ORAL PRESENTATIONS 2C
TRANSPLANT SURGERY

O65 CD8 T CELLS PROCESS ALLOANTIGEN ACQUIRED FROM MHC-I ON GRAFT CELLS AND PROVIDE HELP TO INDIRECT PATHWAY CD4 T CELLS

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Introduction: CD4 T cells play a pivotal role in allograft rejection, providing help for cytotoxic CD8 T cells. During direct allorecognition, CD4 and CD8 T cells recognise intact MHC II and MHC I respectively on a donor APC. We investigate how indirect-pathway CD4 T cells that recognize processed alloantigen presented by recipient APCs provide 'unlinked' help for cytotoxic CD8 T cells recognizing intact allo-MHC I on donor cells directly.

Method: We have developed a murine heart transplant model in which rejection is mediated by cytotoxic CD8 T cells, but help is limited to monoclonal populations of adoptively transferred TCR-transgenic CD4 T cells restricted to the direct or indirect pathway.

Result: B6 Rag-/- mice acutely rejected BALB/c grafts (MST 12.5d) when reconstituted with CD8 T cells from TCR75 mice but not MHCII-/- (MST 21d) or H-2DMa mice (unable to process antigen; MST 38d). MHCII-/- CD8 T cells prompted rapid allograft rejection when first 'parked' as a bone-marrow chimeric population in MHC II positive hosts. We suggest a novel mechanism, where indirect pathway CD4 T cells provide help to CD8 T cells through recognition of alloantigen that is internalized by CD8 T cells via the TCR and presented as processed allopeptide on acquired MHCII, analogous to the provision of cognate T cell help to B cells. CONCLUSION: Indirect pathway CD4 T cells provide help to allospecific CD8 T cells through recognition of MHC I derived alloantigen that is internalized by CD8 T cells and presented as processed allopeptide on acquired MHC II.

Take-home message:
Indirect pathway CD4 T cells provide help to allospecific CD8 T cells through recognition of MHC I derived alloantigen that is internalized by CD8 T cells and presented as processed allopeptide on acquired MHC II.

O66 A COMPARISON BETWEEN STATIC COLD STORAGE AND NON-OXYGENATED, PORTAL HYPOTHERMIC MACHINE PERFUSION FOR THE PRESERVATION OF DONATED HUMAN LIVERS

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Introduction: The shortage of organs for liver transplantation has increased the demand for ECDs. Organs from ECDs are more likely to suffer preservation injury, which may result in either early non-function or primary dysfunction of the graft after transplantation. SCS is the only method used for liver preservation. It has been suggested that HMP could be a better technique to preserve livers from ECDs. HMP may allow the liver to receive nutrients and get rid of metabolic wastes. The aim of this study is to assess the benefits of non-oxygenated, portal HMP of human livers through the histological and immunohistochemical analysis of liver biopsies.

Method: 12 livers rejected from different transplant centres were preserved for 4 hours under two different methods: 6 livers underwent SCS, and other 6 livers underwent non-oxygenated, portal HMP. Tissue biopsies were taken before and after the experiments. They were analysed through histological scores on H&E-stains and immunohistochemical expression of caspase-3. Results were compared in both groups.

Result: There were no significant differences regarding histological scores and the number of immunostain-positive cells before and after preservation in both groups. Cells expressing caspase-3 were found on immunohistochemical sections while apoptotic cell bodies were not found on their corresponding H&E-sections.

Conclusion: Non-oxygenated, portal HMP did not attenuate morphological changes after a 4-hour-preservation, neither did it attenuate the expression of caspase-3 compared to SCS. Non-oxygenated, portal HMP showed no advantages over SCS. ECDs: Extended criteria donors; H&E: Haematoxylin and eosin; HMP: Hypothermic machine perfusion; SCS: Static cold storage;

Take-home message:
Non-oxygenated, portal hypothermic machine perfusion of human livers showed no advantages over static cold storage.

O67 LONG TERM COMPARATIVE OUTCOMES OF INDUCTION AGENTS REGIMENS IN SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION

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Introduction: Alemtuzumab, a humanized monoclonal anti-CD52 antibody, has gained widespread use as an induction agent in pancreas transplantation as it facilitates steroid sparing maintenance immunosuppression. However, it is associated with profound and prolonged lymphocyte depletion with potential deleterious effects. There is limited data on long-term patient and pancreas allograft survival, particularly when compared to the interleukin-2 antagonist, Basiliximab. We aimed to compare

outcomes for both agents.
Method: A retrospective, single centre, non-randomised, sequential study of patients receiving a pancreas transplant was performed (June 2001 - June 2014) Patients receiving their second transplant were analysed separately.
Result: 270 primary transplants were performed of which 164 (61%) received basiliximab and 106 (39%) alemtuzumab induction. There was no significant difference in age or gender between groups. More patients in the alemtuzumab group received organs from a non-heartbeating donor (p=0.042). 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) post-transplant respectively. Alemtuzumab had a significantly better one year patient survival (p=0.017), however this difference did not persist at three (p=0.051) or five years (p=0.155.) Patients receiving a second transplant had no significant differences between either agents for both allograft and patient survival.
Conclusion: 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 definitive and reproducible treatment regimens.
Take-home message:
Alemtuzumab and basiliximab induction immunosuppression offer statistically equivalent mid and long term pancreas allograft survival.

O68 TRANSPLANT RENAL ARTERY STENOSIS IN A LIVING DONOR SERIES: RISK FACTORS AND OUTCOMES

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Introduction: 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 factors and outcomes for patients with TRAS in a living donor series.
Method: A consecutive series of 449 consecutive live donor nephrectomy renal transplants performed in one UK centre during the period 1998-2014 was analysed retrospectively. Donor and recipient demographics and ischaemic times were recorded. TRAS was diagnosed by CT or MR angiography. Recipients were followed up for a minimum of 1 year.
Result: In this series, 21(4.7%) recipients developed TRAS. Baseline donors and recipient demographics were comparable in TRAS and non-TRAS groups (donor age, p=0.44; recipient age, p=0.84; donor CMV, p=0.26). Multiple renal arteries were present more often in patients who developed TRAS (43 vs 19%, p=0.02). Ischaemic times were longer in the TRAS group (CIT 3.7 v 3.2hrs, p=0.02; WIT 6 v 4.3mins, p=0.02). The proportion of IIAGR was higher in the TRAS cohort (23.8% vs 4.1%, p=0.0002). There was no significant difference in the ratio of left to right kidneys in the TRAS and non-TRAS groups (p=0.34). There were no graft losses associated with TRAS.
Conclusion: Higher rates of TRAS are associated with longer ischaemic times, multiple-renal artery donor kidneys and IIAGR. However, in this series there were no premature allograft losses associated with TRAS. TRAS Transplant renal artery stenosis CIT Cold Ischaemic Time WIT Warm ischaemic time IIAGR Internal iliac artery graft reconstruction CT computed tomography MR magnetic resonance
Take-home message:
Longer ischaemic times, multiple-renal artery donor kidneys and IIAGR are associated with TRAS. Although there were no premature allograft losses associated with TRAS in this series, vigilant post-transplant monitoring is advised in these particular cohorts.

O69 PRE-EMPTIVE IMMUNOSUPPRESSION USING TACROLIMUS FOR LIVING KIDNEY TRANSPLANTATION

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Introduction: Renal transplantation from live donors offers the opportunity to start recipient immunosuppression pre-emptively. The aim of this study was to determine the effect of pre-emptive immunosuppression on acute rejection rates after live donor kidney transplantation.
Method: In a consecutive series of 199 live donor transplants, the first 100 patients received immunosuppression with basiliximab, tacrolimus, mycophenolate mofetil and steroids commencing on the day of transplantation (control group). The next 99 patients received pre-emptive immunosuppression with tacrolimus monotherapy for two weeks prior to transplantation, followed by the same post-transplant regimen used in the control group (PET group). The main outcome measure was the incidence of biopsy proven rejection (BPAR) in the first 3 months post-transplantation.
Result: BPAR was numerically higher in patients receiving pre-emptive immunosuppression but this difference did not reach statistical significance (PET 13/99 vs. Control 6/100; p=0.097). There were no differences in allograft function measured by serum creatinine at one year (PET 130±36 vs. Control 142±69 µmol/L; p=0.6829). One-year graft survival was equivalent in both groups (PET 96.9 vs. Control 97.0%; p=0.9915). There were no differences in trough tacrolimus levels in the blood at one week post-transplantation in the two groups (PET 12.7±3.9 vs. Control 12.3±7.4 ng/mL; p=0.6356). CONCLUSION: This study demonstrates that pre-emptive immunosuppression with tacrolimus mono-

therapy does not have a beneficial effect on early acute rejection rates or other outcomes in live donor kidney transplantation.

Take-home message:

Pre-emptive immunosupression with tacrolimus has no beneficial effect on early acute rejection rates.

O70 SKELETAL MUSCLE MASS USING COMPUTED TOMOGRAPHY BODY MORPHOMETRIC ASSESSMENT– DEFINING THE NORMAL RANGE

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Introduction: Sarcopenia, the loss of skeletal muscle mass defined using preoperative staging CT scan has increasingly been used for stratifying surgical prognosis. In such studies there is absence of suitable normal control data to accurately define sarcopenia. The aim of this study is to define normal range of CT derived skeletal muscle mass using standard techniques and compare with data from other studies.

Method: Using a published technique of quantifying L3 Skeletal muscle index (L3SMI) from standardised CT scans a cohort of healthy live kidney donors (LKD) were analysed in a transplant centre.

Result: LKD (n=73; 38m: 34f) with an age range 23-75years were assessed for baseline nutritional characteristics and L3SMI. Mean L3SMI +/- SD was 57.7 cm2/m2 +/- 11.0 for males and 43.2 cm2/m2 +/- 6.7 for females which was normally distributed. Defining sarcopenia threshold levels as 2SD below normal results in cutoffs of 35.7 cm2/m2 for males and 29.8 cm2/m2 for females in LKDs. This is considerable lower than the published reference values of L3 SMI < 52.4 cm2/m2 for men and <38.5 cm2/m2 for women (Prado et al 2008) which when tested on the LKD group demonstrated 28.9% (11/38) of males and 38.2% (13/34) of females would be considered sarcopenic.

Conclusion: Studies predicting surgical outcomes using published values (L3SMI) may overestimate sarcopenia. The present study using an age spectrum of healthy LKD may be a more representative population for the definition of sarcopenia for studying surgical patients and correlating with outcomes.

Take-home message:

CT analysis of a healthy population represented by living donor nephrectomies may assist in defining normal skeletal muscle mass and sarcopenia.

O71 SUBSTANTIAL INCREASES IN DECEASED DONOR TRANSPLANT RATES COULD BE ACHIEVED BY EXPANDING THE THRESHOLDS OF SUITABILITY FOR MARGINAL DONORS

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Introduction: Expansion in donor numbers has not realised a proportional expansion in transplant numbers.

Method: We performed a retrospective review of organ offers to our centre from April 2005 to March 2012: donor characteristics, numbers of kidney, liver and pancreas offers for each study year were recorded. As a marker for organ quality, the organ-specific donor risk index (DRI) was calculated.

Result: A total of 5628 organs were offered, numbers increasing substantially from 392 in 2005 to 1230 in 2012. This reflects an expansion in DCD offers; with proportions of DCD kidney, liver and pancreas offers increasing from 19-77%, 6-64%, and 1-62%, respectively. Transplant numbers have increased (kidneys 68-127, livers 57-96, pancreases 4-21). There has been a significant increase in the mean DRI of each type of organ implanted ($p<0.001$), in 2005 the mean DRI of offered organs was similar to those implanted, by 2012 the DRI of offered organs was significantly higher than the DRI of those used. There was no observed difference in one-year graft survival [kidney (HR 0.42, 95% CI 0.8-2.25), liver (HR 1.07, 95%CI 0.43-2.65), pancreases (HR 1.47, 95% CI 0.1-2.18). CONCLUSION: Numbers of organs offered for transplantation have increased markedly, however, numbers of organ transplants have increased to a much smaller extent, principally because the majority of those organs offered are of poorer quality than are currently accepted for transplantation. Our results suggest that either these marginal donors should not be offered for transplantation or that novel strategies should be implemented to enable their use.

Take-home message:

Numbers of organs offered for transplantation have increased markedly, however, numbers of organ transplants have increased to a much smaller extent, our results suggest that either these marginal donors should not be offered for transplantation or that novel strategies should be implemented to enable their use.

O72 QUALITY ASSESSMENT OF DISCARDED HUMAN KIDNEYS: A COMPARISON OF HYPOTHERMIC MACHINE PERFUSION AND EX-VIVO NORMOTHERMIC PERFUSION TECHNIQUES

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Introduction: In renal transplantation accurate means of viability and quality assessment are essential to ensure the efficient use and allocation of organs. The aim of this study was to compare HMP and ex-vivo EVNP assessment techniques.

Method: Ethical approval was granted for the study by the national research ethics commission in the UK. Ten human kidneys rejected for transplantation underwent 60 minutes of HMP (Lifeport Kidney

Transporter) with KPS-1 solution at 4°C. At 60 minutes the RR was recorded. After HMP, kidneys underwent 60 minutes of EVNP with an oxygenated packed red cell based solution at 36°C. Functional parameters were measured after 60 minutes.
Result: The mean donor age was 54±9y and the cold ischaemic time 43.9±11.6h. During HMP the RR fell in all kidneys but remained above 0.3mmHg/ml/min in 9/10 kidneys at 60 minutes (mean 0.6±0.4mmHg/ml/min). During EVNP the mean RBF was 94±33ml/min/100g and IRR 0.4±2.5mmHg/ml. Seven out of ten kidneys produced a significant quantity of urine (range 100–330ml) and all kidneys appeared evenly perfused. The mean oxygen consumption was 74±23ml/min/g. The RR after HMP did not correlate with any of the perfusion parameters during EVNP ($P>0.05$).
Conclusion: There was no association between the parameters measured during HMP and EVNP. The level of RR during HMP was indicative of a high level of injury. However, the majority of kidneys during EVNP demonstrated a good level of recovery and function. Restoring function using EVNP allows a more comprehensive assessment of the kidney prior to transplantation. EVNP Ex-vivo normothermic perfusion HMP Hypothermic machine perfusion IRR Intra-renal resistance RBF Renal blood flow RR Renal resistance.
Take-home message:
Restoring function using ex-vivo normothermic perfusion allows a more comprehensive assessment of the kidney prior to transplantation.