year follow-up period. This builds upon evidence from the Cincinnati transplant registry (Penn 1995) and series of 43 patients transplanted with tumour-excised kidneys in Australia (Nichol 2007) which have shown very low recurrence of malignancy in kidneys transplanted with clear resection margins. The aim of this study was to assess the size and quality of the potential donor pool from tumour excised kidneys.

Methods

Three years of data from 2012-2014 was provided by the British Association of Urological Surgeons (BAUS) national database and analysed using Microsoft Excel 2010. Patients who fulfilled the 3 primary criteria (creatinine <120, tumour size <5cm, 1a/b tumour stage) were identified. Patients with incomplete data sets were excluded.

Results

From 4236 radical nephrectomies entered into the BAUS database 4005 were categorised as stage 1a/b. Mean pre-operative creatinine was 94 mmol/l (standard deviation (SD) 69 mmol/l) and 4049 of the 4236 patients had a pre-op creatinine <120 mmol/l. Tumour size <5cm in 3839 cases with a mean 3.89cm (SD 2.19cm). 2463 patients met all three criteria of suitability for transplantation currently used by our centre.

Discussion

Tumour excised kidneys provide a large potential pool of organs for transplantation. Advantages of short ischaemic times and those of live donation work to offset the reduced nephron numbers from the cancer resection. Recipients with multiple co-morbidities and those at highest risk on dialysis will benefit maximally from utilising this new organ source.

Kidneys declined for paediatric transplantation can have good short-term renal allograft survival if eventually transplanted

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Introduction

Kidneys offered for paediatric transplantation may be declined for a variety of donor or recipient specific factors. The outcome of organs which have been declined for paediatric recipients is not known. The aims of this study were to determine the outcome of kidneys which were declined for paediatric recipients and establish renal allograft survival in kidneys that were eventually transplanted.

Methods

Data were collected for all kidneys offered and declined for paediatric recipients (aged under 18 years) in the UK from 2009-2014. The eventual outcome of declined kidneys was recorded, as well as 3-year renal allograft survival in those that were eventually transplanted. The outcome for children who had a kidney declined on their behalf was also analysed, with time to transplant calculated for those children who eventually went on to get a transplant. Ethical principles were adhered to.

Results

615 kidneys were available for transplantation from donors initially declined for kidney transplantation to 204 different paediatric recipients from 2009-2014 in the UK. 82% of the 615 declined kidneys were eventually transplanted, 7% of kidneys went to paediatric recipients and 62% of kidneys went to adult recipients. 3-year renal allograft survival in the kidneys that went to paediatric recipients was 82% (95% CI 67-91%). 84% of the 204 children who initially had an offer declined on their behalf were eventually transplanted and have a functioning graft, 11% of children are still waiting for a kidney transplant, 1 child died waiting for a kidney transplant. The median waiting time for a child to be transplanted with a DBD kidney after an offer was declined for them was 198 days (range 0-1701 days).

Discussion

This study reports good short-term renal allograft survival in kidneys that were initially declined for paediatric recipients and then subsequently transplanted. Whilst most children who have a kidney declined on their behalf will eventually be transplanted, they wait more than 6 months on average to get a kidney transplant. In view of the significant advantages of transplantation over other forms of renal replacement therapy in children, criteria for accepting kidneys for paediatric recipients could be reviewed.

Organ selection strategies in double adult kidney transplantation: are pre-implantation kidney biopsies really necessary?

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Introduction

Innovative approaches are required in order to achieve adequate graft outcomes from increasingly elderly deceased donor kidney donors. Double Adult Kidney Transplantation (DAKT) offers a potential solution, but the accurate selection of kidneys suitable for DAKT is essential, avoiding inappropriate discard or implantation. The use of pre-implantation kidney biopsies (PIKB) and histological scoring of elderly kidneys has been widely described in the literature (the Remuzzi approach), but few UK units have 24/7 access to such a service. Our unit can perform PIKB during limited daylight hours only. We compared the outcomes of kidneys selected using standard assessment versus those selected using the Remuzzi approach.

Methods

We retrospectively analysed all DAKTs performed between April 2012 and September 2015 in our unit. PIKBs were used to aid decision-making when the emergency histopathology service was available (Remuzzi score 0-3 = single kidney transplants; 4-6 = DAKT; 7-12 = discard). Time-zero biopsies were routinely taken in the non-PIKB group and analysed electively. Recipients were stratified into two groups based on whether a PIKB was performed (PIKB group), or not (non-PIKB). Variables included delayed graft function (DGF), donor and recipient eGFR (4-variable MDRD equation), UK Kidney Donor Risk Index (CJ Watson et al, Transplantation 2012), death-censored graft survival, and patient survival. The chi-squared test was used to compare categorical variables, the Mann Whitney U test for continuous variables, and the log-rank test to compare survivals.

Results

Forty-two DAKTs were performed; 13 after PIKB and 29 without PIKB. There were no significant differences between PIKB and non-PIKB groups in median donor age (74 versus 72 years), DCD status (73% versus 58%), UKKDRI (1.9 versus 1.8), median donor eGFR at retrieval, or median recipient age (66 versus 63 years). Cold ischaemic times for the first and second kidneys in the pair (CIT1 and CIT2) were significantly higher in the PIKB group (CIT1 14 versus 12 hours, $p=0.01$; CIT2 17 versus 13 hours, $p=0.03$). The median (range) graft PIKB or time-zero Remuzzi scores were not significantly different between the two groups (PIKB 5 (3-6) versus non-PIKB 4 (2-7), $p=0.15$). There were no significant differences in graft or patient outcomes between PIKB and non-PIKB groups: DGF 69% versus 62% ($p=0.65$); median inpatient stay 11 versus 11 days ($p=0.95$); three-month eGFR 48 versus 35 ml/min/1.73m² ($p=0.20$); and 12-month eGFR 39 versus 54 ml/min/1.73m² ($p=0.94$). There were four graft losses (all in the non-PIKB group) but no significant difference in death-censored graft survival compared to the PIKB group ($p=0.17$). Two patient deaths occurred, both in the non-PIKB group, but there was no significant difference in patient survival ($p=0.35$).

Discussion

These results suggest that satisfactory outcomes can be achieved for DAKTs implanted on the basis of standard assessment alone, though it is notable that all graft and patient losses occurred in the non-PIKB group. Although basic donor characteristics were similar between the two groups, it is possible that there were differences in donor risk that were not captured by the above data. PIKBs provide some reassurance to clinicians and patients pre-transplant, but their benefits should be balanced against the risks of slightly prolonged CITs in kidney transplants from DCD donors. The role of PIKBs in elderly deceased donor kidney transplantation has yet to be fully characterised.

Flow studies in hypothermic machine perfusion of donor kidneys and long term graft function

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Introduction

Ex-vivo perfusion of donor organs has shown potential in improving graft function in the recipient. However, flow characteristics have not been utilised as a prognostic tool to predict long term graft outcome. Previous guidelines, in fact, discouraged the making of a decision to transplant a donor organ based on flow data. Few studies have analysed data from hypothermic machine perfusion (HMP), though anecdotal accounts of poor function with poor flow characteristics abound.

Methods

Data from all deceased donor kidney transplants was collected prospectively from Jan 2010 to August 2015. This was entered prospectively in an Excel datasheet designed and maintained at the transplant unit and updated regularly. Lifeport® kidney transporter was utilised universally for HMP. Pulsatile perfusion pressure was set at 30 mm Hg and data was recorded continuously during perfusion, including duration, flow rates and resistance. Graft function was then followed up in the recipients in both groups (HMP and Standard Cold Storage [SCS]). Data was analysed using SPSS® version 20.

Results

A total of 438 transplant recipients were followed up. Of these 115 (26.2 %) received HMP. Average donor age in the HMP group was 59.4 years (median 63.2) and donor BMI was 27.1 (median 26.7). The average Cold Ischaemia Time was 15 hours (median 14.5). HMP and SCS groups are compared in another study.

Total HMP Time (HMPT) was variable but averaged at 8.6 hours (median 8.2) and ranged from 1.5 to 16.9 hours. Initial Flow Rates (InitFR) averaged at 62.4 ml/min (median 55), rose to 104.4 at one hour (1hFR)(median 99), 102.9 at three hours (3hFR)(median 102.5) and peaked at end of machine perfusion (End Flow Rate or EndFR)(mean 106.9, median 103.5). Mean Change in flow rate (ChangeFR) was +44.6 mls/min (median 41), and ranged from -20 to +167 mls/min. Average eGFR (estimated Glomerular Filtration Rate) was 45.8 at one year (median 46) and 44.3 at two years (median 41).

Donor age had an inverse correlation with InitFR ($P=0.029$) i.e. older donor kidneys had lower flow rates, however, mean change in flow rate (ChangeFR) was less strongly related to age ($P=0.288$) as flow is less likely to improve with older kidneys. Donor age had a negative impact on one, two and three year eGFRs ($P=0.000$) in the recipient. Total HMP Time had a limited effect on eGFR at one year (1yrGFR), but impacted 2yrGFR significantly ($P=0.029$). Similarly, InitFR had a significant effect on eGFR at two years ($P=0.027$). One hour flow rate (1hrFR) had a positive effect on eGFR at one month ($P=0.047$), but this wasn't significant at one and two years. Similarly, three hour flow rates (3hrFR) had a positive effect on eGFR but remained statistically insignificant upto two years after transplantation (P at one year 0.319, and at two years 0.505). EndFR and & ChangeFR also had a positive effect on eGFR but this wasn't significant at one year ($P=0.067$ & 0.644) or two years ($P=0.106$ & 0.930).

Discussion

Donor age has a negative impact on eGFR as shown by numerous studies. Older donor kidneys tend to have lower initial flow rates (probably as a result of vascular changes) and improvement in flow rate is lower than that for younger kidneys. Initial flow rates correlate strongly with two year eGFR suggesting a role of this modality in predicting long term graft function and possibly the implantation of borderline kidneys.

Flow rates at one hour, three hours and at the end of HMP impact positively on the eGFR but this isn't statistically significant. However, duration of machine perfusion correlates well with two year eGFR suggesting a positive effect of prolonged pulsatile flow and negating the benefits of short-term HMP suggested by some authors. Inclusion of data from multiple centres would be required to consolidate these findings.

P193

What is the optimum extraction site in laparoscopic donor nephrectomy?

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Introduction

Laparoscopic donor nephrectomy can be performed totally laparoscopic (LDN), hand-assisted laparoscopic (HALDN) or open. A proposed advantage of minimally invasive surgery is a reduction in wound complications. However some HALDN series report significant incisional hernia rates. Our aim was to review our wound problems after surgery and compare to historic series.

Methods

LDN in our unit is performed totally laparoscopically with the kidney removed using a 15 endocatch bag via a 6cm non-muscle cutting pfannensteil incision. A prospectively collated database of 500 consecutive patients undergoing LDN in our unit was interrogated to investigate wound complications following surgery. Patients are routinely reviewed at 3 months. A literature review focusing on wound complications in LDN was also performed.

Results

There were no conversions to open surgery in our LDN cohort. 3 monthly follow up data was available for 303 patients. In the first 30 day period post-operatively there were 2 wound dehiscences – both were superficial with the sheath intact. One was closed on the ward (calvien 2) and one closed in theatre (clavien 3). Documented wound infection rate requiring antibiotic was 2%. No incisional hernias were identified. The incisional hernia rate in published series of hand-assisted laparoscopic donor nephrectomy is 0.1% -5%.

Discussion

The largest hand-assisted laparoscopic donor nephrectomy series in the UK was presented at the BTS in 2015 and revealed a moderate incisional hernia rate from an epigastric port site. Some authors have suggested that a pfannensteil incision reduces the risk of incisional herniation. We believe that totally laparoscopic donor nephrectomy represents the gold standard for donor nephrectomy. Despite the limitation of short follow-up time and some absent data from within this study, a non-muscle cutting pfanensteil incision would appear to confer an advantage with respect to hernia and dehiscence rate. Regular auditing of donor nephrectomy outcomes may help clarify optimal techniques.

P194

Retroperitoneal versus intraperitoneal hand assisted laparoscopic donor nephrectomy: a case matched study

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Introduction

Although hand assisted laparoscopic donor nephrectomy (HALDN) has become a standard of care for living kidney procurement in most centres it is not clear if a retroperitoneal approach offers any advantage over an intraperitoneal approach. Recent RCT data has been published on the subject but the results have been biased by small patient numbers and significant demographic and operative heterogeneity between groups. We therefore conducted a case matched study of retroperitoneal versus intraperitoneal HALDN.

Methods

61 retroperitoneal HALDNs were matched 2:1 with 122 intraperitoneal HALDNs for age, sex, laterality, multiplicity of arteries and obesity status (BMI > 30) characteristics using a propensity matching score approach using Stata SE 12. Outcomes assessed were Clavien grade 2, 3 and 4 complications, infective episodes, readmission, need for reoperation, postoperative hospital stay, creatinine change at Day 30 and development of incisional hernia.

Results

The mean age of the cohort was 44.1 years (SD11) with 52.5% female. The mean length of surgery was greater in the retroperitoneal cohort (225 mins v 200 mins, p=0.001). Hospital stay (4.2 v 3.9 days p=0.11) and readmission rates (9.1 v 9.6% p=0.12) were similar. Incidence of postoperative surgical site infection (9.9% v 10.1% p=0.1) and the occurrence of minor complications (Clavien 2) were also equivalent (16.3 v 17.3% p=0.45). The abdominal reoperation rate was lower in the retroperitoneal group (1.6% v 3.3% p=0.009) as was the rate of incisional hernia development at one year (0% v 5% p=0.08). Day 2 peak CRP levels were less in the retroperitoneal group (111 v 123 p=0.035). Creatinine rise at day 30 was similar (+34 v +37 p=0.35).

Discussion

Retroperitoneal HALDN has similar minor complication outcomes compared to the intraperitoneal approach with similar lengths of hospital stay and readmission rates. However there is evidence from this study that it may exhibit a reduced systemic inflammatory response (as measured by Day 2 CRP) and also reduce more serious surgical complications thereby reducing the need for reoperation and ultimately reducing the overall donor morbidity burden.

P195

Radical nephrectomies done for pT1a and pT1b renal tumours: a national audit of the hospitals involved and logistics of a synchronised National program promoting use of the kidneys for transplantation

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Introduction

The shortage of suitable organs for transplant and ever expanding donor wait list has led to investigations into novel sources of organs. One such source is use of kidneys for transplants after radical nephrectomy for pT1a (<4 cm) and pT1b (<7cm) tumours after ex-vivo tumour resection. These kidneys have historically been shown to possess no added risk to the recipient (Cincinnati Registry, Nicol et al). This audit aims to assess the scope of this donor organ pool in the United Kingdom focusing on a better logistical and training approach in National Urology and Transplant catchment areas.

Methods

Two year data (2013/14) relating to the number of Radical Nephrectomies performed for pT1a (<4cm) and pT1b (<7cm) and the hospital performing these surgeries was obtained from BAUS National registry. Urology and Transplant centre catchment areas were obtained from respective trusts/centres. These were co-related with the hospital involved in carrying out the procedures and thus mapping of prospective 'Tumour-kidney' catchment areas was attempted.

Results

1042 Radical nephrectomies were performed for pT1a lesions and 1497 for pT1b tumours. Nearly 160 trusts perform these procedures, many being district general hospitals. Dedicated teams and extra resources leading to linking these trusts to regional Urology and/or Transplant Units is feasible which will lead to potential harvest of these kidneys for transplant.

Discussion

Tumour excised kidneys are a potential source of organs for transplant. More than 1000 Kidneys resected for pT1a and pT1b tumours are discarded per year in the United Kingdom. In the presence of a National program, these can be utilised for transplantation after ex-vivo tumour resection and careful recipient selection.

P196

Explanted internal iliac grafts are an independent risk factor for transplant renal artery stenosis

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Introduction

Transplant renal artery stenosis (TRAS) is a major determinant in allograft survival and premature mortality. Prompt diagnosis and management significantly reduces these risks. This study aims to identify the associated risk factors and outcomes for patients with TRAS in a living donor series with particular emphasis on the type of arterial anastomosis.

Methods

A series of 506 consecutive live donor nephrectomy transplants at a single UK institution from 1998-2014 were analysed retrospectively. Baseline donor and recipient characteristics and ischaemic times were recorded. TRAS was diagnosed by CT/MR angiography. Independent risk factors for TRAS were identified using a multivariate analysis model. Recipients were followed up for a minimum of 1 year.

Results

Twenty-one recipients (4.1%) developed TRAS. TRAS and non-TRAS groups were well matched for donor and recipient characteristics. Explanted internal iliac graft anastomosis (Odds Ratio 4.95, 95% Confidence Interval 1.26-19.50, p=0.02) and total ischaemic times (OR 1.82, 95% CI 1.11-2.96, p=0.01) were identified as independent risk factors for TRAS. TRAS was managed by angioplasty ± stent. Patient survival was comparable between TRAS and non-TRAS (p=0.11). TRAS was associated with a decreased 10-year allograft survival (TRAS 80.9% vs non-TRAS 88.7%, p=0.03). All causes of reduced allograft survival in the TRAS group were attributable to non-TRAS related complications.

Discussion

Explanted internal iliac grafts and total ischaemic times were independent risk factors for the development of TRAS in our series. Having a low threshold of clinical suspicion with timely diagnosis and management demonstrates no additional recipient morbidity or mortality.

Expanding the deceased donor pool by transplantation of kidneys from increased infectious risk donors (IIRDs)

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Introduction

Kidneys from increased infectious risk donors (IIRDs) are commonly declined by most transplant centres, due to the risk of viral transmission to the recipient. However, this risk may be diminished with the appropriate use of nucleic acid testing (NAT) in specific donor categories, with negative serology for hepatitis B, hepatitis C and HIV at the time of donation. A national guidance for the use of organs from IIRDs is currently lacking, hence organs from such, usually young, donors are being underutilised.

Methods

We developed a local protocol for the use of NAT for screening IIRDs at the time of donation, which enables kidney transplantation in appropriately selected recipients, followed by an intensive virology surveillance schedule in the post-transplant period. Herein, we report the feasibility, safety and outcomes of a series of successful transplants from IIRDs in our centre, since the implementation of the protocol in December 2014.

Results

Four kidney grafts from three IIRDs (2 DBD, 1 DCD) with a history of IV drug use were transplanted in four recipients. All donors and recipients had negative serology for hepatitis B and C, and HIV at the time of donation. Pre-transplant NAT testing was negative in all cases. Recipients were appropriately consented for risk of viral transmission, according to the protocol. Mean donor and recipient age was 38.7 and 54 years, respectively. All recipients were established on haemodialysis with a median waiting time on the transplant list of 900 days (interquartile range - IQR 639.8). The two DCD recipients were moderately sensitized with a calculated reaction frequency (cRF) of 56% and 70%, respectively. The mean cold ischemia time (CIT) of the kidney grafts was 695 min. The two DCD grafts had DGF, which resolved within few days. No rejection episodes were recorded within the first three months. The mean eGFR at three months post-transplant was 38.8 ml/min/1.73m². All recipients remained negative for hepatitis B and C, and HIV at three months after transplantation.

Discussion

Kidney grafts from seronegative IIRDs with negative NAT testing may be safely transplanted in carefully selected recipients, e.g. highly sensitised, with a long waiting time on the transplant list. Appropriate consenting for the risk of viral transmission and adherence to an intensive post-transplant surveillance protocol are of paramount importance. The short-term graft function is comparable to non-IIRDs. The development and implementation of a similar protocol at a national level could expand the deceased donor pool with good quality organs and subsequently reduce the waiting time for a kidney transplant.

P198

Review of practice of dual listing of patients on the transplant waiting list: a single centre 5-year experience

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Introduction

Practices vary amongst units when it comes to keeping potential kidney transplant patients on the deceased donor waiting list who have an identified potential living kidney donor. In our centre, patients remain on the deceased donor list until a theatre date is booked for the transplant, allowing for them to receive a deceased donor kidney should it become available while waiting.

This project specifically compares the outcomes between those patients who while being worked up for a living donor kidney transplant received a deceased donor transplant and those patients who proceeded to receive a living donor transplant.

Methods

Over a 5-year period from 2010-2015, recipients being worked-up for a living donor kidney transplant at the OTC were categorized into two groups based on whether they received a deceased or living donor kidney. Primary outcomes compared were incidence of delayed graft function (DGF), estimated GFR at 1 year and incidence of graft failure in first year.

Results

291 recipients on the living donor list were identified between 2010 and 2014. Of these, 49 (16.8%) received a deceased donor kidney. Incidence of DGF was higher in the deceased donor group (27.3%) compared to the living donor group (2.8%). There was no significant difference in eGFR and incidence of graft failure at 1 year between the two groups.

Discussion

This study has shown that in the medium-term, receiving a deceased donor kidney does not disadvantage kidney transplant recipients who were previously waiting for a living donor kidney. The current policy at our centre can therefore be deemed appropriate pending studies on longer-term outcomes. We are currently collecting data on longer-term outcomes as well as collecting donor information (age, kidney function, co-morbidities) as we recognise that this has a significant impact on both long- and short-term outcomes.

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Zero-ischemia zero-transfusion transplant kidney partial nephrectomy

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Introduction

De novo renal cell carcinoma (RCC) in a renal transplant kidney (RTx) is rare. Demand for RTx is increasing; so partial nephrectomy (PN) where possible can maintain a functioning RTx. We describe our experience with RCC in renal transplant kidneys.

Methods

We identified 3 RTx PNs performed at our institution in the last 17 years. Our last 2 cases, both in 2015, were performed with zero ischemia and zero blood transfusion including the first case for an endophytic RCC.

Results

Case 1: A 27 year old male had CT performed for pancreatitis 2 years post living donor RTx. An incidental 2cm inter-polar endophytic mass was identified in the RTx kidney, confirmed as Type 1 Papillary RCC by percutaneous biopsy. Open PN was performed via the old RTx incision. The RTx kidney was fully mobilised controlling iliac vessels proximal and distal to RTx artery and vein. Intra-operative USS identified the exact location and margin of the endophytic RTx mass. Renal capsule over the mass was marked with diathermy. The mass was excised with sharp dissection. Hemostasis was achieved with manual compression of adjacent edges, sutures to major bleeders, argon laser to parenchyma, pro-coagulant products to cavity and closure of renal capsule. Estimated blood loss ~ 500ml; operation time 3.5 hours. Patient discharged on day 5. Pre-op Hemoglobin (Hb) was 136g/L and 113g/L on day 1. He did not require blood transfusion. Pre- and 2 month post-surgery creatinine was identical (91umol/L). Histology confirmed a 15mm type 1 papillary RCC with clear margin.

Case 2: A 68 year old man had staging CT performed for melanoma 10 years post-RTx. An incidental exophytic 3cm RTx mass was detected. A similar surgical approach was taken but without intra-operative ultrasound. This patient had a longer hospital stay, as recovery was complicated by a urine leak requiring drain and catheter for 2 weeks. He made an otherwise uneventful recovery. Histology confirmed a 30mm Fuhrman grade 3 clear cell RCC.

Discussion

63 PNs for RTx RCC have been reported in the world literature since 1977. The majority describe segmental clamping of vessels with subsequent ischemic insult. 2 cases of zero ischemia PN were reported for exophytic masses in RTx, but no zero ischemia endophytic PNs have been reported. We believe the key steps to a zero ischaemia /transfusion PN maintaining excellent RTx function are: a team of a RTx urologist, uro-radiologist for identification of endophytic tumors and urologist experienced in open PN of solitary kidneys; an adequate Hb with 'planned' blood loss ~ 500ml and hemostatic products. Our cases highlight the importance of a highly skilled multi-disciplinary approach to provide a successful oncological and functional outcome.

P200

Does hypothermic machine perfusion neutralise 'age effects' on DCD kidneys?

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Introduction

Delayed graft function is an unwanted outcome in some transplanted kidneys, with organs from DCD (circulatory death donors) being affected more than DBD (brainstem death donors). One reason for this trend is a longer warm ischaemic time in DCD donors leading to tissue damage in the organs. It is well established that hypothermic machine perfusion (HMP) allows for better early post-operative graft function when compared to static cold storage (SCS). Long-term benefits, however, remain a topic of discussion. We aim to ascertain whether there are significant differences in one-year outcomes from older DCD donors whose kidneys have been statically stored vs machine perfused to aid future decision making in our unit.

Methods

Data from all kidneys transplanted in our unit are collected prospectively on a secure, central database. A retrospective analysis of the data, including donor and recipient demographics, donor eGFR and one-year GFR, from 162 DCD transplants (109 SCD > 40 years old and 53 ECD > 65 years old) performed between 01/2010 and 08/2015 was undertaken. The data was analysed using 'IBM SPSS Statistics 23' to determine if there were any significant differences in one-year GFR between the HMP and SCS groups.

Results

There were no significant differences in donor age or donor eGFR in both groups. Cold ischaemic time (CIT) was significantly longer in ECD kidneys on HMP vs SCS ($p=0.004$), there was no significant difference in CIT in the SCD groups ($p=0.105$). There were no significant differences in one-year GFR for HMP vs SCS kidneys between the two groups (ECD $p=0.872$, SCD $p=0.612$). Similarly there were no significant differences in the change of GFR at one year in both groups (ECD $p=0.684$, SCS $p=0.971$).

Discussion

Whilst it is well established that HMP is beneficial for reducing the rates of DGF and primary non-function in DCD kidney transplants, it is also a costly, labour-intensive process. This study suggests that there is little long-term benefit in using HMP in older DCD kidneys, as any immediately beneficial effects are lost by one year post-transplantation. The reason for this is that the donor changes are likely to be chronic and irreversible. To ensure that these conclusions are accurate, a future, higher powered study would need to be undertaken.

P201

A retrospective review of the use of donor kidneys with acute kidney injury in renal transplantation

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Introduction

The use of extended criteria donors is increasingly common as efforts are made to bridge the disparity between the number of patients awaiting deceased donor transplantation and the number of donor kidneys available. The use of donor kidneys with acute kidney injury (AKI) is an emerging aspect of this. However guidance on the acceptance of such kidneys is not included in our unit's current guidelines and clinicians consider offers on a case by case basis. We sought to better understand the current practice of our own unit in this regard and to evaluate the outcomes of the recipients of donor kidneys with AKI.

Methods

We undertook a retrospective review of all renal transplants performed locally over a 12 month period from April 2013 to March 2014. Data was collected from our electronic patient records (VitalData) and the NHSBT Organ Donation and Transplantation Electronic Offering System. Donor AKI was defined according to the AKIN criteria on the basis of the donor creatinine results and donor urine outputs. Data regarding the recipient (age and BMI), transplant (HLA mismatch and cold ischaemic time), and donor (age) was collected. Outcome data was also collected, including graft function at 6 months and 1 year, the incidence of delayed graft function (DGF), and the incidence of biopsy-proven acute rejection (BPAR) in first 6 months. Statistical analysis was performed to compare these outcomes between the AKI and non-AKI groups, using linear and logistic regression analyses to reduce confounding factors.

Results

A total of 45 of the 72 renal transplants performed were from deceased donors. The mean age of recipients was 52 years and mean age of donors was 53 years. Six out of 45 donors (13%) had an AKI according to AKIN criteria (stage 1, n=3; stage 2, n=2; stage 3, n=1). The differences in the incidences of DGF (33.3% vs 36.8%), BPAR (16.6% vs 15.8%) and mean eGFR at 1 year (50 vs 41 mL/min/1.73 m²) between the AKI and non-AKI groups respectively were not statistically significant. This finding persisted when other variables (donor age, recipient age, recipient BMI, HLA mismatch and cold ischaemic time) were accounted for. A higher recipient BMI was associated with higher likelihood of delayed graft function (p value 0.033).

Discussion

Our experience is that the acceptance of donor kidneys with AKI does not negatively impact upon outcomes including BPAR and graft function at 1 year. This is in keeping with the recent published literature. It was outside of the scope of this review to determine the number of offers declined by our centre due to the presence of AKI in the donor kidney. However, it seems likely that there is scope to increase our utilisation of donors with AKI locally and this review suggests that our outcomes would not suffer as a result. Referring centres should be encouraged to provide historic creatinine results in order to aid the differentiation of AKI from chronic kidney disease in donors.

This review found comparable rates of DGF between the two groups. This is counter-intuitive, at odds with the associations seen in the published literature, and probably due to the relatively small sample size in the population included in this study.

P202

Frozen kidney, a serious but avoidable complication of inadequate hypothermic renal preservation for transplantation

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Introduction

Hypothermic static storage is the standard of kidney preservation for transplantation. Following in-situ flush, the kidney is stored in a preservation solution on ice at 0-4°C. Freezing of kidney during storage is associated with the formation of ice crystals, which in conjunction with subsequent thawing, destroys the integrity of the cells rendering the kidney non-transplantable. An unexpected drop in temperature, inadequate volume of preservation fluid or a rise of the freezing point (by mixing other solution or ice/slush to the preservation fluid) may lead to freezing of the kidney during preservation. We describe two cases of frozen kidney where kidney could not be transplanted and one case of a near miss where freezing was avoided due to timely intervention.

Methods

3 kidneys received at our centre in the past 24 months met the criteria for inclusion in this review of practice. Kidney 1 was part of a 3-way live-donor exchange, was imminently frozen and proceeded to transplantation. Kidney 2 and Kidney 3 were frozen and were not transplanted.

Results

Kidney 1 was packed with ice blocks and with scanty preservation fluid. Timely intervention prevented imminent freezing of this kidney. The recipient of Kidney 1 had primary function with, 3month and 12month creatinine of 99, and 127µmol/L. Kidney 2 was noted to be frozen when opened immediately prior to implantation. The kidney was stored in scanty preservation fluid again with ice blocks. This kidney was benched, re-packed and re-iced in our centre. Kidney 3 arrived frozen with scanty perfusion fluid, again with ice blocks. Analysis of fluid biochemistry in one case confirmed contamination of preservation fluid with a sodium rich fluid.

Conclusion

Freezing renders the kidney non-transplantable. In most cases freezing occurs due to either scanty preservation fluid or placing saline ice blocks in direct contact with the kidney. Contamination with saline may raise the freezing point of the kidney. Appropriate icing & packaging is crucial to prevent freezing.

P203

Are diseased donor kidneys declining inq?

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Introduction

There has been some concern in the UK transplant community regarding the deterioration in quality of diseased donor organs over the last five years. The data from NHSBT is generally reassuring but centre-specific reports are inevitably historic when reporting 1 and 5 year outcomes. The six month eGFR permits a more contemporary assessment of performance and here we use this method to analyse the performance of one of the UKs busiest transplant units including a subanalysis of Fast Track kidneys.

Methods

We searched our regional electronic database for kidney function at 6 months after transplantation in cadaveric grafts from 2010 to 2015. We excluded diseased patients and assigned an eGFR of 0 to failed grafts. We also analysed kidneys obtained under the Fast Track scheme for 2013 to 2015.

Results

The results for renal function are shown in the table below:

| Year | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | FT13 | FT14 | FT15 |
|---|---------------|----------------|----------------|---------------|---------------|---------------|---------------|---------------|---------------|
| n | 80 | 98 | 117 | 152 | 149 | 57 | 39 | 26 | 20 |
| 6/12 eGFR (mls/min/1.73m ²) Mean±SD | 44.0± 20.3 | 40.4 ± 21.0 | 44.3 ± 19.8 | 40.4± 20.5 | 38.8± 21.1 | 41.8± 19.4 | 38.2± 19.4 | 44.1± 19.6 | 36.1± 15.2 |
| Median | 41 | 38 | 43 | 40 | 38 | 42 | 37 | 42 | 39.5 |

There were no significant differences between different years nor between fast track and non-fast track kidneys for any given year.

Discussion

These results are reassuring since average renal function is being maintained despite the perceived drop in quality of cadaveric organs. Kidneys transplanted under the fast track scheme are not inferior at our centre. Monitoring six month eGFR allows a contemporary examination of transplant outcomes.

P204

Live-related kidney transplantation after ex-vivo repair of the donor renal artery aneurysm (RAA): a case report

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Introduction

Kidney transplantation is the definite surgical treatment for end-stage renal disease. Shortage of organs and the increasing number of patients with end stage renal disease has led to expansion of the selection criteria promoting use of organs from marginal donors. Use of kidneys with renal artery aneurysm (RAA) is one such example.

Case

We report a case of living-related kidney transplantation from a 46-year-old female donor with unilateral RAA to her 68-year-old father. The pre-operative donor's assessment with a computed tomography angiogram, revealed a saccular aneurysm of the left renal artery. The transplant team proceeded to the left nephrectomy, surgical ex vivo repair of the aneurysm and transplantation of this kidney to the recipient, with the total ischemic time of 130 minutes. At revascularization there was no anastomotic leak with good perfusion of the organ and normal postoperative kidney function.

Discussion

RAA is a rare renal anatomical abnormality with unproven clinical significance. Advanced microvascular surgical techniques can be used to repair the aneurysm with subsequent successful use for transplantation.