Mini Oral Sessions

Sunday, 4 September 2011

Kidney I

MO-001

CD8DR EXPRESSION IN GRAFT-INFILTRATING LYMPHOCYTES ACCURATELY IDENTIFY ACUTE REJECTION IN KIDNEY TRANSPLANTS

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Background: Flow cytometry analysis of fine-needle aspiration biopsy (FNAB) samples achieved high diagnostic performance in kidney transplants (KTx) treated with cyclosporine-azathioprine-prednisolone. We tested its accuracy under modern immunosuppression regimens.
Methods: One hundred and twenty-nine KTx were studied, all treated with calcineurin inhibitors, mycophenolate mofetil and prednisolone from the beginning with eight exceptions who received thymoglobulin induction, 92 remained rejection-free, group I and 37 developed an acute rejection episode, group II. Acute rejection diagnosis was confirmed by a Biopty-gun biopsy read by an independent pathologist using Banff 97 classification and occurred at 15±430 days post-KTx. A FNAB was obtained from each case along with a simultaneous blood sample, on day 7 post-KTx in I and on rejection day in II. Both samples were analysed by a FACScan from Becton-Dickinson for several T subsets and for CD19.
Results: Several T subsets displayed significant changes when comparing stable with rejecting cases both in FNAB samples and in peripheral blood. CD3CD8, CD8, CD3DR, CD8DR, DR, CD3CD69 and CD69 showed the most significant up-regulation while CD4 subsets showed significant down-regulation in rejection. By combining the results in FNAB samples for DR plus CD8DR plus CD3CD69 minus CD4 we defined a cut-off of $\geq$ 36 points for acute rejection which achieved a sensitivity of 97.3%, a specificity of 90.9%, positive predictive value of 83.7% and negative predictive value of 98.6%. We did not observe a correlation between the score value and response to rejection treatment.
Conclusions: We confirmed that cytofluorometric analysis of FNAB samples of KTx reach a very high diagnostic accuracy just by the combination of a small set of lymphocyte subsets in a group of patients under modern immunosuppressive regimens. Peripheral blood analysis did not prove so reliable but the results showed the same trend.

MO-002

POSTTRANSPLANT SOLUBLE CD30 SERUM CONCENTRATION DOES NOT AFFECT DECEASED-DONOR KIDNEY GRAFT OUTCOME THREE YEARS AFTER TRANSPLANTATION

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Introduction: An elevated serum concentration of sCD30 has been reported as a predictive factor for acute rejections and poor graft outcome. In this study we hypothesized that the post-transplant sCD30 serum concentration in kidney transplant recipients treated with current immunosuppression with induction was not a predictive factor of immunologic risk associated with the kidney graft function and survival three years after transplantation.
Methods: The post-transplant sera of 234 adult deceased-donor kidney graft recipients were tested for sCD30 content (microsphere flow-cytometry assay (CD30 (soluble) Singleplex Bead Kit, Invitrogen, CA, USA)). The immunosuppression consisted of an induction therapy with anti-CD25 antibodies and a maintenance therapy with cyclosporine A microemulsion, mycophenolate mofetil, and methylprednisolone. The kidney graft function was estimated (eGFR) by the four-variable MDRD Study equation. Incidences of graft loss were calculated with the use of Kaplan-Maier survival-analysis and compared with the log-rank test.
Results: The vast majority of the post-transplant sCD30 levels in our cohort (91.4%) were lower than the lowest detectable level determined with this method (864 pg/mL). We compared the group with sCD30 content lower than 864 pg/mL (N=214) to the group with higher sCD30 levels (N=20). Results are presented in the table.

Transplantation related clinical characteristics and outcome at three years according to post-transplant soluble CD30 (sCD30) serum concentrations

Clinical characteristics	sCD30 <864 pg/mL (n=214)	sCD30 >864 pg/mL (n=20)	P value
Recipient age (years)	48±11	47±11	0.81
Recipient sex (female:male)	93:121	7:13	0.47
Last PRA value	6.2±12.4%	3.3±5.0%	0.29
HLA mismatch	2.8±1.0	2.6±1.2	0.29
Cold ischemia time (hr)	21±7	22±7	0.69
Acute rejection (yes:no)	19:195	0:20	0.16
Delayed graft function (yes:no)	55:159	4:6	0.57
eGFR, 3 years (mL/min per 1.73m2)	64±18	66±22	0.72

Data are total numbers or means ± SD. Abbreviations: eGFR, estimated glomerular filtration rate (MDRD equation); HLA, human leukocyte antigen; PRA, panel reactive antibody.

Three years after transplantation eGFR was not significantly different between two groups (P=0.72), and the incidences of acute rejections (P=0.16) or delayed graft function (P=0.57) were not significantly different between groups. Grafts survival rates three years after transplantation were also not significantly different (95% versus 90%; P=0.41).
Conclusions: This study shows that the post-transplant sCD30 serum concentration in our adult recipients of deceased-donor kidney transplants is not a predictive factor of immunologic risk associated with the kidney graft function neither it affects kidney graft survival three years after transplantation.

MO-003

ADIPOSE TISSUE DERIVED MESENCHYMAL STEM CELLS ARE NOT AFFECTED BY END STAGE RENAL DISEASE

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Background: Mesenchymal stem cells (MSC) are a potential therapeutic agent for a variety of conditions, including end-stage renal disease (ESRD) and kidney transplantation. In kidney transplantation, autologous cell use is preferential to avoid anti-HLA reactivity. However, the influence of ESRD on MSC is unknown. Therefore, we investigated the functionality and genetic stability of MSC from ESRD patients and examined the effect of uremic serum conditions on these cells.
Methods: MSC were isolated from subcutaneous adipose tissue of healthy controls (MSC-HC) and ESRD patients (MSC-RD) and phenotypically and functionally compared. Genetic stability of MSC-RD after expansion was investigated by whole genome SNP analysis. Finally, the influence of uremic conditions on MSC-RD was evaluated.
Results: MSC-HC and MSC-RD showed a similar morphology and differentiation capacity and were both over 90% positive for CD73, CD105 and CD166 and negative for CD31 and CD45. They demonstrated comparable population doubling times and apoptosis rates. MSC-HC and MSC-RD had similar capacity of inhibiting allo-antigen and anti-CD3/CD28 activated PBMC proliferation and responded to immune-activation by increased expression of pro-inflammatory (IL-1β, IL-6, IL8) and anti-inflammatory factors (IDO, TGF-β, PD-L1). MSC-RD were genetically stable after expansion to up to 200 million cells. Importantly, MSC-RD were not affected by uremic serum conditions.
Conclusions: This study demonstrated that MSC of ESRD patients have similar characteristics and functionality as MSC from healthy controls and that uremic conditions do not impair MSC functionality. These results indicate feasibility of isolation and expansion of MSC from ESRD patients for autologous cell therapy.

MO-004

FRACTIONAL EXCRETION OF PROTEIN MAY HAVE SUPERIOR PREDICTIVE VALUE OVER TRADITIONAL MEASURES OF PROTEINURIA IN DETERMINING THOSE AT HIGHER RISK OF TRANSPLANT FAILURE

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Background: Proteinuria is associated with poorer outcomes in transplant recipients. Fractional excretion of total protein (FePr) may better reflect renal excretion of protein than protein:creatinine ratio (PCR). We assessed FePr and PCR as predictors of transplant failure.
Methods: Data were collected from the electronic patient record for recipients

of a first renal transplant (Tx) between 01/01/00 and 31/12/2008. FePr and PCR were calculated (FePr = (Serum creatine * Urine protein)/(Serum protein * Urine creatinine)%, PCR = ((Urinary Protein/Urinary Creatinine) * 1000). Primary endpoint was Tx failure. ROC analysis was performed for each test and patients were stratified into high/low risk groups. Kaplan Meier and Cox surivival analysis were performed for each test.
Results: 219 recipients were followed up for a median of 4.9 years (1-11.1). 11.4% (n=25) of the transplants failed at a median of 2.7 years (1.2-7.3 years). Mean eGFr at 1 year post Tx was 48.5mls/min/1.73m^2 (SD 16.7). Using ROC analysis, both FePr and PCR predict transplant failure. FePr had the higher sensitivity and specificity. Those in the higher group of FePr had a 3.4 fold increased risk of transplant failure than those in the lower group (p=0.03). They had a significantly lower 1 year eGFR ($p<0.001$). For PCR, the higher group had a 2.1 fold increased risk of transplant failure. In multivariate analysis, both tests remain independently predictive of transplant failure.
Conclusion: FePR and PCR accurately predict transplant failure but FePr is more sensitive and specific. It may be superior at predicting those at risk of transplant failure. Our study is limited by its retrospective nature and the small number of events. Comparison should be made between these tests and measures of albuminuria.

MO-005 STRONG ASSOCIATION OF PHENYLALANINE AND TRYPTOPHAN METABOLITES WITH ACTIVATED CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Polyomavirus BK (BKV) and CMV are important viral infections after kidney transplantation. Previous studies reported on increased plasma levels of the amino acid phenylalanine in patients with certain viral infections. On the other hand, tryptophan and its metabolites were shown to be linked to immune responses and to exhibit immunoregulatory properties. In the present study, we focused on the amino acids phenylalanine and tryptophan (and its metabolites) in kidney transplant recipients in the context of BKV and CMV infections.
Patients and Methods: phenylalanine, tryptophan, tryptophan metabolites (kynurenine, quinolinic acid) plasma levels, and kynurenine/tryptophan as well as quinolinic acid/tryptophan ratios were analyzed in kidney transplant patients with post-transplant reactivation of CMV (CMV+BKV-: n=12) or BK virus infection (BKV+CMV-: n=37). Stable patients without active infections (CMV-BKV-: n=28) and CMV-BKV- healthy individuals (HCs: n=50) were used as controls.
Results: CMV+BKV- patients showed higher phenylalanine and tryptophan metabolite (but not tryptophan) levels than CMV-negative patients with ($p\leq0.002$) or without active BKV infections ($p<0.001$). Healthy controls behaved similar to CMV-negative patients. Kynurenine/tryptophan and quinolinic acid/tryptophan ratios were also significantly higher in CMV+ than in CMV- patients, regardless of BKV status ($p<0.003$). ROC-curve analysis showed an exceptionally high sensitivity (100%) and specificity (94%) of phenylalanine with activated CMV infections. For kynurenine (cut-off: 3.0 μmol/L) the sensitivity was 75% and specificity 73%. Likewise, quinolinic acid (cut off: 1 μmol/L) showed a sensitivity of 75% and specificity of 85%.
Conclusion: In contrast to polyomavirus BK, activated cytomegalovirus infections are tightly linked to increased phenylalanine and to a lesser extent to increased tryptophan metabolite plasma levels in kidney allograft recipients. The relevance of this finding for the prognosis and therapy of kidney allograft outcome remains to be studied.

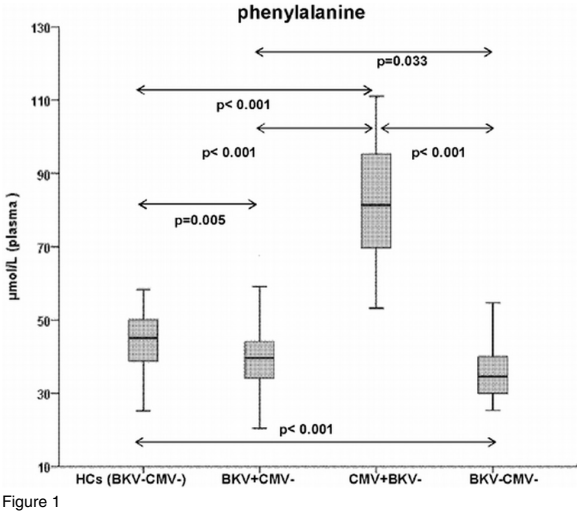

Figure 1

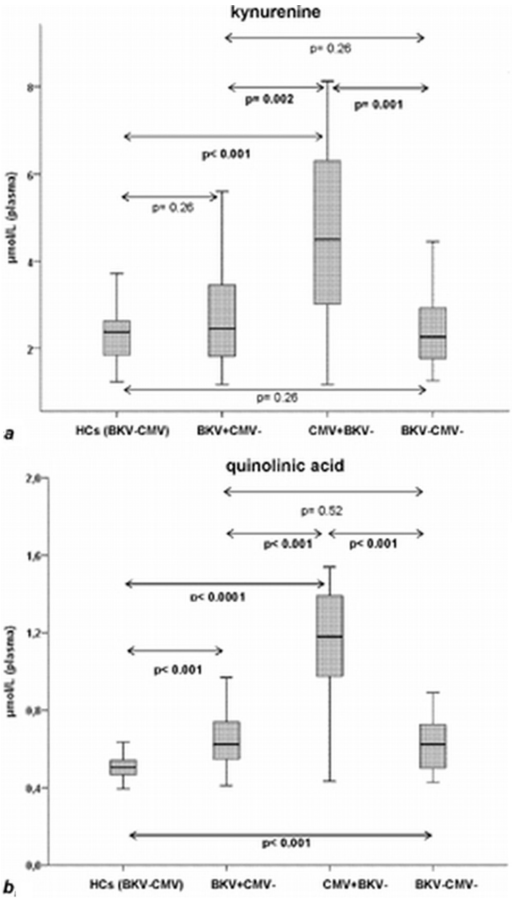

Figure 2

MO-006 SERIAL ANALYSIS OF SERUM NEUTROPHIL GERATINASE-ASSOCIATED LIPOCALIN PREDICTS ORGAN RECOVERY FROM DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION FROM DONORS AFTER CARDIAC DEATH

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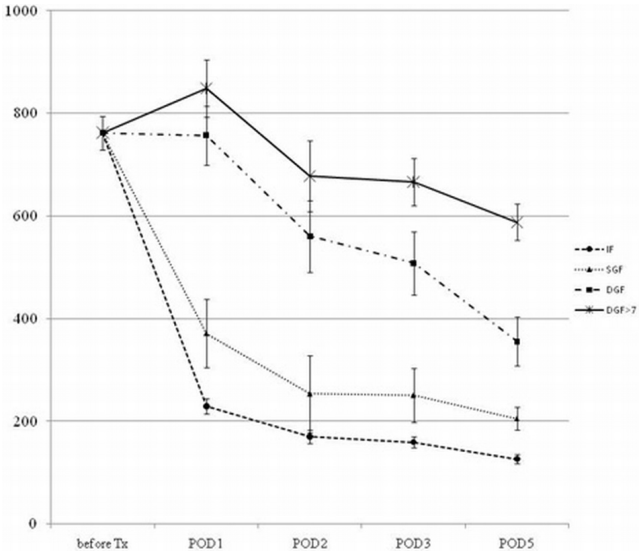
The kidneys procured from donors after cardiac death (DCD) hold great potential to expand the donor pool but have not yet been fully utilized, in part because of initial graft dysfunction. In the early period after transplantation, kidneys from DCD often required dialysis (HD) (delayed graft function (DGF)) and few percent of the kidneys never recovered. This study evaluated serum NGAL as a potential biomarker to predict early functional recovery of transplanted DCD kidneys. Consecutive patients undergoing living-related (LD (n=39)) or DCD (n=27) kidney transplantation (KTx) were prospectively enrolled. Serum samples were collected serially before and after KTx. Serum NGAL level was measured by ARCHITECT assay. The average serum NGAL level of Pre-KTx was markedly raised at 735±22 ng/ml. In KTx from LD, serum NGAL level decreased rapidly (immediate function (IF)). In contrast, serum NGAL decreased slowly in slow graft function (SGF), gradually decreased in DGF, and delayed to decrease in DGF cases HD requiring longer than 1 week (DGF >7days). Analysis of receiver-operating-characteristic curves demonstrated that SGF can be predicted with 88% sensitivity (SE) & 96% specificity (SP) at a cut off of 350 ng/ml on POD 1 (AUC 0.98). DGF can be predicted with 91% SE &



97% SP at cut off 500 on POD 1 (AUC 0.99) and 86% SE & 90% SP at 350 on POD 2 (AUC 0.94). Moreover, DGF >7days predicted 82% SE & 83% SP at 700 on POD 1 (AUC 0.93) and 73% SE & 85% SP at 600 on POD 2 (AUC 0.85). These data suggest that serially monitoring of serum NGAL levels may allow us to predict IF, SGF and graft recovery (DGF) from DCD.

MO-007 UNRECOGNISED GRADE II T-CELL MEDIATED REJECTION IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Background: Acute renal allograft rejection is classified according to the Banff classification system and has prognostic and therapeutic implications. Acute T-cell mediated rejection (TCMR) is diagnosed by the presence of tubulo-interstitial inflammation (grade I) or arteritis (grade II-III). Therefore, the diagnosis of Grade II or III TCMR requires the presence of a large artery on biopsy. In many cases arteritis will be accompanied by tubulo-interstitial inflammation however in cases where arteritis occurs without tubulo-interstitial changes, TCMR could go undiagnosed if a large vessel is absent on biopsy. We sought to establish the incidence of grade II/III TCMR in our cohort of paediatric renal transplant recipients and estimate the frequency of undiagnosed TCMR due to absence of large artery on biopsy.
Methods: 103 unselected renal transplant biopsies from 66 patients, performed for investigation of acute or acute on chronic renal allograft dysfunction between 2008 and 2010, were reviewed. The proportion of biopsies in which a large artery was present was ascertained and the frequency of grade II TCMR within these biopsies was calculated. In all biopsies graded as Grade II or III TCMR, the presence of tubulo-interstitial inflammation fulfilling the criteria for Grade I TCMR was noted.
Results: 70 (68%) biopsies contained a large vessel. Of these, 15 (21%) had evidence of arteritis fulfilling the criteria for grade II/III TCMR. In 60% of biopsies with grade II TCMR, arteritis was observed in the absence of significant tubulo-interstitial inflammation.
Conclusion: A significant proportion of biopsies classified as "normal" or "borderline change" in the absence of a large vessel may represent undiagnosed grade II TCMR. This may result in a delay in treatment or non-optimal therapy and has important prognostic and therapeutic implications for the management of acute allograft dysfunction.

MO-010 MEDICAL WEB BROWSING- RENAL TRANSPLANT PATIENT'S VIEWPOINT

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Background: The current literature encourages the use of the Internet to support patients with chronic illnesses. The complexity of renal transplantation, its risks and attendant ethical considerations mean that open ongoing access to information is essential for informed consent and patient understanding. This study explored the pattern of internet use by renal transplant patients in the West of Scotland.

Methods: A 31 items questionnaire was developed, validated and used for obtaining information from post renal transplant patients about Internet use and the relationships between Internet use and gender, age, education and health requirements. The information obtained by the questionnaire was analysed by SPSS 15.0.
Results: The validation of questionnaire showed an Intraclass Corelation Coefficient 0.77 to 0.96 with 95% confidence interval (CI 0.75-0.99). The overall response rate was 65% (n= 84/130). Responses are given in figures 1 and 2. 87% (n=73/84) had access to Internet and it was a preferred source of health information for 70% (n=59/84). 90% (n=53/59) looked up information on transplantation. 92% (n=52/59) successfully found the information they searched. 85% patients (n=71/84) would like the transplant team to develop a website for information on transplantation and 52 (62%) would like to receive health advice by email. 85% (n=50/59) commented that transplant websites are an effective way of obtaining information.

Figure 1 Trends of Web browsing in renal transplant patients

Survey responses (Respondents n=84/130)	Percentage and number	P value
Access to computer	87% (n=73/84)	NA
Access to Internet	87% (n=73/84)	NA
Age 21-60 years	94% (n=60/64)	
Age 61-70 years	67% (n=12/18)	
Age 71-80	100% (n=1)	
Preferred source of heath information	70% (n=59/84)	*0.003
Internet	17% (n=14/84)	*0.001
Books	12% (n=10/84)	
Magazines		
Health Topics searched (70%, n=59/84)	***Total n= 59***	NA
Transplant operations	69% (n=41)	
Rejection	66% (n= 39)	
Immunosuppressive medicines	59% (n=35)	
Complications	54% (n=32)	
Donor related	52% (n=31)	
Quality of life	52% (n=31)	
Transplant risks	52% (n=31)	
Survival rates	46% (n=27)	
Travel	44% (n=26)	
Exercise	41% (n=24)	

NA not applicable, n number, *student t test

Figure 2 Patient's views on transplant websites visited

Questions asked from patients (n=59) who consulted a transplant website for medical information	Yes n (%)	No n (%)	Do not know n (%)	No answer	P value
Did you find the information you were looking for?	54 (92)	2 (3)	1 (2%)	2	0.001
Did you think that the information was accurate?	44 (75)	2 (3)	10 (17)	3	0.001
Was the website easy to understand?	51 (86)	3 (5)	3 (5)	2	0.001
Was the information useful?	53 (90)	1 (2)	1 (2)	4	0.001
Was the information the same or different to what your GP told you?	33 (56)	10 (17)	8 (14)	8	0.002
. Was the information the same or different to what the Transplant Team told you?	45(76)	7(12)	4 (7)	3	0.002
Did you find information that your GP had not given you?	24 (40)	26 (44)	3 (5)	6	0.08
Did you find information which the Transplant Team had not given you?	9 (15)	39 (66)		11	0.003
Do you think that transplant websites are an effective way of obtaining information?	50 (85)	6 (10)		3	0.001

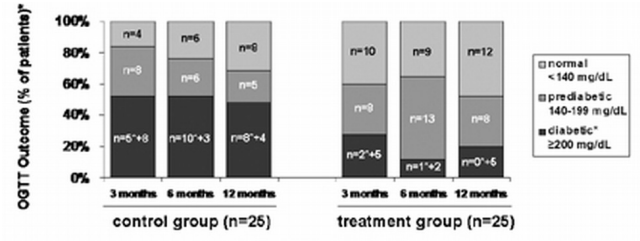
Student t test

Conclusion: The majority of renal transplant patients use the Internet for information on transplantation. Almost all patients under 60 years old access the internet for this purpose suggesting a trend towards the internet as the favoured modality for information gathering, mirroring changes in society as a whole. Transplant units should develop flexible, web-based sources of transplant related information. This would allow rapid adaptation to changes in prevalent practice as well as reflecting the preferences of the patient population.

MO-008 EARLY BASAL INSULIN THERAPY DECREASES NEW-ONSET DIABETES AFTER RENAL TRANSPLANTATION BY PROTECTING ENDOGENOUS INSULIN SECRETION

Manfred Hecking[1], Michael Haidinger[1], Dominik Döller[1], Johannes Werzowa[1], Andrea Tura[2], Jinyao Zhang[3], Susanne Rasoul-Rockenschaub[4], Ferdinand Mühlbacher[4], Walter H. Hörl[1], Giovanni Pacini[2], Friedrich K. Port[3], Marcus D. Säemann[1]. *[1]Nephrology, Medical University of Vienna, Vienna, Austria; [2]Metabolic Unit, National Research Council's Institute of Biomedical Engineering, Padova, Italy; [3]Arbor Research, Collaborative for Health, Ann Arbor, MI, USA; [4]Surgery, Medical University of Vienna, Vienna, Austria*

We tested efficacy and safety of early basal insulin therapy for post-transplant hyperglycemia and evaluated the development of new-onset diabetes after renal transplantation (NODAT). Fifty non-diabetic patients were randomly assigned to standard of care or basal insulin isophane treatment, and followed over 12 months. Twenty-three of 25 control patients had postoperative blood glucose greater or equal to 200 mg/dL, 18 required intermittent treatment with insulin and/or oral hypoglycemic agents. All 25 treatment patients had postoperative blood glucose levels greater or equal to 140 mg/dL, received and were discharged with insulin. Hypoglycemia of 41 to 60 mg/dL occurred once in the control versus 5 times in the treatment group, but was asymptomatic. At 3, 6 and 12 months post-transplantation, the prevalence of NODAT, diagnosed by oral glucose tolerance test or need for antidiabetic therapy, was consistently greater or equal to 48% in the control versus smaller or equal to 28% in the treatment group (odds ratio 0.27, p smaller than 0.05 at 12 months).

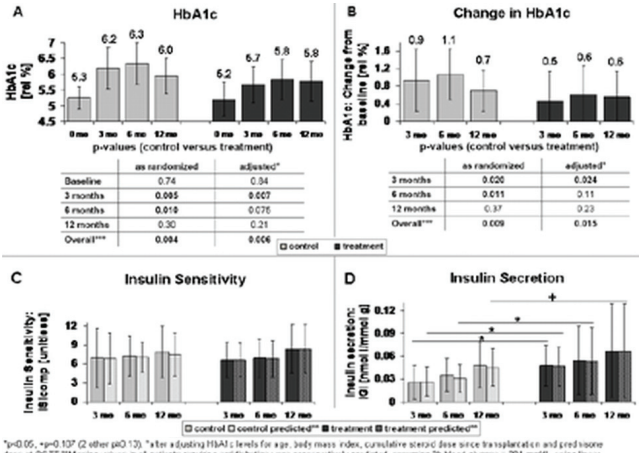


Odds Ratios [95% CI]

	Diabetic + Prediabetic versus Normal		Diabetic versus Non-diabetic	
	as randomized	adjusted**	as randomized	adjusted**
3 months	0.29 [0.08-1.09]	0.43 [0.09-2.08]	0.36 [0.11-1.16]	0.43 [0.11-1.59]
6 months	0.56 [0.16-1.92]	0.75 [0.16-3.47]	**0.13 [0.03-0.53]**	**0.13 [0.03-0.64]**
12 months	0.51 [0.16-1.61]	0.61 [0.14-2.65]	**0.27 [0.08-0.95]**	0.31 [0.08-1.25]
Overall***	0.43 [0.16-1.14]	0.55 [0.19-1.62]	**0.27 [0.10-0.72]**	**0.33 [0.12-0.91]**

*Patients on antidiabetics were counted as diabetic (without OGTT being performed).
**Adjusted for age, body mass index, cumulative steroid dose since transplantation and prednisone dose at OGTT, using multiple logistic regression analysis.
***Generalized Estimating Equations were used to determine overall odds ratios over the 1-year follow-up time, accounting for within-patient repeated measures.
Boldface numbers indicate findings with p<0.05. **Abbreviations:** CI: confidence interval.

Insulin sensitivity was not different between treatment and control patients, but insulin secretion and HbA1c (primary endpoint) were significantly better in the treatment group at 3 months, remaining at improved levels through months 6 and 12.



*p<0.05, •p=0.107 (2 other p≥0.13). *after adjusting HbA1c levels for age, body mass index, cumulative steroid dose since transplantation and prednisone dose at OGTT. **Missing values in all patients requiring antidiabetics were conservatively predicted, assuming 2h blood glucose = 201 mg/dL, using linear regression models that accounted also for age and body mass index. ***Generalized Estimating Equations were used to determine overall p-values for group differences over the 1 year follow-up time, accounting for within-patient repeated measures.

Unlike type 2 diabetics in the general population, untreated transplant patients (control group) with NODAT had similarly low insulin secretion, but higher insulin sensitivity levels. In conclusion, basal insulin treatment immediately following renal transplantation effectively decreased NODAT presumably by providing temporary beta cell protection. Further expansion or refinements of this strategy could potentially maximize insulin secretion to enable long-term glycemic control post-transplantation.

MO-009 TRANSITION FROM PAEDIATRIC TO ADULT CARE AFTER RENAL TRANSPLANT: AN ESSENTIAL LINK TO IMPROVE SURVIVAL

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Background: Arranging an efficient and caring transition service has been highlighted as one of the great challenges facing health service provision for the next century. For young people with functioning transplants, transition to adult services is a significant life event which needs careful planning and consideration. The majority of young people make their way into adult services in an unplanned and uncoordinated fashion. According to Watson et al, 8 out of 20 kidney transplants failed within 36 months of the transfer to adult services, with 35% of these failures being unexpected. Each year in UK approximately 40 renal transplant recipients are transferred from paediatric to adult post transplant care. Adolescents following transfer are particularly vulnerable and are at high risk of adopting non-concordant behaviour and are at risk of losing their transplant. To improve patient and graft survival we have developed a transition pathway to accommodate the clinical, social and psychological needs of our paediatric renal transplant patients. This present study describes our experience over the last 20 years.
Methods: This study comprises of two mile stone retrospective audits performed in our unit over the last two decades. The first audit period namely, pre-transitional audit was from 1980 to 1997 and the second period namely, post-transitional audit was from 2001 to 2010. The three important end points were rate of DNA (did not attend) at outpatient clinics, patient and graft survival at 1 and 5 years.
Results: These results have shown that after introduction of the transition pathway for paediatric transplant patients there have been a statistically significant improvement in patient and graft survivals.

Comparison of pre and post transitional pathway in paediatric transplant patients

	Pre Transition	Post Transition
Period	1980-1997	2001-2009
No of patients	58	78
DNA at 1 year	10%	6%
DNA at 3 year	24%	25%
DNA at 5 year	15%	9%
Unexpected graft loss at 1 year	1.72% (n=1)	0
Unexpected graft loss at 3 year	5.17% (n=4)	1.28% (n=1)*
Unexpected graft loss at 5 year	10.34% (n=6)	3.84% (n=3)*
Graft survival at 1 year	93.11% (n=54)	98.72% (n=77)
Graft survival at 3 year	89.66% (n=52)	94.88% (n=74)*
Graft survival at 5 year	86.20% (n=50)	94.88% (n=74)*
Patient survival at 1 year	94.83% (n=55)	100% (n=78)
Patient survival at 3 year	91.4% (n=53)	100% (n=78)*
Patient survival at 5 year	88% (n=51)	96.15% (n=75)*

*Mean results.

Conclusion: We recommend that a flexible and tailor made approach should be adopted to maximise the outcome from a transition care pathway.

Donation, retrieval and allocation

MO-011 THE CHALLENGE OF LIVE KIDNEY DONOR EVALUATION: PERCENTAGE OF EXCLUSIONS

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Objective: Inclusion criteria for kidney donation are extremely strict and a consistent percentage of candidates will not be suitable for donation. The aim of this study is to review the percentage and causes of exclusion for kidney donation at a single tertiary institution.
Material and methods: A retrospective analysis of our database was performed from 2003 to 2011. Nephrologists were in charge of filtering the queries for donation by excluding donors with absolute contraindications such body mass index > 35, uncontrolled high blood pressure, diabetes, known medical history of malignancy or systemic disease and psychological issues. Following this initial filter, potential donors were further evaluated by a multidisciplinary committee formed by urologists, nephrologists, cardiologists, radiologists and psychologists.

Results: After the initial filter by nephrology was applied, 344 potentially ideal living kidney donors were identified from 2003 to 2011. Despite the initial filter, 42% (146 donors) of donors were considered not suitable for donation. Further analysis revealed that 30% (44 donors) of donors regretted their decision to donate, and 10% (15 donors) were found to be ABO incompatible and/or had positive cross match. 7% (10 donors) had their recipient transplanted during the decision process from a cadaveric donor. 18% (27 donors) were excluded for anatomical reasons. 2% (3 donors) were excluded for uncontrolled high blood pressure and 5% (7donors) for glucose intolerance. 3% (4 donors) were found to have prostate cancer and 1% (2 donors) was excluded due to exitus of their recipient. Proteinuria, microscopic hematuria and systemic disease accounted for the rest of exclusions. (24%)
Conclusions: These results highlight the importance of a multidisciplinary donor selection during the process of kidney donation. Even when an initial filter is applied, a consistent percentage of potential donors (42% in our series) will not be considered suitable for donation.

MO-012 HAS THE DONOR TYPE ANY IMPACT IN THE WILLINGNESS TO DONATE?

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Introduction: The different types of donors: Brain Death (BD), Non Heart Beating (NHB) or Cardiac Arrest (CA) implies different schedule and settings to approach families for request about organ or tissues donation and can influence final decision.
Objectives: Study the differences between refusal and acceptance rates in the different donor types, and the reasons for refusal.
Material and methods: Descriptive study of family refusals (FR) for organ or tissue donors in all potential donors (PD) between January 2008 and December 2010 in our hospital. Study variables: donor type, age and sex of the deceased, the rate of FR and reasons for refusal.
Results:

Table 1. Characteristics of the population

Donor type	Number of cases	Average age (X ± SD)	Gender (Female / Male) %	Refusal Rate %
BD	174	53,9±20,4 (1–80)	51,5% / 49,4%	38 / 174 (21%)
NHB	208	45,0±13,2 (18–65)	27,0% / 73,0%	24 / 208 (11%)
CA	1680	67,8±14,0 (1–85)	38,4% / 61,6%	830 / 1680 (49%)

Table 2. Reasons for FR

Reasons for FR	BD	NHB	CA	Total
Explained as refusal in live	31%	9%	30%	29%
Family doesn't want to decide	0%	9%	19%	18%
No reasons	15%	27%	22%	21%
Do not harm the body	23%	36%	21%	23%
Ethic or religious reasons	23%	9%	2%	3,5%
Controversies with health attention	8%	9%	1%	1,5%
Other	0%	1%	5%	4%

Conclusions: Further studies are required to discriminate if the conditions and settings of the family interview in the different types of donors can influence the final decision. Considering that the transplant coordinator's team that approach families was always the same, the big difference observed in FR between the different donor's types can be explained by the fact that CA donors can't provide to society organs for transplantation.

MO-013 LONG TERM PROSPECTIVE ASSESSMENT Of LIVING KIDNEY DONORS: SINGLE CENTER EXPERIANCE

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Introduction: Virtually all studies reporting the outcomes of living kidney donation beyond the first year from donation were retrospective.
Methodology: In this prospective study the outcome of 81 consecutive living kidney donors, who donated their kidneys between December 2007 and November 2008 in our center, was thoroughly evaluated. Clinical, psychological assessment via FS36, laboratory and radiological assessments were carred out at pre-donation (basal), 3, 6, 12, and 24 months post-donation.
Results: The mean age at time of donation was 37.8±9.8 years (range: 22-64 years) and the majority were females (61, 75.3%). They were; 45 parents, 28 siblings, and 8 emotionally-related. The mean BMI (kg/m^2) was 29.7±5.4, 30.1±5.7, 30.4±5.8, 30.8±5.8 and 30.9±6.1 at basal, 3, 6, 12, and 24 months respectively ($p<0.0004$).The mean serum creatinine levels (mg/dl) were; 0.75±0.14, 1.01±0.22, 0.99±0.21, 0.98±0.20, and 0.94±0.20 ($p<0.0001$). Likewise, the mean levels of measured creatinine clearance (ml/min) were 148.8±35.7, 94.7±26.6, 95.5±24.6, 96.7±20.2 and 101.6±26.2 ($p<0.0001$).The mean 24 hours urinary protein excretion (mg/dl) were 0.09±0.03, 0.19±0.18, 0.16±0.09, 0.18±0.25, and 0.17±0.12 ($p<0.0001$).The mean serum cholesterol levels (mg/dl) were 179.3±33.6, 182.8±31.6, 185.6±34.3, 189.9±40.3, and192.4±39.4 ($p< 0.018$).The mean serum uric acid levels (mg/dl) were, 4.5±1.03, 5.2±1.1, 5.27±1.19, 5.18±1.16, and 5.37±1.14 (<0.001). There were no significant difference between the means of the basal FS 36 (pre-donation) and 1 year post-donation regarding emotional role and social functioning. On the other hand there were significant difference regarding physical health and living conditions. One year post-donation 3 donors developed hypertension and one of them developed diabetes mellitus. On the other hand, 10 female donors have got successful post-donation pregnancies.
Conclusions: We highly recommend assessment of all risk factors before and after donation. Long-term follow-up is necessary for all living donors.
Keywords: Live Kidney donors, post-donation monitoring.

MO-014 COMPUTER-AIDED ALTRUISTIC UNBALANCED PAIRED KIDNEY EXCHANGES BASED ON VIRTUAL CROSSMATCHING AND PREDICTED POST-TRANSPLANT CREATININE CLERANCE

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Background: Paired kidney exchange (PKE) programs often involve large numbers of pairs, and suitable exhanges are difficult to be found manually. Furthermore stagnation of blood group 0 recipients in PKE programs has encouraged the development of even more complex programs termed altruistic unbalanced PKE (AUPKE): here a lot of variables should be considered in order not to expose altruistic pairs to any additional risk factor.
Methods: We developed and tested a new software on the pair pool on the waiting list at the Pisa Transplant Centre as of January 2011, consisting of 29 recipients with no compatible donor and 39 recipients with at least a compatible donor (so called altruistic recipients).
Results: The software aims at assisting the physician in the matching process. First, it allows to inspect the situation of the candidate recipient with the set of direct (i.e. emotionally-related) donors. Then, if no suitable donor can be found, it allows to search for exchanges considering both PKE and AUPKE. A set of parameters can be customized to find desired exchange, including sum of mean fluorescence intensities (MFI) of donor-specific antibodies (DSA) for the n pairs involved in the exchange and sum of predicted minimal post-transplant creatinine clearances (according to nomograms by Tiong et al, J Urology, 2009). Finally, the software allows to compute a solution for the whole pool, by maximizing the number of satisfied pairs via a greedy algorithm using local heuristics.
Conclusion: This computer-aided allocation software has the potential to solve mixed pools containing recipients with either AB0 or DSA incompatibilities.

MO-015 PROSPECTIVE EVALUATION OF THE US-AMERICAN DONOR RISK INDEX FOR THE ACCEPTANCE OF LIVER GRAFTS IN GERMANY

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Background: Organ quality has a major impact on the postoperative result of orthotopic liver transplantation (OLT). The US-american donor risk index (DRI) (Feng S et al, Am J Transplant 2006Apr6(4):783-790) stratifies the risk for patient death following OLT with the following parameters: donor age, DCD-donation, splitliver transplantation, donor race, donor size, cold ischemia time and reason for braindeath.
Material and Methods: We used the DRI prospectively as an acceptance criterion from 08/2007 until 12/2008. In every organ offer, DRI was calculated and high risk organs were refused for high risk patients.
Results: N=420 organ offers were included. Donor age was below 40 years in 22.9%, between 40 and 60 in 40.8% and in 36.4% older than 60. Brain death was traumatic in 18.3% and non-traumatic in 81.7%. All donors were caucasians. No splitlivers or DCD-donors were used. Organ allocation was local

in 4%, regional in 6.5% and national in 89.5%. Mean DRI was 1.91±0.44 (1-2.89), 65.2% had a DRI greater than 1.7 (n=274). N=49 organs (11.7%) were accepted for OLT and n=371 organs were denied (88.3%). All organs showed primary function, no retransplantation was needed. Patients with a DRI below 1.7 had a significant 3 year survival benefit compared to those greater than 1.7 (Kaplan Meier analysis, 80% vs. 54.2%, logrank p=0.045). Local and regional allocated organs showed a significant better survival than national allocated organs (Kaplan Meier anaylsis 90% vs. 61%, logrank p=0.05). Organs from donors with traumatic brain death showed a 3 year survival rate of 90%.
Conclusion: DRI is a useful tool to assess organ quality on an evidence based level. Donors in Germany show significant higher DRIs compared to the USA, although specific USA typical risk factors are not relevant in Germany.

MO-016 TRENDS IN DECEASED ORGAN DONATION IN THE UK

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Introduction: The number of donors after brain death (DBD) in the UK declined gradually in the last 2 decades, leading to two key initiatives aimed at providing more organs for the 8000 patients on the transplant waiting list.
In 2003, a national audit of all deaths in ICUs in the UK was established to identify accurately the real potential for organ donation from ICU and determine the reasons for lack of consent for donation. Then in 2006, the Department of Health established an Organ Donation Taskforce to identify barriers to all parts of the organ transplant process and to recommend solutions to increase the number of transplants performed. The recommendations aimed to increase the number of donors by 50% over 5 years and are now largely implemented.
Results: Over the last ten years, due at least in part to significant investment in a new organ donation infrastructure and a better understanding of the donation process, the number of deceased organ donors in the UK has risen. There has been a 9-fold increase in DCD donors, and in addition the number of DBD donors has also started to increase.
Donor characteristics have also changed markedly: in 2001, 14% of deceased organ donors were aged over 60 years compared with 30% in 2010. A decrease in donors resulting from trauma has been seen: 19% of donors in 2001, 7% in 2010. Donor body mass index has increased: 11% of donors had BMI$\geq$30 in 2001 rising to 20% in 2010.
Conclusions: Major initiatives coupled with a change in donor acceptance criteria have led to an increase in the number of deceased organ donors in the UK over recent years such that the number of people receiving a deceased donor organ transplant in the UK has increased by 23% since 2005.

MO-017 THE UK NATIONAL PANCREAS ALLOCATION SCHEME

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Background: There are 8 pancreas transplant units in the UK and historically deceased donor pancreases have been allocated by the nearest centre to patients on their local waiting list. However with the introduction of a national pancreatic islet transplant scheme and a national organ retrieval service, which dissociated organ retrieval from implantation, there was a need to revise the traditional centre-based allocation system. Since 1 December 2010 all deceased donor pancreases (DBD and DCD) have been allocated to named patients listed nationally for either a vascularised pancreas or pancreatic islet transplant.
Methods: Using the UK Transplant Registry and UNOS registry data, factors affecting outcome of pancreas transplantation and a patient's relative chance of transplant were identified. Applying simulation modelling techniques, these factors were used to develop a computer-based points scoring system to prioritise patients for a donor pancreas. This scoring system gives priority to patients with prolonged waiting times, higher levels of sensitisation (based on a standardised calculated reaction frequency), dialysis requirements, listed at a centre close to the donor hospital (to assist in minimising cold ischaemia times), that are not poorly HLA mismatched and, to a lesser extent, to patients of a similar age to the donor. Donor body mass index (BMI kg/m^2) is also used to help decide whether a pancreas should be preferentially allocated to a patient listed for a vascularised pancreas (low BMI donors) or a pancreatic islet graft (higher BMI donors).
Conclusion: On 1 December 2010 the UK introduced a new patient based National Pancreas Allocation Scheme. The scheme allocates all pancreases from both DBD and DCD donors and prioritises patients listed for vascularised pancreas or pancreatic islet transplantation using a single computer-based matching algorithm.

MO-018 DONOR-RECIPIENT MATCHING IN LIVER TRANSPLANTATION BASED ON A RULE-SYSTEM BUILT ON A MULTIOBJECTIVE ARTIFICIAL NEURAL NETWORK

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The aim of this study was to provide a preliminary understanding of Artificial Neural Networks (ANNs) applied to donor-recipient (D-R) matching in liver transplantation (LT) from a multicenter spanish dataset.
A retrospective analysis from 11 spanish LT centers was conducted, including all the consecutive liver transplants performed during 2007 and 2008. Nineteen recipient, 20 donor and 3 operative factors were reported for each donor-recipient pair. The end-point variable for logistic regression and artificial neural network modelling was 3-month graft mortality. The follow-up period was fulfilled in 1003 liver transplants.
For each D-R pair, two probabilities were calculated using 2 different ANN models: The acceptance model (NN-AC) consists of a neural network which predicts (classify) the probability of survival of the graft at 3 months following LT. The rejection model (NN-MS) consists of a neural network which give us the probability of graft loss at 3 months following LT.
The parameters of D-R were set with a subset of the database (training set) and tested with the rest of the database (generalization set). These 2 models, NN-C and NN-MS, were compared with 2 logistic regression models and 3 deterministic machine learning methods by Correct Classification Rate (CCR), Minimum Sensitivity (MS) and AUROC. These algorithms were run with WEKA Machine Learning Workbench.
NN-C methodology obtains the best performance in predicting the probability for graft survival for each D-R pair with a percentage of CCR in the generalization set of 88.49%.
NN-MS methodology offers an excellent capability of graft loss prediction of 62.06% for the best NN-MS model.
We used subsequently a rule-based system consisting of five rules and two preconditions. This system would allow specialists to make a more appropriate decision-making, without removing the principles of justice, efficiency and equity.

MO-019 ORGAN PROCUREMENT AFTER EUTHANASIA PROCEDURE, RESPECTING PATIENT'S WILL

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Euthanasia was legalized in Belgium in 2002 for adults under strict conditions. The patient must be in a medically futile condition, of constant and unbearable physical or mental suffering that cannot be alleviated, resulting from a serious and incurable disorder caused by illness. If the person is not in the terminal phase of his illness, the 2 doctors performing the act of euthanasia must consult with a third doctor, either a psychiatrist or a specialist in the disease concerned.
Between 2005-2010, 5 patients (43-50 y) expressed voluntary their will for organ donation after their request for euthanasia was granted. Patients were all suffering from a debilitating neurological disease, either after severe CVA or primary progressive multiple sclerosis. They were totally dependent on third parties for personal care and without quality of life. Written informed consent about the procedure, after extensive explanation, was given by the patient and their relatives. The Institutional Ethics Committee requested this full written scenario with informed consent. There had to be clear separation between the euthanasia request, the euthanasia procedure and the organ procurement procedure. The procedures had to be performed by senior staff members and nursing staff on a voluntary basis.
The euthanasia procedure was carried out by three physicians, in the operating room. After clinical diagnosis of cardiac death, the organ retrieval was done as a non-heart beating donor procedure. In all patients liver and two kidneys were procured and additionally in three patients also lungs pancreatic islets. Organ allocation was done by Eurotransplant (allocation 4 hrs before), only in Belgium and the Netherlands, the only two countries with euthanasia legislation. Transplant centers were informed about the nature of the case and the elements of organ procurement. There was primary function of all organs.

MO-020 MILD HYPONATREMIA HAS A SUBSTANTIAL INFLUENCE ON CLINICAL OUTCOME OF PATIENTS ON THE WAITING LIST AND AFTER LIVER TRANSPLANTATION

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Background: Waiting list mortality is high in patients awaiting liver transplantation (LT). Despite the use of the Model for End-stage Liver Disease (MELD) score, patients with severe hyponatremia have an even worse waiting list survival. We assessed the impact of mild hyponatremia on LT waiting list survival and overall survival. We also aim to identify if there are any patient groups that are underserved in the MELD based allocation system.
Methods: Data were collected from 3 transplant centers located in The Netherlands, Germany, and the United States of America. Serum bilirubin, creatinine, sodium, and international normalized ratio (INR) were collected and MELD scores calculated accordingly. Mild hyponatremia was defined as serum sodium level of 130-134 mmol/L.
Results: In total 1658 patients were included in this study. A strong correlation was found between serum sodium and overall and waiting list survival ($P < 0.001$). Post-LT survival was also significantly decreased in the mild hyponatremia group ($P < 0.001$). Waiting list survival for patients with serum sodium levels 130-134 mmol/L was worse compared to patients with normal sodium levels in all three centers together and each center individually ($P < 0.001$). Waiting list and overall survival was significantly worse in the 166 patients with cholestatic liver disease compared to patients with non-cholestatic liver disease ($P = 0.041$; $P = 0.005$). Post-LT survival also was significantly worse in this group ($P = 0.022$).
Conclusion: Mild hyponatremia is associated with significantly worse waiting list survival in patients awaiting LT. It is also associated with increased post-LT mortality. Patients listed for cholestatic liver disease may be underserved in the current allocation model. Serum sodium should therefore have a more prominent role in liver allocation.

Clinical immunosuppression

MO-021 HIGH TACROLIMUS INTRAPATIENT VARIABILITY IS ASSOCIATED WITH ACUTE REJECTION AND GRAFT LOSS

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Introduction: Tacrolimus shows substantial intrapatient variability in pharmacokinetics requiring therapeutic drug monitoring and frequent dose adjustments. Borra et. al. (NDT Vol 25 2010) described an association between high intrapatient variability and worse clinical outcomes. In an era of alternative Tacrolimus formulations including generics licensed on broad pharmacokinetic equivalence criteria, the effects of variability may be extremely important to patient outcomes. We investigated the relationship of Tacrolimus trough level variability with graft survival, acute rejection (AR) and New onset diabetes post transplant (NODAT).
Methods: Data were collected from the prospectively-compiled electronic patient record for 255 adult kidney transplants performed between 01/01/07 and 01/03/09. 7 cases were excluded due to early graft loss. Median variability was calculated from all Tacrolimus trough levels in the 1st year post transplant. High variability (HV) was defined as variability $>$ observed median and low variability (LV) as $</=$ observed median. HV patients were compared with LV for AR, graft survival and NODAT in univariate analysis and multivariate analysis including potential confounding factors. A P value of 0.05 was considered as statistically significant.
Results: Median variability of tacrolimus trough levels was 27.7% (Range 10.9-54.7%).
HV patients showed an acute rejection rate of 19.4% (24/124) compared with 8.2% (10/122) for LV patients (P=0.02 Chi2). HV patients showed a 1 year graft survival of 91.9% (114/124) compared with 99.2% (121/122) for LV (P=0.01 Chi2). There was no significant difference in rates of NODAT between the 2 goups.
Discussion: This data supports the assertion that high intrapatient variability in Tacrolimus clearance is associated with inferior clinical outcomes and is consistent with the observations of Borra et.al. Strategies to reduce variability have the potential to address this effect and require prospective evaluation. Caution should be exercised when conversion to alternative Tacrolimus preparations, with potentially greater variability, is considered.

MO-022 CONVERSION FROM Prograf® TO Advagraf® IN LIVER TRANSPLANT. OBSERVATIONAL MULTICENTRIC STUDY

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Introduction: Compliance to immunosuppressive therapy in liver transplant (LT) patients is critical to prevent acute organ rejection and/or late graft loss. Strategies to simplify the therapeutic scheme may improve adherence.
Aim: Evaluate safety and efficacy of conversion from twice-daily tacrolimus formulation (Prograf®) to once-daily formulation (Advagraf®) in LT patients.
Patient and Methods: This prospective observational multicentric study included 187 LT patients between three hospitals in Barcelona, Spain (Hospital Vall d'Hebron, Hospital Bellvitge and Hospital CIInic). Inclusion criteria were: at least 10 month post-LT follow-up, no rejection episodes during the last 3 months and creatinine levels <2 mg/dL. Conversion from Prograf® to Advagraf® was based on 1:1 proportion. Doses and serum levels of tacrolimus, liver and renal function, acute rejection episodes, arterial hypertension, diabetes mellitus and dyslipidemia were recorded at 4 weeks, 6 months and 1 year after conversion.
Results: Mean age was 69 years $\pm$11.34, 64% were male and 36% were female. The main indications for liver transplant were alcoholic cirrhosis in 30%, hepatocellular carcinoma in 24% and HCV positive cirrhosis in 20%. Median time of conversion was 55m (r: 10-215m). Serum levels of tacrolimus decreased at one month after conversion (pre-conversion levels = 5.4$\pm$3.0ng/dL vs post-conversion levels = 4.4$\pm$2.4ng/dL, $p = 0.013$); however, these values are normalized at 6 months post-conversion with no changes in liver function and no increase in acute rejection ratio was observed. No significant differences in renal function, incidence of diabetes mellitus, dyslipidemia or arterial hypertension were recorded during follow-up.
Conclusion: Conversion from Prograf® to Advagraf® is a safe and effective strategy in management of stable LT patients.

MO-023 IS THE PRIMARY IMMUNOSUPPRESSION DRUG (CYCLOSPORIN A OR TACROLIMUS) PLAYING A ROLE ON THE RESPONSE TO ANTIVIRAL TREATMENT FOR POST-TRANSPLANT HCV RECURRENCE?

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Background: HCV-related cirrhosis is the most common indication for liver transplantation. Standard immunosuppression, based on Calcineurin inhibitors (CNI) may also affect HCV replication and response to antiviral therapy.
Aim: to evaluate the impact of CNI on SVR in a population of HCV transplanted patients undergoing antiviral therapy for HCV recurrence.
Patients and methods: A multicenter database of 12 Italian Centres was set up to carry on a retrospective analysis of 464 liver transplant recipients, treated for HCV recurrence, from 1992 to 2008. Patients were considered eligible for combination interferon plus ribavirin-based therapy according to defined criteria. Antiviral treatment was aimed for 48 weeks regardless of viral genotype (73,9% genotype 1); median follow up was 87$\pm$45 months. Immunosuppressive therapy was based on cyclosporine in 39% of cases, on tacrolimus in 56,9%.
Results: SVR rate was 34,1%. EOT was significantly higher in the Cyclosporine group (64%) compared with the Tacrolimus (54,5%) (p= 0,04): a longer interval between OLT and starting of antiviral therapy (32,7 vs 19,2 months), higher daily dose of Ribavirin (659,9 versus 561,9 mg) were associated with virological response in the Cyclosporin group. Acute and chronic rejection rate (p=0,536 and p=0,585 respectively) and pre-treatment staging score, were no different between the two groups. No difference in SVR rate and in patients survival was observed (88% survival in Cyclosporin group vs 87%).
At multivariate analysis Cyclosporine was confirmed as an independent significant predictor of EOT (p=0,04), regardless of viremia, donor and recipient

features, genotype, distance from OLT, olt-recurrence interval, fibrosis stage and treatment dose and duration.
Conclusions: EOT response to antiviral treatment for post-OLT HCV recurrence is significantly higher among Cyclosporin treated recipients, however no differences in SVR and patient survival was observed.

MO-024 THE IMPACT OF EVEROLIMUS BASED IMMUNOSUPPRESSION ON HCV RECURRENCE AFTER LIVER TRANSPLANTATION: CASE-CONTROL STUDY

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Introduction: There is in vitro evidence that mTOR proteins protect Hepatitis C (HCV) infected cells and inhibit hepatic fibrosis by attenuating different profibrogenic pathways. The aim of this study was to evaluate the effect of everolimus (EVL) on HCV recurrence in liver transplant (LT) recipients.
Patients and Methods: A case-control study (1:3) was designed including patients who underwent LT due to HCV infection from 2005 to 2009 and follow-up of 1 year. Patients that received EVL during the first 6 months post-transplant (study group) were compared with those who never received EVL (control group) and were on Tacrolimus (TAC)-based immunosuppression. HCV recurrence was defined by liver biopsy under Ishak score. The reasons of introduction of EVR were severe acute rejection, prevention of HCC recurrence in patients with microvascular invasion and calcineurin inbitor (CNI) side effects.
Results: Fourteen patients received EVL compared with 42 who continued on TAC-based immunosuppression. No differences were found between both groups regarding HCC indication,donor age and cold ischemia time (p ns). Median time to HCV recurrence was 5.2m (r: 2-12 m) in EVL group vs 8.3m (r: 1-12 m) in control group (p ns). Liver biopsy showed acute hepatitis, fibrosis stage I, fibrosis stage II- IV and cirrhosis in 62%, 8%, 30% and 0% respectively in EVL group and 52%, 5%, 36% and 7% respectively in control group (p ns). Anti-HCV therapy treatment was indicated in 54% in EVL vs 72% in control group (p ns), of whom sustained virological response was observed in 43% in EVL group vs 48% in control group (p ns).The histologic progression of disease at one year liver biopsy (fibrosis stage $>$2/3) was observed in 43% in EVL vs 41% in control group (p ns).
Conclusions: Despite the limits of this study due to reduced number of patients, we conclude that significant differences in fibrosis progression was not observed in HCV recurrence at one year post-LT for patients receiving EVL vs TAC-based regimens.

MO-025 BETTER RENAL FUNCTION WITH EARLY EVEROLIMUS (EVL) INTRODUCTION AND CALCINEURIN INHIBITOR (CNI) WITHDRAWAL AT THIRD MONTH IN KIDNEY RECIPIENTS AT MONTH 12: RESULTS OF THE ERIC STUDY

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Introduction: EVL is a proliferation signal inhibitor with good tolerability and low rejection rate on reduced or no cyclosporine therapy. Additional data are needed on theuse and long term results of EVL with CNI elimination.
Methods: This ongoing multicenter, randomized, open-label trial included 196 de novo renal transplant (RT) recipients treated until month 3 (M3) with tacrolimus (TAC), sodium mycophenolate and steroids. 111 were randomized at M3 to: continue with TAC (n=54) or TAC withdrawal and EVL introduction (n=54). Randomization requirements: serum creatinine $<$2.5 mg/dl, proteinuria $<$1g/day, and no previous severe biopsy-proven acute rejection (BPAR) or subclinical rejection. Primary endpoint: renal function (RF) estimated by glomerular filtration rate (GFR) (MDRD) at month 12 post-randomization (M12-PR). Protocol biopsies scheduled at M3 and 27. We present an interim analysis at M12-PR.
Results: Baseline donor and recipient characteristics were comparable. Pre-randomization protocol biopsies were normal in 52.7% of patients. Borderline changes were found in 13.5%, chronic allograft nephropathy in 6.5% and CNI toxicity in 11.5%. There were no significant differences between groups in RF at M12-PR (GFR 53.38 TAC and 57.27ml/min EVL,p=0.254), but a significant improvement from M3 to M12-PR was observedwithEVL: GFR-M3 52.72 vs 57.27ml/min M12-PR,p$<$0.05). This also reflects in a significant increase in the creatinine slope: 1/Cr=0.0048,p$<$0.05. No difference in 24h-proteinuria was observed (0.31 EVL vs 0.31g/L TAC,p=ns). Patient and graft survival: 100% at M12-PR in the ITT population. 10 patients presented BPAR (17.5%), all with EVL. A significant lower CMV incidence was detected in the EVL group (3.3% vs 10.1%,p$<$0.05).
Conclusions: Early TAC withdrawal and replacement by EVL in RT allows a significant improvement in RF and seems to be a safe procedure with an acceptable and low-intensity rejection rate.

MO-026 CYCLOSPORINE VERY LOW DOSE WITH EVEROLIMUS HIGH DOSE IS ASSOCIATED WITH EXCELLENT OUTCOMES IN RENAL TRANSPLANT PATIENTS

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Aim of this study was to compare the efficacy and safety of CyA "very low exposure" with Everolimus "very low exposure" respect to CyA "very low exposure" with EC-MPS.
In a randomized, prospective, monocenter study, renal transplant patients were enrolled to receive either everolimus (C0 8-10ng/ml) + CyA (C2 250-300ng/ml) + steroids or EC-MPS (1440g/day) + CyA (C2 500-700ng/ml) + steroids. Efficacy was evaluated at 24 months. Data analysis has been made per protocol. The 2 groups were comparable for demographic and transplant data. After 2 years 41 EC-MPS and 46 Everolimus patients have been evaluated. Biopsy proven acute rejection rate was higher in CyA standard exposure with respect to CyA very low exposure (24% vs 18.8%;RR=1.4). We observed a trend towards a better 2-year graft survival rate in patients with CyA very low exposure (95% vs 85%;p=NS). CyA dose at 2 years was lower in E group (1.35$\pm$0.49 vs 2.3$\pm$0.64mg/kg;p$<$0.0001. At 2 years eGFR (Cockcroft-Gault) was higher in Everolimus group (77.78$\pm$31.9 vs 54.76$\pm$18.76 ml/min;p$<$0.001). The 2-year systolic blood pressure was lower in everolimus group (125.3$\pm$13.96 vs 129.8$\pm$16.23 mmHg;p=0.03). The 2-year serum cholesterol levels were higher in everolimus group (229$\pm$47.08 vs 206.7$\pm$42.2mg/dL;p$<$0.01). 24 hours proteinuria was low and similar in both groups (387.6$\pm$42.5 in everolimus vs 409.3$\pm$76.8 mg/24 hours in EC-MPS.
Examining our population per protocol we observed a significant 2-year higher eGFR in patients with CyA very low exposure together with a significant lower systolic blood pressure. Our prospective study documented the safety and efficacy of an immunosuppressive regimen based on CyA very low exposure associated with unusual high everolimus exposure.

MO-027 EVEROLIMUS MONOTHERAPY AS MAINTENANCE IMMUNOSUPPRESSION AFTER RENAL TRANSPLANTATION

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Introduction: The aim of this study was to analyse the safety and feasibility of everolimus monotherapy in kidney transplant recipients (KTR) with low inmunological risk.
Material/Patients: Study of medical records of 26 KTR on everolimus therapy in a our Center. Mean time period between transplantation and the beginning of everolimus monotherapy was 181,57 months (SD 56,6). Mean follow-up from conversion to everolimus to initial monotherapy was 28,6 months (SD 10,18). Tipe of conversion: de novo (3 patients) and profilaxis of CNI toxicity (23p). Inclusion criteria: creatinine $<$ 1,6 mg/dL, MDRD $>$ 42 ml/min, proteinuria $<$ 400 mg/day, no malignancy, absence of previous severe acute rejection, optimal donors, follow-up more than 6 months. Objectives: 1) Evaluate the incidence of acute rejection, nephrotoxicity, malignancy and discontinuation to treatment. 2) Compare the levels of creatinine, albuminuria, uric acid, hemoglobin, dose and levels of EVE at 1-3-6 months with baseline.
Results: Twenty KTR were elegible for analysis. Most frequent inmunosuppression regimen preconversion was CyA (22), Tacrolimus (4), Azatioprina (14), MMF (5), Prednisona (8), De novo (3). At baseline: mean dose of EVE was 1,75 mg/day, mean GFR (MDRD) of 59,3 ml/min (SD 14,3), mean albuminuria of 34,2 mg/24h (SD 45,8). One patient died because of postconversion gastric tumor and two other patientes developped breast cancer. None of them discontinued everolimus treatment. Good tolerance to EVE. No acute rejection. At the end of the 6 month period, mean creatinine 1,01 (SD 0,25), mean MDRD 76,16 (SD 16,14) p$<$0.05, there is a significative decrease in uric acid (27,6%) from the start of initial conversion.
Conclusions: Everolimus monotherapy can be a good alternative in long term KTR. We found no apparent nephrotoxicity, no acute rejection and an slight increase in albuminuria. We report 3 tumors. A long term follow-up will be needed to have more consistent data.

MO-028 THE ROLE OF SURVEILLANCE BIOPSIES IN CLINICAL RENAL TRANSPLANTATION

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Background: Previous data suggested that surveillance biopsies were useful to detect and treat early subclinical rejection (SCR) improving graft outcomes. It has been argued that current more potent immunosuppression has reduced the prevalence of SCR. Furthermore, tailoring of calcineurin inhibitors (CNI) has reduced CNI nephrotoxicity. Thus, the role of surveillance biopsies has been questioned.
Methods: We retrospectively examined the histological findings and detailed clinical action taken in 280 surveillance biopsies from 100 kidney and combined kidney-pancreas transplant recipients transplanted between January 2008 and July 2009. Only patients biopsied with stable graft function were considered as having surveillance biopsies. Biopsies were classified using Banff 97 criteria by pathologists blinded to clinical data. Biopsies were carried out at implantation, 1, 3 and 12 months. Decision to alter immunosuppression was dependent on combined clinical and histologic criteria.
Results: 50% of all biopsies were abnormal. Major findings were interstitial fibrosis and tubular atrophy (IF/TA, 20%), borderline changes (i1t1/i1t2; 13%), SCR (i2t2 or above; 6%), acute tubular necrosis (8%), CNI toxicity (5%), recurrent disease (3%), and BK virus-associated nephropathy (1%).
At 1, 3 and 12 months the prevalence of SCR was 20%, 15% and 19%, and IF/TA was 9%, 17% and 34%. 32% of all surveillance biopsies led to a decrease, 16% an increase, and 8% a switch in immunosuppression.
Following treatment of SCR, Cockcroft & Gault creatinine clearance (CrCl) improved from 65±26 to 73±33ml/min at one year from transplant. Mean i,t scores fell from 2.65±0.24 to 0.88±0.29 (mean±SEM, $p<0.001$). Chronic scores did not change (mean ci,ct score 1.1±0.24 vs 1.3±0.27).
Conclusions: Early routine surveillance biopsies reveal a high frequency of findings undetected by clinical surveillance and often unveil pathology that, if left undetected and untreated, may lead to worse graft outcome.

MO-029 THERAPY OF CHRONIC HUMORAL REJECTION AFTER KIDNEY TRANSPLANTATION

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Chronic humoral rejection is increasingly recognized as a cause of chronic allograft dysfunction and failure, established therapy is still missing.
We report 11 patients with biopsy proven transplant glomerulopathy, 9/11 with diffuse C4d staining; median 37 months (8-71) after KTx. Immunosuppression consisted of tacrolimus (9/11), rapamycin (2/11), MPA and prednisone (11/11). Deterioration of graft function and/or de novo proteinuria was an indication for biopsy. Donor specific antibodies (DSA) (FlowPRA) were detected in 7/9 Ps (anti HLA class I -1x, anti DQ - 4x, anti DRB – 2x). All patients were treated with methylprednisolone, 3 boluses of IvIg over 3 months, 140 g each; and one dose of rituximab (375 mg/m2). Patients on rapamycin were converted to tacrolimus. Minimum follow up after the therapy was 6 months.
Drop of GFR (MDRD formula) was 4.2±1.8 ml/min (mean ± SEM) during 6 months before therapy. Graft function improved in 7/11 (gain of GFR over next 6 months 6.9±1.7 ml/min), worsened in 4/11 (another drop of GFR 3.8±1.3 ml/min). Re-biopsy was available in 8 Ps, with reduced C4d staining in 5/8. DSA disappeared in 2/8 Ps only. Five from 7 improved patients had follow-up for 12 months, 2/5 continued to improve, 2/5 remained stable and 1/5 worsened again. No serious infections were recorded during the follow up.
Therapy used to treat acute antibody mediated rejection helped to improve/stabilize graft function in nearly 2/3 of kidney transplant recipients with chronic humoral rejection. Long term success remains to be determined. Protocol biopsies in later post transplant period can help us to make the diagnosis and attempt for therapy earlier, before progression of chronic irreversible changes.

MO-030 CONVERSION OF STABLE CYSTIC FIBROSIS (CF) LUNG TRANSPLANT RECIPIENTS FROM A TWICE-DAILY PROGRAF-BASED REGIMEN TO A ONCE-DAILY MODIFIED RELEASE TACROLIMUS-BASED REGIMEN: PRELIMINARY RESULTS OF THE FQ-UST-01 TRIAL

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Background: The purpose of this pharmacokinetic (PK) study was to evaluate tacrolimus exposure in stable cystic fibrosis lung transplant recipients, converted from Prograf® twice a day to MR tacrolimus (Advagraf®) once daily.
Material and methods: This was a pilot open-label, single centre study with two periods and a single sequence design. Eligible patients were 18 to 65 years of age, post transplant with stable lung function and receiving stable doses of Prograf® twice a day for at least 4 weeks prior to enrolment. Patients who signed informed consent and fulfilled selection criteria received Prograf® twice a day on day 1 and were then converted to the same milligram-for-milligram daily dose of MR once daily from day 2 onwards. Twenty-four-hour PK steady stage profiles were obtained for each. Laboratory and safety parameters were also evaluated.
Results: Interim results from 6 patients are presented in the table below:

Table 1. Pharmacokinetic Parameters

	AUC 0-24		Cmin	
	Prograf	Advagraf	Prograf	Advagraf
N	6	5	6	5
Mean	439.12	408.27	12.38	11.16
SD	108.76	141.46	3.02	4.51
Minimum	296.48	245.3	10.5	6.4
Maximum	626.95	616.6	18.7	17.4
Percentage 25	371.51	289.46	11.1	6.85
Percentage 50 (Median)	422.38	377.73	12.2	11.3
Percentage 75	509.24	542.35	15.78	15.4

We found that 66% of recipients on Advagraf® needed significantly higher tacrolimus doses per kg than those on Prograf® (0.15 vs 0.18 mg/kg). MR tacrolimus was well tolerated. Lung function remained stable in all but one patient who experienced a sepsis secondary to acute cholecystitis. This patient recovered without sequelae.
Conclusions: The steady-state tacrolimus exposure of Advagraf® once daily was equivalent to Prograf® twice a day after a milligram-for-milligram conversion in stable lung transplant cystic fibrosis recipients. To reach this similar exposure, it was necessary to use up to a 20% higher dose of MR tacrolimus than Prograf®. Despite dose adjustments, non-clinically relevant lower trough levels were seen in patients receiving the extended released tacrolimus formulation.

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Immunobiology / basic science

MO-031 NUTRACEUTICALS AMELIORATE KIDNEY ISCHEMIA/REPERFUSION INJURY IN RATS VIA HO-1 INDUCTION

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Background: The induceable Hemeoxygenase-1 (HO-1) is the rate limiting step in the conversion of heme into biliverdin, carbon monoxide (CO) and free iron (Fe2+). Up-regulation of HO-1 might be among the most critical cytoprotective mechanism that are activated during cellular stress e.g. inflammation, hyperthermia and ischemia/reperfusion. The elicitors used are mainly hepatotoxic and consequently not adaptable for clinical use. Some nutraceuticals are inducers of HO-1 and ameliorate kidney ischemia-reperfusion-injury (IRI).
Methods: Different nutraceuticals were tested for their potential in up-regulating HO-1 in mice. In a well-established renal artery clamping model in Lewis-rats weighting 250-300g an IRI was set, parameters for kidney function, HO-1 expression and tissue damage were observed at fixed time points. Nutraceuticals were applied orally 24hrs before ischemia and immediately after reperfusion.
Results: Two of the tested nutraceuticals led to a distinct induction of HO-1 expression. (N18519: 11-fold; N791419: 17-fold). In the renal artery clamping model serum creatinine and urea levels after 48h of reperfusion (3,06±0,86 mg/dl) were significant higher compared to the sham operated group (0,38±0,07 mg/dl; $p<0,001$). The administration of 10mg/kg bw (N18519, 48h after reperfusion, creatinine: 0,54±0,23 mg/dl; $p<0,001$) and 30mg/kg bw (N791419, 48h after reperfusion, serum creatinine: 0,53±0,06 mg/dl; $p<0,001$) led to a significant amelioration of kidney function, respectively. The competitive antagonist Sn-PP (5mg/kg bw) anticipated this positive effect. Histological analysis and dose dependent drug studies as well as HO-1 expression analysis encourage support the study.

Conclusion: The use of non- toxic nutraceuticals is a promising new possibility for inducing HO-1 and hence ameliorating ischemia-reperfusion-injury in rat kidney.

MO-032 AUTOPHAGY PROTECTS HUMAN HEPATOCYTES FROM CELL DEATH DURING HYPOXIA AND HYPOXIA-REOXYGENATION (H-R)

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Introduction: The precise role of autophagy in shaping the response of human hepatocyte to oxidative stress remains controversial. The delineation of the role of autophagy in human hepatocytes will have profound implications for the understanding of the responses of hepatocytes during and after liver surgery. Previous studies have reported that autophagy may be a separate and distinct form of cell death whilst other studies support the role of autophagy in promoting cell survival.
Aim: To delinate the precise role of autophagy in human hepatocytes during hypoxia and hypoxia-reoxygenation (H-R).
Methods: We isolated human hepatocytes from liver tissue (1) and exposed them to an *in vitro* model of hypoxia and H-R (2). Human hepatocyte reactive oxygen species (ROS) production, apoptosis, necrosis and autophagy was determined using a four-colour reporter assay and then subjecting cells to flow cytometry.
Results: Hypoxia and H-R increased human hepatocyte ROS production which was associated with increased levels of autophagy.

Figure 1. Intracellular ROS Accumulation is Associated with Increased Autophagy within Human Hepatocytes

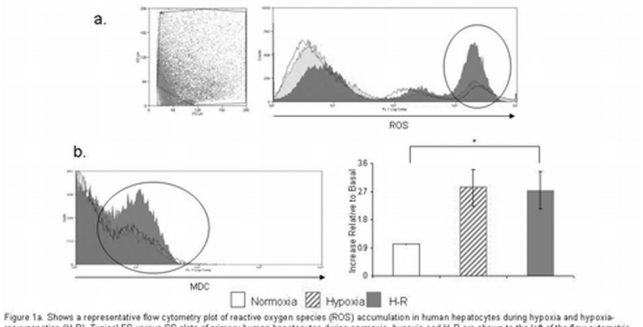

Figure 1a. Shows a representative flow cytometry plot of reactive oxygen species (ROS) accumulation in human hepatocytes during hypoxia and hypoxia-reoxygenation (H-R). Typical FS versus SS plots of primary human hepatocytes during normoxia, hypoxia and H-R are shown to the left of the flow cytometric plot. The FS versus SS plots shown is from the H-R alone sample of a liver preparation but similar plots were obtained during normoxia and hypoxia (data not shown). The areas of interest on the flow cytometric plots are marked by the vertical ellipses. The area on the left of each ellipse represents cell debris. Cell debris is included within the plot as human hepatocytes vary considerably in size and therefore to include all viable human hepatocytes in the analysis a large gate is required on the flow cytometer, this by necessity includes the cell debris. Figure 1b shows a representative plot to illustrate the effect of hypoxia and H-R upon autophagy in human hepatocytes during normoxia, hypoxia and H-R. Again, the area of interest within the flow cytometric plots is marked by the vertical ellipse. The same gate has been applied to primary human hepatocytes for these plots as those shown in Figure 1a. The bar chart represents data from three separate experiments. Data is expresses as increases relative to basal, were basal refers to the level of autophagy during normoxia. (*p<0.05, Mann-Whitney test)

Specifically, ROS derived from the mitochondrion and NADPH Oxidase mediated autophagy during hypoxia and H-R. Class III phosphatidylinositol 3-kinase (PI3-K) is integrally involved in the induction of autophagy. PI3-K function can be inhibited with the specific PI3-K inhbitor 3-Methyladenine (3-MA). Inhibition of autophagy, with 3-MA, increased human hepatocyte apoptosis during H-R.

Figure 2. Inhibition of Autophagy Increases Apoptosis in Human Hepatocytes During H-R

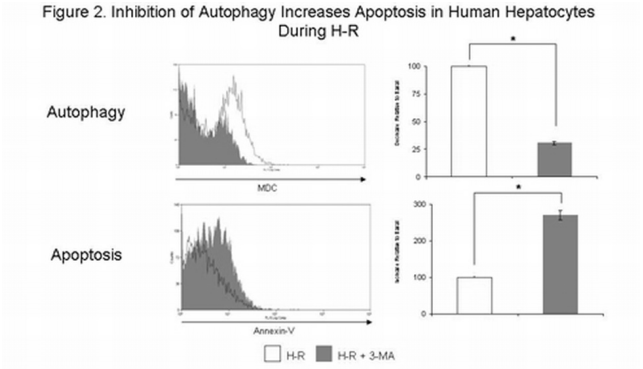

Figure 2. Shows a representative flow cytometry plot to illustrate the effects of inhibition of autophagy with the PI3-K inhibitor 3-MA upon human hepatocyte autophgay and apoptosis. The same gating protocol was in flow cytometric analysis as that shown in Figure 1a. Inhibition of PI3-K significantly reduced autophagy in human hepatocytes during H-R. This caused a concomitant increase in apoptosis. The bar charts represents data from three separate experiments. Data is expresses as increases or decrease relative to basal, were basal refers to the level of autophagy during H-R. (*p<0.05, Mann-Whitney test)

Specifically, peri-venular, and not peri-portal human hepatocytes, were more susceptible to apoptosis after the inhibition of autophagy during H-R.
Conclusion: These findings conclusively show that during oxidative stress autophagy serves as a cell survival mechanism within human hepatocytes. The activation of PI3-K may provide an important therapeutic target for improving human hepatocyte survival after liver transplantation.
References:
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MO-033 RENAL ALLOGRAFT FUNCTION AT SIX MONTHS POST TRANSPLANT IS ASSOCIATED WITH DONOR CHROMOSOMAL TELOMERE LENGTH

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Background: Bio-age, as defined by CDKN2A expression, has recently been demonstrated to be a superior pre-transplant predictive marker for post-transplant function. Traditionally however, bio-ageing has been assessed through a measurement of telomere length. We measured renal pre-implantation telomere length and determined associations with organ function at six months post-transplant with a view to using it as a further biomarker, in combination with CDKN2A and donor chronological age.
Methods: DNA was extracted from time zero biopsies (n=32) using a Maxwell® 16 DNA purification robot and quantified using a Nanodrop® apparatus. Telomere length determination was by Q-PCR using a specified assay protocol. Telomere length was then analysed with respect to donor age and sex, cold ischaemic time and renal function 6 months post-transplant as determined by serum creatinine (SC) levels.
Results: Donor telomere length was observed to shorten as a function of increasing chronological age (p=0.018). We also observed significantly inferior renal function, in those who received organs with shorter telomere lengths (p=0.025) as measured by recipient creatinine at six months. Linear regression analyses indicated that at 6 months post-transplant, donor age explains 12.0% of the variability in SC levels, while telomere length accounted for 7.9%.
Conclusions: This study confirms that measurement of donor bio-age pre-transplant can predict post-transplant function. It indicates that telomere length is inferior to donor chronological age when it is used as a bio-marker. This is in keeping with previous observations indicating that CDKN2A is a superior biomarker. Telomere length in addition to donor age and other promising biomarkers of ageing may provide a valuable pre-transplant prognostic score on organ quality, allowing improved and objective patient counselling and providing the possibility for targeted intervention strategies to preserve graft function.

MO-034 $CD4^+CD25^+Foxp3^+IFN\text{-}g^+$ INDUCED HUMAN Treg ARE A HETEROGENOUS CELL POPULATION SUPPRESSING ALLORESPONSES SPECIFICALLY AS WELL AS UNSPECIFICALLY

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IFN-g-producing $CD3^+CD4^+CD25^+Foxp3^+$ PBL are more frequently detectable in patients with good than in patients with impaired long-term kidney graft function, suggesting an immunoregulatory role of this induced Treg (iTreg) subtype.
We investigated the in-vitro function of separated $CD3^+CD4^+CD25^+Foxp3^+IFN\text{-}g^+$ PBL that were induced by phorbol 12-myristate 13-acetate (PMA)/Ionomycin or alloantigenic stimulation.
$CD4^+CD25^+Foxp3^+IFN\text{-}g^+$ PBL increased up to 36% in 16h PMA/Ionomycin-stimulated cell cultures. Induction of $CD4^+CD25^+Foxp3^+IFN\text{-}g^+$ PBL was suppressed in the presence of anti-IFN-g monoclonal antibody. Part of $CD4^+CD25^+$ and $CD4^+Foxp3^+$ PBL with intracellular IFN-g expression showed IFN-g on the cell surface (autocrine IFN-g production). The proportion of $CD4^+CD25^+$ and $CD4^+Foxp3^+$PBL expressing IFN-g only on the cell surface but not intracellularly was in the background region (paracrine IFN-g). Surface IFN-g was bound to IFN-g receptors on the cell surface. Expression of surface IFN-g allowed separation of $CD4^+CD25^+IFN\text{-}g^+$ PBL with 98% purity using antibody-coupled magnetic beads. Addition of enriched $CD4^+CD25^+IFN\text{-}g^+$ PBL to autologous PMA/Ionomycin-stimulated PBL suppressed blast formation in contrast to $CD4^+CD25^+IFN\text{-}g^-$ PBL. All blasts in $CD4^+CD25^+IFN\text{-}g^+$ PBL-containing cultures showed strong carboxyfluorescein-diacetat-succinimidyl-ester staining, indicating total suppression of cell proliferation in the presence of $CD4^+CD25^+IFN\text{-}g^+$ PBL. $CD4^+CD25^+IFN\text{-}g^+$ PBL separated from primary MLC and added to secondary MLC suppressed allogeneic T-cell activation mainly unspecifically. However, the strongest suppression was observed in

autologous MLC/iTreg combinations. In contrast, secondary MLC was less strongly suppressed by $CD4^+CD25^+IFN\text{-}g^+$ PBL when $CD4^+CD25^+IFN\text{-}g^+$ PBL were separated from primary MLC stimulated with a stimulator different from the secondary MLC. These data suggest antigen-specific suppression by a subset of $CD4^+CD25^+IFN\text{-}g^+$ PBL.
We conclude that $CD4^+CD25^+Foxp3^+IFN\text{-}g^+$ PBL represent a heterogenous population containing iTreg that suppress allogeneic T-cell responses and may be involved in inhibition of the specific posttransplant alloresponse.

MO-035 IL-17 PRODUCING CELLS HOME TO THE GRAFT EARLY AFTER HEART TRANSPLANTATION

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Purpose: While IL-17 is predominantly a proinflammatory cytokine, it has pleiotropic and environmental specific functions. Therefore, it is tempting to speculate that IL-17 is important in inflammatory responses seen in organ transplant patients. We determined IL-17 mRNA expression in the transplanted heart and donor-specific IL-17 producing cells in peripheral blood cells during early and late acute rejection episodes, and during immunological quiescence after heart transplantation.
Methods and materials: Endomyocardial biopsies (n=41) from heart transplant recipients (n=29) who experienced an early or late acute rejection were analysed for the presence of IL-17 mRNA. Moreover, we determined the frequency of donor-specific IL-17 producing peripheral blood cells by Elispot assay (n=35).
Results: Twenty-two percent (9/41) of the biopsies were positive for IL-17 mRNA. All (9/26) were observed in the early period ($\leq$3 months) after transplantation, while none (0/15) of the late (>3 months) biopsies expressed IL-17 mRNA (p=0.02). During early acute rejection, 56% (5/9) of the biopsies did express IL-17 mRNA, while biopsies from late acute rejections (0/5) did not express IL-17 mRNA (p=0.09). In contrast to the findings in the graft, we detected donor-specific IL-17 producing cells in peripheral blood predominantly late after transplantation (early 1/15 vs. late 7/20, p=0.10).
Conclusion: Early after transplantation IL-17 producing cells may home to the graft contributing to the rejection process, while late after transplantation this homing phenomenon does not occur.

MO-036 BELATACEPT DOES NOT ACTIVATE INDOLEAMINE 2,3-DIOXYGENASE (IDO) IN DE NOVO LIVER TRANSPLANT RECIPIENTS

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Background: Indoleamine 2,3-dioxygenase (IDO) is an immunomodulating enzyme catalyzing the degradation of tryptophan (trp) to kynurenine (kyn). Experimental studies have proposed that IDO activation is a key mechanism of action of CTLA4Ig. Belatacept is a 2nd generation CTLA4Ig which is under clinical development in organ transplantation. We therefore investigated whether belatacept treatment leads to IDO induction in patients undergoing liver transplantation.
Methods: A prospective, investigator-driven substudy of the phase II multicenter trial IM103-045 on belatacept in de novo liver transplantation was performed. At four participating transplant centers serum samples were collected and frozen at five pre-defined time points during a period when the immune system is exposed to belatacept for the first time. Samples were analyzed in batch for trp and kyn levels (indicative of IDO activity) by HPLC. Thirty consecutive patients were enrolled, who were treated either with belatacept-based (n=23) or tacrolimus-based immunosuppression (n=7). Time and group effects were analyzed employing a mixed linear regression model for longitudinal data.
Results: Trp levels significantly decreased in both groups in the immediate postoperative period ($p<0.01$). Trp levels, kyn levels and calculated kyn/trp ratios were not significantly different between patients receiving belatacept and patients receiving tacrolimus ($p>0.05$ for all three parameters) (see Fig. 1).
Conclusion: IDO activity is comparable in liver transplant recipients receiving either belatacept or tacrolimus. Thus the immunosuppressive mechanisms of action of the costimulation blocker belatacept do not involve IDO induction in the clinical setting.

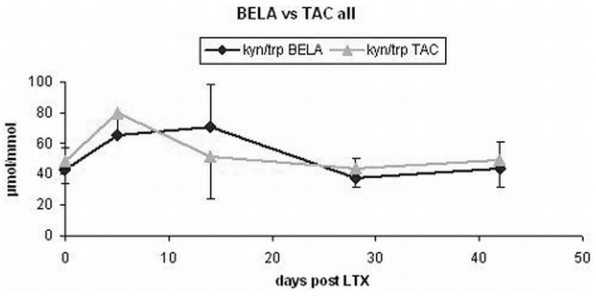

Figure 1. kyn/trp ratio in belatacept and tacrolimus treated patients after liver transplantation (medians & 95% CI).

MO-037 NO PRIVILEGED ROLE FOR VASCULAR ENDOTHELIAL CELLS DURING CYTOMEGALOVIRUS DISSEMINATION

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Introduction: The course of systemic viral infections is determined by the virus productivity of infected cell types and the efficiency of virus dissemination. We had recently developed a cell-type-specific virus labeling system to quantitatively track virus progeny during murine cytomegalovirus (MCMV) infection. With this model we could recently show that MCMV is produced by endothelial cells and hepatocytes. Remarkably, virus produced in the liver did not disseminate to other organs. Here, we aimed to investigate the role of endothelial cells in CMV dissemination in a murine heart transplant model.
Methods: Mice expressing Cre recombinase selectively in vascular endothelial cells (Tie2-cre) were infected with a modified MCMV that is converted to a fluorescently (EGFP) labeled virus by Cre-mediated recombination. HTx and NTx were performed from Tie2-cre to B6 and from B6 to Tie2-cre mice. Transplanted mice were infected and animals were sacrificed 5 days post infection. Virus load was measured in different organs using plaque assay. EC derived virus was quantified by fluorescence microscopy.
Results: After infection of B6 animals transplanted with a Tie2-cre heart modified MCMV could be detected in all analyzed organs, including the transplant. In the transplanted transgenic heart the majority of virus was recombined (43-81% PFU). However, no dissemination of the recombined EC derived MCMV to other organs was detected. When Tie2-cre animals were transplanted with a B6 heart and infected with the MCMV thereafter, recombined virus was found only in recipient organs but not in the transplanted non-transgenic heart. Finally, in B6 mice transplanted with acutely infected transgenic hearts most of virus found in organs of the recipient was recombined.
In summary, we could show that MCMV poorly disseminates from one organ to another and that EC do not play a privileged role in this process.

MO-038 ARTEMISIAE CAPILLARIS HERBA INDUCED PROLONGED SURVIVAL OF FULLY CARDIAC ALLOGRAFTS AND GENERATED REGULATORY CELLS

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Background: Inchingorei-san (TJ-117), a 6-component Japanese herbal medicine, is used for the treatment of vomiting, urticaria, liver and kidney disorders, with few side effects. In this study, we investigated the effect of TJ-117 on alloimmune responses in a murine model of cardiac allograft transplantation.
Methods: CBA mice ($H2^k$) underwent transplantation of a C57BL/6 (B6, $H2^b$) heart and received oral administration of 1g/kg/day of TJ-117 or one component of TJ-117 from the day of transplantation until 7 days afterward. An adoptive transfer study was conducted to determine whether regulatory cells were generated. Immunohistochemical and cell-proliferation studies, cytokine measurements, and flow cytometry analyses were also performed.
Results: Untreated CBA mice rejected B6 cardiac grafts acutely (median survival time [MST], 7 days). CBA transplant recipients given 1g/kg/day of TJ-117 had prolonged B6 allograft survival (MST, 23 days). However, the majority of CBA transplant recipients given 1g/kg/day of Artemisiae capillaris herba (ACH), one component of TJ-117, accepted B6 allograft indefinitely (MST, >100 days). ACH also suppressed proliferation of splenocytes and production of interferon-γ. Secondary CBA recipients given whole splenocytes from primary ACH-treated CBA recipients with B6 cardiac allografts 30 days after grafting had prolonged survival of B6 hearts (MST, >50 days) compared to that in the secondary recipients with adoptive transfer of naive splenocytes (MST, 12 days). The immunohistochemical studies showed that cardiac allografts from

ACH-treated recipients had sparse cell infiltration and only slight myocardial damage. Flow cytometry studies showed that the $CD4^+CD25^+Foxp3^+$ regulatory cell population was increased in transplant recipients given ACH.
Conclusion: Not only TJ-117 but also ACH, one component of TJ-117, induced hyporesponsiveness to fully allogeneic cardiac allografts and may generate $CD4^+CD25^+Foxp3^+$ regulatory cells in our model.

MO-039 CLINICAL RELEVANCE OF DEFINING EQUIVALENCES BETWEEN HUMAN AND MOUSE IMMUNOREGULATORY CELLS

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Although the induction and adoptive transfer of allograft tolerance with immunoregulatory cells are common methods in experimental Immunology, their translation to the clinic has met many obstacles. One fundamental difficulty lies in defining precise equivalences between immunoregulatory cells studied in animals and their supposed counterparts in man. Work in our laboratory centers on the regulatory macrophage (M reg) as a means of attenuating responses against donor alloantigen and has culminated in inclusion of M reg treatment in The ONE Study, a multinational clinical trial of cell therapy in renal transplantation. Mouse models prove convenient to test the combined effect of M reg treatment and conventional immunosuppression, but their relevance hinges on the degree of similarity between mouse and human M regs. M regs of both species arise from monocytes under analogous conditions and express unique markers and T cell-suppressive activities distinguishing them from monocytes, monocyte-derived DCs, and M0-, M1-, M2a-, M2b- and M2c-polarised macrophages. However, differences between mouse and human M regs exist, and weighing these differences against the likenesses is necessarily subjective. Therefore, gene expression profiling by microarray was adopted as an unbiased approach to evaluating their true similarity.

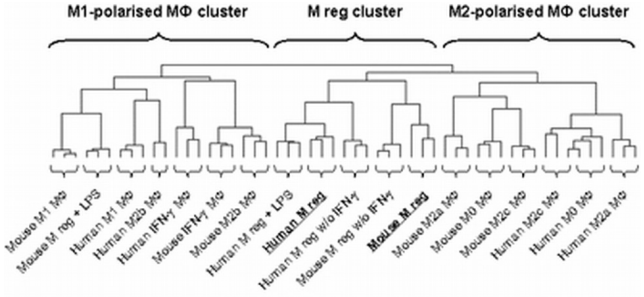

Figure: Hierarchical clustering (Pearson uncentered, average linked) of gene-wise median centered log2 signal intensities of genes with clear orthology between mouse and human

In co-clustering analyses, M regs from the two species grouped together when the entire orthologous gene set was considered, but gene set enrichment analyses returned inconsistent results. Thus, human M regs are the closest counterpart of mouse M regs, but an unambiguous equivalence could not be demonstrated. This may reflect a biological limit to resolving interspecies homologies or show no closer equivalents exist. The imperfect correspondence of mouse and human M regs does not invalidate results from mice, but cautions against their direct extrapolation to the clinic. These arguments should be applied to other potentially therapeutic immunoregulatory cell types.

MO-039A EARLY INCREASE IN N(EPSILON)-CARBOXY-METHYL-LYSINE AND DECREASE IN sRAGE PLASMA VALUES IN DE NOVO LIVER TRANSPLANTATION

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Background: Advanced glycation end-products (AGEs) - such as the N(epsilon)-carboxy-methyl-lysine, CML) - and the soluble form of receptor for AGEs (sRAGE) have been reported as emerging biomarker in cardiovascular, metabolic and inflammatory diseases. Their behavior in the setting of liver transplantation (LT) is poorly understood.
Methods: Seventeen patients undergoing LT were included in a prospective study. CML and sRAGE were determined before LT, after graft reperfusion and 1, 2, 7, 30 and 90 days after LT.
Results: Baseline CML plasma levels decreased after graft reperfusion (15.7 ± 4.6 and 8.8 ± 2.7 μg/mL, before LT and after graft reperfusion, respectively) while returned progressively to baseline values during the follow-p (15.1 ± 5.6 μg/mL at 90 days after LT) (ANOVA, $p < 0.0001$). The plasma levels of sRAGE did not change significantly soon after LT (median: 872, 1277, 1310, 835 pg/mL, before LT, after graft reperfusion, 1 and 2 days after LT, respectively), while they decreased from the seventh day after LT and remained constantly low during the follow-up (274, 391 and 233 pg/mL, respectively 7, 30 and 90 days after OLT) (ANOVA, $p < 0.0001$).
Conclusions: Our study provides further evidence to the role of the liver in the metabolism and/or clearance of CML, while the early decline of sRAGE might be accounted for by use of immunosuppressive medication. CML accumulation and decrease of protective titers of sRAGE might account for the negative metabolic impact of immunosuppression in the setting of LT and be of relevance to current clinical practice.

Kidney II

MO-040 STIMULATION OF THE CHOLINERGIC ANTI-INFLAMMATORY PATHWAY IN BRAIN DEAD DONOR RATS IMPROVES LONG-TERM ALLOGRAFT OUTCOME IN RECIPIENTS

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We have previously demonstrated that the parasympathetic nervous system is impaired in brain dead (BD) donor rats. Vagus nerve stimulation in these rats variably affected the expression of pro-inflammatory genes in different donor organs and improved renal function in recipients in an acute allograft rejection model. Since chronic allograft nephropathy is a major cause for late renal graft loss, the present study was conducted to assess the influence of donor vagus nerve stimulation on renal function and histology in long term transplantation experiments.
To this end, BD was induced in Fisher rats. In 1 group the vagus nerve was electrically stimulated (BD+STIM) during the whole course of BD (6 hours). Unstimulated BD Fisher donor rats served as controls. Renal transplantations were performed into allogeneic Lewis rats, without installation of immunosuppression. Blood and urine samples were collected every second week. Banff classification was assessed from harvested allografts.
Long term renal function was significantly better in recipients that received a graft from a BD+STIM donor. This was reflected by a better creatinine clearance. Banff classification revealed significantly reduced vasculopathy and less tubulopathy in the BD+STIM group. Altogether vagal stimulation of donors resulted in an improved survival of recipients.
In conclusion, our data demonstrate a long lasting beneficial effect of vagus nerve stimulation in BD donors on renal transplantation outcome. Since vagus nerve stimulation down-regulates BD induced expression of pro-inflammatory genes in the kidney, a reduced immunogenicity of renal allografts in the BD+STIM donors might underlie this beneficial effect. Hence activation of the cholinergic anti-inflammatory pathway in BD donors may represent a novel therapeutic modality to maintain organ quality in these donors.

MO-041 A COMPARISON OF THE PERIPHERAL BLOOD mRNA TRANSCRIPTIONAL PROFILES OF BELATACEPT- AND CYCLOSPORINE-TREATED RENAL TRANSPLANT PATIENTS

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Introduction: In an ongoing, phase III clinical trial (BENEFIT), the RNA expression profiles of renal transplant patients treated with belatacept was compared to that of patients treated with cyclosporine (CsA).
Methods: Whole blood samples were collected from patients receiving either belatacept (n=32 & 61) or CsA (n=19 & 22) at years 1 and 2 post- transplantation, respectively. Microarray analysis was performed on Affymetrix HG-133A whole genome arrays. Genes exhibiting at least a 1.3 fold difference ($p<0.05$) in expression level were considered differentially expressed in belatacept versus CsA treatment patients.
Results: Fifty-five and 61 genes exhibited higher expression, while 10 and 8 genes exhibited lower expression in belatacept-treated patients at years 1 and 2, respectively. Higher expression of genes associated with lipid metabolism and glucose transport was observed in belatacept patients at both years 1 and

2, potentially providing insight into the lower cholesterol, triglyceride and blood pressure observed in belatacept-treated patients. Genes associated with the regulation of epithelial inflammation and repair mechanisms were higher in belatacept patients, primarily at year 2. Interferon and viral infection response genes were also expressed at higher levels in belatacept patients, primarily at year 2, implying less inhibition of innate immunity.
Humoral immunity genes were expressed at a lower level in belatacept-treated patients. These included the complement gene, C4A/C4B, at year 1 and 2, as well as the immunoglobulin genes IGHA1 and IGHG1, at year 2. These findings are consistent with pre-clinical data demonstrating that belatacept inhibits T cell-dependent allo-antibody responses and the lower prevalence of anti-donor HLA antibodies in belatacept-treated patients.
Conclusion: Genes associated with innate immunity, response to epithelial inflammation and metabolic processes exhibited higher expression, and those associated with humoral immunity exhibited lower expression in belatacept- versus CsA-treated patients.

MO-042 EPITHELIAL TO MESENCHYMAL TRANSITION IN TRANSPLANTED KIDNEY, RELATION TO ALLOGRAFT FUNCTION AND MORPHOLOGY

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Introduction: The chief mechanism leading to renal fibrosis is fenotypic transition of tubular epithelial cells to mesenchymal cells. Tubular Epithelial Cells actively respond to posttransplant immunological and nonimmunological injury and can undergo transition to mesenchymal myofibroblast cells. Factors which force this process can be related to sustained morphological changes. The aim of the study was to evaluate correlations between epithelial to mesenchymal transition (EMT) and allograft function and histology.
Methods: 130 kidney allograft recipients from deceased donors had accomplished clinically indicated biopsy for graft dysfunction. 21 had implantation biopsy and 17 surveilance biopsy at 6th month. Biopsies were classified according to Banff criteria and immunostained for epithelial markers (cytoceratin and E-cadherin) and mesenchymal markers (vimentin and S100A4). Dual labeling was performed for E-cadherin and S100A4 to evaluate EMT in tubular cells. Correlations between histology, graft function and EMT were assesed.
Results: There was significant reduction of epithelial markers and increase of mesenchymal markers in tubular cells in 6th month protocol biopsies compared to implantation biopsies. Acute rejection and TA/IF was strongly correlated with EMT markers ($p < 0.05$). Tubular cells with lymphocyte infiltration had increased expression of mesenchymal markers compared to biopsies with ATN. Vimentin expression significantly positively correlated with serum creatinine ($r = 0.25$, $p = 0.006$). TEC's of grafts in recipients with proteinuria vs nonproteinuric, had sigificantly reduced expression of cytocerain (80.3 vs 85.3 (p= 0.03); and E-cadherin (58.6 16.8 vs 67.2, p = 0.03), increased expression of vimentin (39.3+_15.8 vs 26.8 10.4, $p<0.001$) and S100A4 (21.4 9.7 vs 14.5 9.3, p = 0.001).
Conclusions: EMT in tubular cells is closely related to functional allograft impairment, acute rejection, extent of fibrosis and tubular atrophy.

MO-043 A PRE-CLINICAL EVALUATION OF RENAL TRANSPLANT FROM DECEASED AFTER CARDIAC ARREST DONORS

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Background: Because of graft shortage, transplantation teams have to widen selection criteria in particular to deceased after cardiac arrest (DCA) donors. Kidneys from these donors have allowed good results especially if regional normothermic circulation (RNC) and perfusion machine are used for procurement and preservation. The aim of this study is to develop a pre-clinical model of DCA donors in accordance with recommendations of French Biomedical Agency, in order to describe the effects of RNC on renal transplant and to study the impact of static conservation or perfusion machine.
Methods/material: After 30 minutes' cardiac arrest, RNC was set up between inferior vena cava and abdominal aorta on Large White pigs of 30-40kg. The pump flow rate was between 2.5 and 3L/min. After 2 or 4 hours of RNC kidneys are removed and preserved 18 hours in a static UW solution or with ORS perfusion machine using KPS.
Results: This pre-clinical porcine model of DCA donor was reproducible. RNC have been performed during 2 hours (n=4) versus 4 hours (n=6). About renal transplant, length of RNC does not seem to affect inflammatory/immunological response. On the other hand kidney's response to hypoxia/oxidative stress is better after 4 hours of RNC than after 2 hours. In fact there is an activation of the mechanisms of response to hypoxia using of the ways of HIF1-a. The method of conservation during cold ischemia does not affect kidney's response to hypoxia/oxidative stress. However, conservation using perfusion machine keeps expression level of inflammatory/immunological response's genes.
Conclusion: RNC seems to allow a best response to hypoxia from the renal transplant. We need to study allotransplantation of these kidneys. This model can also be enhanced to be closer of clinical conditions.

MO-044 DO THE OXIDOREDUCTASES (ENDOTHELIAL NO SYNTHASE, CATALASE, GLUTATHIONE PEROXIDASE, SUPEROXIDE DISMUTASES) GENES POLYMORPHISMS HAVE AN ASSOCIATION WITH DELAYED GRAFT FUNCTION OF KIDNEY ALLOGRAFTS

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Background: Enhanced oxidative stress has been implicated in the development of complications after organ transplantations, especially ischemia-reperfusion injury and delayed graft function (DGF). It can therefore be hypothesized that genetic variability of antioxidant enzymes may play a role in the development of these complications. Endothelial NO synthase (eNOS) is seen as a protective enzyme. Catalase plays a significant role in the development of tolerance to oxidative stress in the adaptive response of organism. The glutathione peroxidase (GPX) is a major defense in oxidative stress. The superoxide dismutases (SODs) are involved in the defense against reactive oxygen species. The aim of the study was to examine the association of oxidoreductases genes polymorphisms with delayed graft function of kidney allografts.
Methods/materials: 187 recipients of kidney allografts were included in the study (59% males, mean: 43.1 years). The histories of the patients were analyzed taking into the account DGF, which was defined as the need for hemodialysis within the first 7 days after transplantation. All studied polymorphisms were analyzed using the PCR-RFLP method.
Results: With regard to the ENOS VNTR polymorphism probability of DGF was significantly increased in carriers of a allele compared with patients with bb genotype OR= 2.31, 95% CI=1.25-4.27, p=0.012. The risk of DGF was significantly lower in T allele carriers of the catalse gene polymorphism compared with CC homozygotes: OR=0.34, 95%CI=0.17-0.67, p=0.001.
Conclusions: The results of our study suggest that individuals with the a allele of NOS intron 4 VNTR polymorphism may be exposed to the delayed graft function. The -262C/T polymorphism in the catalase gene is associated with the delayed graft function in kidney allograft recipients. Glutathione peroxidase, SOD1 and SOD2 genes polymorphisms have no influence on the graft function.

MO-045 SAFETY AND EFFICACY OF EVEROLIMUS AND LOW DOSE CYCLOSPORINE IN PEDIATRIC KIDNEY TRANSPLANTATION

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Introduction: The aim of this study was to assess the safety and the efficacy of a low-dose Cyclosporine (CYA)-Everolimus (EVE) combination in pediatric kidney transplant recipients (kTx).
Materials and Methods: From 2008 to 2010 we enrolled 41 pediatric patients from 5 different pediatric programs. Mean age of the recipients was 9.1 ± 5.4yrs. Immunosuppressive regimen included: CYA (10mg/kg/die) and MMF (600mg/m2 BID) from POD#1 and delay introduction of EVE on POD#21 (0.8 mg/m2 BID, adjusted to a trough level 5-10ng/ml.) with simultaneous discontinuation of MMF and 50% reduction of CYA initial dose. CYA dose was tar-

geted to a 2nd hour post-dose concentration of 500-700 ng/ml (#21-#60 POD), 400-600 ng/ml (#61-#90POD) and 200-400 (>#61POD). Blood pressure values, sCreatinine, sCholesterol, sTriglyceride, PCR-CMV, PCR-EBV,PCR-BKV and uProtein were recorded 7, 14, 28, 90, 180, 270 and 360 POD as well as any immunological and non immunological adverse events. Protocol kidney biopsies were obtained on POD#180 and #360.
Results: Four patients were dropped before EVE administration because of hypercholesterolemia, surgical complication, chronic low platelet count and exitus. One year patients' and graft's survivals after EVE introduction were 100%. We experienced 18% of acute rejection, 5% of subclinical rejection and 6% of chronic allograft nephropathy. Any adverse event was recorded. Renal function, blood pressure values, lipid profile and virus infections were not impaired by EVE introduction and were comparable with our historical controls. After 1 year of follow up only 9% of patients showed histological patterns of CNI toxicity.
Conclusions: Low- dose CYA and EVE provide a safe and effective immunosuppression in pediatric kidney transplant recipients and seems to reduce CNI toxicity.

MO-046 REDUCTION IN COLD ISCHAEMIA TIMES OVER A DECADE OF DECEASED DONOR RENAL TRANSPLANTS IN THE UNITED KINGDOM

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Background: Prolonged cold ischaemia time (CIT) is associated with poorer outcome following kidney transplantation, with higher incidences of delayed graft function, acute rejection and reduced long term graft survival. The present study aims to determine trends in cold ischaemic times in the United Kingdom over the last decade.
Methods: UK Transplant Registry data on over 12000 adult, deceased donor kidney only transplants performed from 2000 to 2009 throughout the UK were reviewed. Activity for each of the 23 transplant centres including the number of donations after cardiac death (DCD) and after brain death (DBD) kidney transplants and CITs were reviewed for each year.
Results: 12067 deceased donor kidney only transplants were performed, with the number being performed annually increasing from 1164 in 2000 to 1324 in 2009. Overall, 82.6% of transplant performed were from DBD donors and 17.4% were from DCD donors. The proportion of transplants from DCD donors increased from 3.9% in 2000 to 36.2% in 2009.
After remaining relatively stable between 2000 and 2004, median CIT for national DBD donor transplants declined from 18.5h in 2004 to 16.4h in 2009, ($p<0.001$). Median CIT (2000-2009) fell significantly in 11 of the 23 transplant centres for DBD donor transplants. For DCD donor transplants, the median CIT fell significantly from 18.0h in 2005 to 15.9h in 2009, ($p<0.01$).
Conclusion: These data demonstrate an overall reduction in cold ischaemia in deceased donor kidney transplantation in UK renal transplant centres in the last decade, although the median CIT still exceeded 15h in half the centres in 2009. Further efforts should be made to minimise CIT by identifying and influencing potentially modifiable factors contributing to CIT in order to maximise the outcome for kidney transplants.

MO-047 HIGH INCIDENCE OF ANTI-CMV DRUG RESISTANCE AMONG D+R- KIDNEY TRANSPLANT RECIPIENTS RECEIVING PREEMPTIVE THERAPY

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Background: International guidelines favor the use of anti-CMV prophylaxis over preemptive strategy in D+R- kidney transplant recipients (KTR). However, there is a theorical risk of developing anti-CMV drug resistance with the prophylactic strategy.
Methods: 32 D+R- KTR who received prophylaxis (valganciclovir for 3 months) were compared with 80 D+R- KTR who received a preemptive treatment (IV ganciclovir or oral valganciclovir).
Results: The incidence of CMV infections was higher in the preemptive group than in the prophylactic group (60% vs 34%, p=0.02). A treatment failure (CMV DNAemia at 8 weeks after the initiation of the anti-CMV treatment) occurred more frequently in the preemptive group (31% vs 3%, p= 0.001). Anti-CMV drug resistances (14 UL97, 1 UL54) were also more frequent in the preemptive group than in the prophylactic group (18% vs 3%, p=0.04). 58% of the anti-viral treatment failures were associated with an anti-CMV drug resistance (p=0.0001). Patients with a viral load above 5.25 $\log_{10}$ cop/mL had the highest risk to have an anti-CMV drug resistance (OR=10.91, p=0.001). Finally, one year e-GFR was worse in patients with an anti-CMV drug resistance (43±24 ml/min vs 58±20 ml/min, p=0.04).
Conclusion: In D+R- KTR, preemptive strategy can be associated with a high incidence of anti-CMV drug resistance in patients with high peak viral load and treatment failure.

MO-048 CARDIOVASCULAR RISK IN KIDNEY TRANSPLANT RECIPIENTS RECEIVING mTOR INHIBITORS

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Background: Cardiovascular diseases (CVD), the main reason for death in kidney transplant recipients, should be addressed when tailoring immunosuppressive regimens. mTOR inhibitors showed cardioprotective effects in experimental studies, but their effect on CVD in renal transplantation is unclear.
Study was aimed to estimate cardiovascular risk in kidney transplant recipients receiving mTOR inhibitors.
Materials: The study included 115 kidney recipients, aged 56 years, receiving sirolimus or everolimus and steroids for mean 39.1 months. Additionally, 38 of them received low calcineurin inhibitor doses. Control group consisted of 58 recipients, randomly chosen from the population transplanted at the same period, receiving calcineurin inhibitors with MMF and steroids.
Results: Time after transplantation was 7 years in both groups. No differences in age, duration of pretransplantat dialysis, BMI, HbA1c existed between groups. The prevalence of diabetic, ischemic and hypertensive nephropathy as the reasons for ESRD was similar.
Post-transplant diabetes appeared in 33% of the study group compared to 17% of the control, (P=0.08). Blood pressure and number of antihypertensive agents, HDL-cholesterol and uric acid were similar.
In the study group higher mean cholesterol 249 vs 204.6mg/dl, ($P<0.0001$), LDL 136.5 vs 117.7mg/dl, (P=0.015), triglycerides 202 vs 142mg/dl, ($P<0.0001$) and proteinuria (P=0.0002) were noted. eGFR was lower in the study group (42.9 vs 51.8ml/min P=0.0003).
CVD (myocardial infarction, percutaneous coronary intervention, stroke, aortic aneurysm, pulmonary thromboembolism, sudden cardiac death) appeared in 19 patients from the study group compared to 5 from the control, (P=0.24). The risk of any CVD was higher in patients receiving mTOR inhibitors, HR 1.94; (95% CI 0.83-4.52). No correlation was found between duration of mTOR therapy and CVD.
Conclusion: The risk of cardiovascular events in kidney transplant recipients receiving mTOR inhibitors is increased. The burden of cardiovascular risk factors is greater in these patients.

MO-049 HOMOGENITY OF GENE EXPRESSION PATTERN IN CHRONIC KIDNEY ALLOGRAFT REJECTION

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Background: The main reasons of late kidney allograft loss are chronic rejections. The presented study aimed to show transcriptome differences in chronic T-cell mediated rejection (CTCMR) and chronic antibody mediated rejection (CAMR).
Methods/Materials: Late case biopsies (>3M) were performed in 2007-2009 in CNI/MMF treated patients. Diagnosis of chronic rejection was made according to Banff'09 classification. Intrarenal expressions of 378 genes relating to immune response (T-, B-cell activation, chemokines, cytokines, immune regulators and apoptosis) were analyzed with respect to the graft outcome in patients with CAMR (n=13), CTCMR (n=9) and in control group with stable kidney graft function and normal histological finding in protocol biopsy (n=10).
Results: Patients with CAMR had eGFR 0.49±0.22ml/s/1.73m^2 and proteinuria 2.8±3.9g/day while patients with CTCMR had eGFR 0.34±0.11ml/s/1.73m^2 and proteinuria 1.3±1.1g/day; n.s. Four patients with CAMR and three with CTCMR lost their grafts during the follow-up.
Both types of chronic rejection up-regulated many genes as compared with control group: chemokines (CCL4, CCL5, CXCL9, CXCL10, CXCL11), growth factor TGFB1, MHC class II (HLA-DMA, HLA-DMB, HLA-DRA), genes participating in humoral immune response (ADA, CD53, C4A, C4B, HLA-DRA, UBD) and in T-cell dependent mechanisms (CD3D, CD86, LAG3) including cytotoxic T-cell associated transcripts (CCL4, CCL5, GBP1, GZMK). Expression profile of CAMR did not differ significantly from CTCMR. Patients whose graft failed during the follow-up because of CAMR had higher expression of AGR2, AGR3,

BFAR, CD59, CD9 and IFNGR2, but lower expression of CCL19 and TRADD than patients, whose graft survived. This indicates lowering of apoptotic signals, but also upper regulation of cell migration and adhesion in failing grafts.
Conclusion: In this study, similar immune mechanisms that involved T-cells and B-cells mediated immunity in both chronic antibody- and T-cell mediated rejections were identified.
Supported by grant P301/11/1568.

Liver and intestine

MO-050 OUTCOME FROM RIGHT LOBE EX SITU SPLIT LIVER TRANSPLANTATION: SINGLE CENTRE EXPERIENCE

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The lack of size-matched livers for paediatric liver transplantation (LTx) led to the development of split liver transplantation. By splitting through the left portal fissure, transplantation of the left lateral segment (LLS) gives results comparable to using whole livers in children. To see if the same was true for right grafts, we performed a retrospective analysis of our right lobe split (RLS) liver program which started in 1991.
The majority of donors were <50 years, <5 days in ICU, stable hemodynamically with liver function tests < twice normal. Our technique in the majority was ex-situ, Kelly forceps crush clamping one centimetre to the right of the falciform ligament with partial resection of the adjacent segment IV and I. Segment IV artery and bile duct were sutured if encountered during transection. The majority of implantations were performed starting with the LLS recipient. T-Tube was inserted for duct to duct anastomosis.
Up to December 2010, 189 RLS LTx were performed. Table 1 and Table 2 show donor and recipient characteristics.

Table 1. Donor characteristics

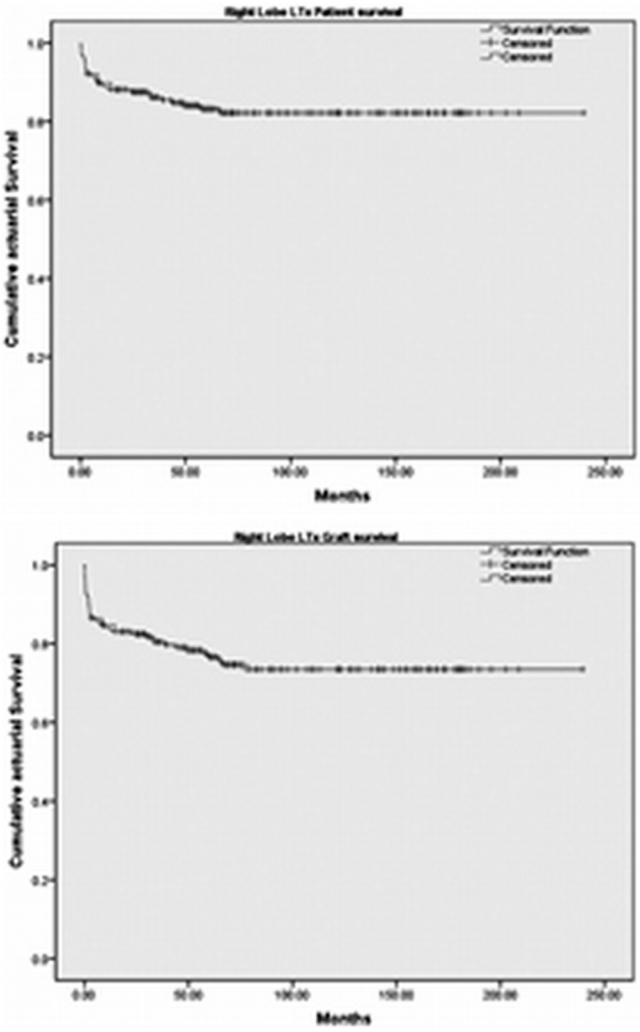
Gender	Female / Male	79 (44.4%) / 99 (55.6%)
Age (years)		26 (1–69)
ICU days		2 (1–14)
Inotropes	Yes / No	131 (73.6%) / 47 (26.4%)
Cause of death	ICB	73 (41%)
	HBI	27 (15.2%)
	NT	60 (33.7%)
	Others	18 (10.1%)
BMI		22.4 (12.3–37.8)
Na+ (mmol/L)		147 (121–175)
AST (IU/L)		36 (8–630)
BIL (umol/L)		10 (1–93)
Liver macroscopical assessment	Optimal	153 (85.9%)
	Non optimal	15 (8.4%)
	N/A	10 (5.6%)

ICU: Intensive Care Unit; BMI: Body Mass Index. Numerical values expressed in Median (range).

Table 2. Recipient pre- and post-transplant characteristics

Gender	Female / Male	100 (56.2%) / 78 (43.8%)
Age		48 (1–70)
Age group	Adult/Paed	147 (82.6%) / 31 (17.4%)
Disease	Toxic	27 (15.2%)
	Viral	37 (20.8%)
	Autoimmune	42 (23.6%)
	Neoplasm	8 (4.5%)
	Congenital cholestatic	12 (6.7%)
	Other	29 (16.3%)
Presentation	ALF / CLD	13 (7.3%) / 165 (92.7%)
CP	A	34 (19.1%)
	B	61 (34.2%)
	C	83 (46.6%)
UNOS	1	13 (7.3%)
	2A	4 (2.2%)
	2B	68 (38.2%)
	3	28 (15.7%)
	N/A	64 (36.5%)
MELD Score		12 (8–45)
CIT (hours)		12.6 (2.4–21.6)
GRWR		1.6 (0.9–4.5)
Post AST Peak (IU/L)		968 (202–11140)
Day 5 INR		1.8 (0.9 -4.2)
Day 5 BIL (umol/L)		66 (6-371)

ALF: Acute Liver Failure; CLD: Chronic Liver Disease; CP: Child Pugh; UNOS: United Network for Organ Sharing; MELD: Model for End stage Liver Disease; CIT: Cold Ischaemia Time; GRWR: Graft/Recipient Weight Ratio; AST: Aspartateaminotransferase; INR: International Normalised Ratio; BIL: Bilirubin; LOS: Length Of Stay. Numerical values expressed in Median (range).



9 patients were lost to follow up, 29 patients died and 43 grafts failed.
Patient and graft actuarial survival at 3 months, 1 and 5 years were 92.7%, 88.7%, 83.2% and 87.1%, 83.6%, 76.6%.
Complications included 7 (3.8%) primary non function, 14 (7.7%) arterial thrombosis and 27 (15%) biliary complications, of which 22 (12.2%) were bile leaks.
We adopted the ex situ technique for logistical reasons, allowing technical decisions to be made during splitting. The cutting plane 1 cm to the right of the falciform ligament was satisfactory, and excision of segments IV and I reduced the risk of parenchymal necrosis and the incidence of bile leaks, particularly from segment I duct. Short term complications did not compromise the long term outcome.

MO-051 EARLY GRAFT FUNCTION IN LIVING DONOR LIVER TRANSPLANTATION IS NOT PREDICTED BY GRAFT SIZE ALONE, BUT IS DETERMINED BY THE CORRELATION BETWEEN GRAFT SIZE, DONOR AGE, AND RECIPIENT STATUS

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Introduction: Graft size is the critical factor affecting the prognosis of living-donor liver transplantation (LDLT), and the occurrence of small-for-size syndrome (SFSS) is a main concern for clinicians. Many centers require the absence of pre-transplant risk factors and a minimal graft size for the prevention of SFSS. We hypothesized that early graft function would depend not only on graft size, but also on donor age and recipient status.
Methods: We retrospectively analyzed 200 consecutive adult LDLT cases, which were divided into two groups. From the 46th case onward, portal mod-

ulation by preoperative splenic artery embolization (SAE) was introduced for the small-for-sized-graft cases.
Results: Hospital mortality and 1-year survival rate in the first 45 cases were 10.8% and 84%, respectively. In multivariate analysis, the perioperative risk factor for post-transplant hospital death was a GW/RBW $<$ 0.8%. After the introduction of portal modulation by SAE in the later 155 cases, the hospital mortality and 1-year survival rate were 7.1% and 88%, respectively. The risk factors were a donor age $\geq$ 53 years-old and MELD $\geq$ 23. A cut-off value of 0.68% for GW/RBW didn't have a significant impact on post-transplant graft function, because of the efficacious portal decompression by SAE. The occurrence of SFSS and hospital death depended upon the specific combination of graft size, donor age, and MELD.
Conclusions: The minimum GW/RBW could be safely lowered to 0.68% with adequate portal modulation. Early graft function were determined not only by graft size, but also by donor age and recipient status. Donor age and graft size should be matched to the recipient status when possible, and when not possible, portal modulation should be considered.

MO-052 EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT FOR LIVERS FROM DONORS AFTER CIRCULATORY DEATH: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Livers from Donors after Circulatory Death (DCDs) are particularly susceptible to the effects of warm ischaemia and ischaemia-reperfusion injury with successful utilization dependent on overcoming these factors. Extracorporeal Membrane Oxygenation (ECMO) acts as a bridge between asystole and successful procurement, enables rehabilitation of marginal DCDs, and permits assessment of the liver under non-ischaemic conditions. This study evaluates the effectiveness of ECMO in supporting liver transplantation from DCDs.
Methods: MEDLINE, EMBASE and Cochrane databases were searched citing the MeSH terms "Extracorporeal Membrane Oxygenation" AND "Donors after Cardiac Death" (and their variants). Primary endpoints included 1-year patient and graft survival. Secondary endpoints included rates of Primary Non Function (PNF) and Ischaemic Cholangiopathy (IC).
Results: The search identified 59 articles of which 3 cohort studies (3 category II) and 1 case-control study (category III) were relevant. Meta-analysis was performed using 44 uncontrolled DCD livers and 100 Donation after Brain Death [DBD] controls. One-year patient survival was comparable between DCDs and DBDs (relative risk 0.955, p = 0.624), but DCD graft survival was lower (RR 0.790, p = 0.148). PNF (RR 7.877, p = 0.002) and IC (RR 4.41 p = 0.013) were significantly higher in DCD grafts. The category III study (11 livers) reported 91% 1-year patient and graft survival, one case (9%) of IC, and no PNF.
Conclusions: ECMO helps recover ischaemically-damaged livers from uncontrolled DCDs thus enabling transplantation with acceptable survival. ECMO support may contribute towards an increased donor pool, but its benefits must still be balanced with recognition of significantly higher rates of PNF and IC. Preliminary results of ECMO for category III DCDs appear promising as more liver grafts from marginal controlled DCDs are offered for transplantation.

MO-053 PATIENT OUTCOMES FOLLOWING PORTAL VENOUS AND HEPATIC ARTERIAL RECONSTRUCTION IN ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: Portal venous and hepatic arterial inflow is frequently insufficient to allow adequate arterial and venous inflow to the liver graft. Donor iliac artery and vein are most commonly used as conduits from aorta and superior mesenteric vein to overcome this problem. In this study we describe the outcome of patients in the Scottish Liver Transplant Programme who underwent cadaveric OLT where arterial and venous grafts were required.
Methods: All patients who underwent OLT at The Royal Infirmary, Edinburgh between 1996 and 2010 were identified from the transplant unit database. Data regarding outcome of patients requiring vascular reconstruction were gathered from the database, hospital case notes and operation notes and compared to those with standard vascular reconstruction. All liver transplants except split grafts were included in the analysis. Data analysis was performed using Microsoft excel and graph pad prism.
Results: Eight hundred and twenty three consecutive patients were analysed. Of these, 66 patients (8%) required a vascular conduit. Fifty of these were arterial and 19 were portal venous (3 patients required both). Mean red cell transfusion was significantly higher in patients who underwent portal venous reconstruction (7 vs 11 units, p$<$0.05). 30 day mortality was almost double in the venous reconstruction group (10.5% vs 5.8%, p$<$0.001). The need for arterial reconstruction did not significantly increase morbidity or mortality. Cold and warm ischaemic times, and operative times were similar in all groups.
Conclusion: The need for portal venous reconstruction results in increased morbidity and mortality in OLT graft recipients. This highlights the essential requirement of pretransplant vascular assessment in order to provide informed consent to the patient and be able to chose suitable grafts for the recipient, potentially avoiding extended criteria donors if a venous conduit is required.

MO-054 THE HISTOPATHOLOGIC RISK FACTORS OF PRIMARY GRAFT DYSFUNCTION AFTER HUMAN LIVER TRANSPLANTATION.

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Introduction: The causes of primary grafts dysfunction (PDF) or non-function (PNF) after liver transplantation (LTx) are multifactorial. Nevertheless many mechanisms of ischemia/reperfusion (I/R) injury responsible for PNF/PDF are unknown.
Purpose: To analyze the factors associated with PDF/PNF after human LTx and outcome
Patients and methods: Between May/02 and Aug/10 were analyzed prospectively 127 LTx performed in 124 patients. Donors' and recipients' demographics data, LTx indication and Meld score, CIT, preservation solutions and patient and grafts survival were studied. In all cases a liver biopsy was taken 2 hour after graft reperfusion and were assessed for the following histological features (HE): steatosis *macro and/or microvesicular*; *parenchymal neutrophilic infiltration*; *portal inflammation*; *hepatocellular necrosis* and *ballonization.* Apoptosis was assessed by the apoptosis index (TUNEL and Caspase-3 cleaved assay) and ICAM-1 by index. Grafts functions were analyzed during the 7 days after LTx by serum levels of AST, ALT, Bilirubin, and Protrombin Time. Primary graft dysfunction (PDF) was defined as initial poor outcome with AST peak level $>$2000 IU/L and PT $\leq$ 50% and primary nonfunction (PNF) needed urgent regraft. It was compared G1 - *Non PDF/PNF group* (n=78) vs. G2 - *PDF/PNF group* (n=49). Results significant when p$<$0.05.
Results: There was no significant difference comparing G1 vs G2 regarding donors age; BMI, ITU stay; AST; ALT and Sodium; and CIT. The main LTx indication was due to end stage liver disease 50 (70.5%) – G1 and 37 (75.5%)-G2, p-0.5 and mean MELD score (pure) was 21$\pm$8 and 22$\pm$11.5, p-0.5.

Groups	Non PDF/PNF (n=78)	PDF/PNF (n=49)	P value
Hepatocellular Necrosis - Zone 1 to 2	12 (15.4%)	21 (43%)	0.006
Mean necrosis	2.4$\pm$9.7	7.6$\pm$13.4	0.01
Apoptosis Index (TUNEL)	0.267$\pm$0.109	0.195$\pm$0.106	0.002
Patient Survival (1, 3, 6 mths)	92, 87, 86%	80, 70, 68%	0.2
Graft Survival (1, 3, 6 mths)	92, 86, 84%	75, 65, 63%	0.03

Conclusion: The presence of high rates of hepatocellular necrosis and low apoptotic index (TUNEL) are associated with increase PDF/PNF and consequently impairment of graft survival rates in human liver transplant.

MO-055 HIV POSITIVE PATIENTS IN THE WAITING LIST FOR LIVER TRANSPLANTATION: HIGH MORTALITY AND LOW ACCESS TO TRANSPLANTATION

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After the introduction of HAART, HIV has no longer been considered a contraindication for transplantation. Yet, liver disease in this population is characterized by an accelerated course that may impact on the waiting list. Aim: To evaluate the experience in Argentina with HIV + patients listed for liver transplantation.
Patients and Methods: We analysed 52 HIV + patients listed between 7/2005 and 3/2010 (Group HIV +). Results were compared with 462 HIV negative patients included in the same period (Group HIV neg). Data was obtained from the INCUCAI, the Argentinian National procurement organism and from the Transplantation Centers.
Results: Etiology of liver disease in the Group HIV + was hepatitis C, n=40; HBV n=3, fulminant hepatitis n= 3, alcohol n=2, re-trasplant n=2 and others n=2. MELD at the time of listing: Group HIV +:16.15 ($<$19 n=40, $>$19 n=8, emergency n=3) vs Group HIV neg: 16.64 (NS). Outcome in the waiting list:

Death 27% (n=14) vs 18.7% (n=61) ($p<0.05$), transplant 13% (n=10) vs 30.4% (n=99) ($p<0.001$). Mean time from listing to death: 270.70±298.11 days vs 267.29±266.53 days, NS. Mean time from listing to transplant: 70.26±74.05 vs 261±187.6 days ($p<0.01$). Mean MELD at the time of death 12.54 (< 15 n=13, >19 n=1) vs 19.6±9.7 ($p<0.05$). Mean MELD at the time of transplantation: 24.33 vs 24.1±7.6, NS. Post transplant survival at 1 year: 70% (n=7) and 83.5% (n=83), NS.

Conclusion: HIV positive patients have a high mortality in the waiting list and a low access to liver transplantation. MELD score underscores the severity of liver disease in this population when compared to HIV negative patients. Yet, post transplant overall survival at 1 year does not differ significantly from HIV negative patients.

MO-056 EFFECTS OF INDUCTION ON HEPATITIS B AND HEPATITIS C VIRUS CO-INFECTED LIVER TRANSPLANTS: AN ANALYSIS OF UNOS DATA

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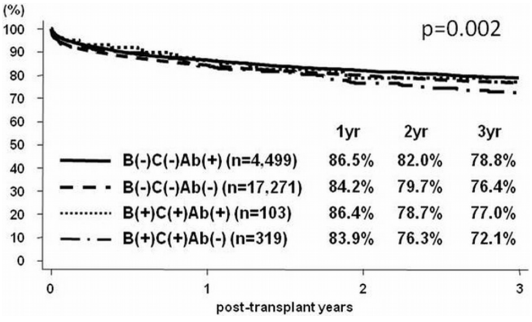
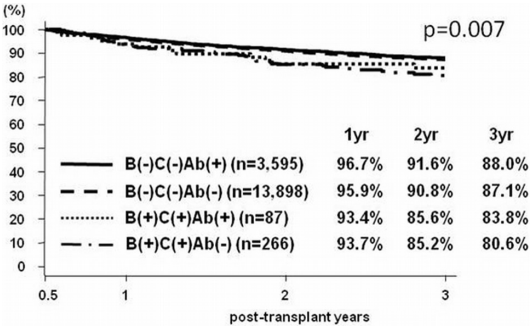
Background: The effect of antibody-based induction therapy (Ab) in hepatitis B (HBV) and hepatitis C (HCV) co-infected patients is inconclusive. We assessed whether after adjustments for confounders Ab was associated with improved graft survival in B(+)C(+) recipients using the UNOS data.

Methods: The data of 422 adults with HBV and HCV co-infection who received deceased-donor primary-only liver transplants that were performed in the MELD era was analyzed. HBV infection was defined by positive results for hepatitis surface antigen. HCV infection was defined by positive HCV serology. Transplants from donors who were HBV-positive or HCV-positive were excluded. We classified recipients into four groups: HBV and HCV co-infected patients who received Ab [B(+)C(+)Ab(+)], HBV and HCV co-infected patients who did not receive Ab [B(+)C(+)Ab(–)], HBV- and HCV-negative patients who received Ab [B(–)C(–)Ab(+)], and HBV- and HCV-negative patients who did not receive Ab [B(–)C(–)Ab(–)]. We used Kaplan-Meier methods to calculate liver graft survival rates, and Cox proportional hazard models to estimate the effect of Ab adjusted for confounders.

Results: Graft survival rates were significantly lower in B(+)C(+)Ab(–) (72.1% at three years) than in other groups.



Graft survival of B(+)C(+)Ab(+) (77.0% at three years) was similar to that of B(–)C(–)Ab(–) (76.4% at three years). Graft survival rates for those surviving more than 6 months depicted similar trend.



After adjusting for confounders and using B(–)C(–)Ab(+) as a reference group three-year survival of B(+)C(+)Ab(–) (hazard ratio [HR], 1.50; 95% CI, 1.06-2.11) showed significantly worse survival. B(+)C(+)Ab(+) (HR, 1.28; 95% CI, 0.68-2.41) and B(–)C(–)Ab(–) (HR, 1.10; 95% CI, 0.97-1.25) had survival similar to that of B(–)C(–)Ab(+).

Conclusion: The use of Ab for HBV and HCV co-infected patients resulted in improved survival, similar to that of patients with no hepatitis.

MO-057 IMMUNOSUPPRESSIVE STRATEGIES IN LIVER TRANSPLANTATION IN HIV CO-INFECTED PATIENTS: UNIVERSITY OF MODENA EXPERIENCE

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Introduction: Highly effective antiretroviral therapy (HAART) in the last decade increased the survival rates in HIV positive patients, determining at the same time a higher number of HIV patients suffering from liver-related disease. Liver transplantation (LT) is the only curative treatment for end-stage liver disease (ESLD) associated or not associated with HCC.

Materials/Methods: From June 2003 to January 2011, 27 patients underwent cadaveric LT for ESLD at our Institution. Three of them were combined liver-kidney transplantation. Inclusion criteria at our Centre followed the Italian Protocol for LT in HIV positive patients. Immunosuppressive regimens were based on Cyclosporine (CsA) or Tacrolimus (FK), conversion to Rapamycin was made in cases of calcineurin inhibitos (CNI) toxicity, de novo neoplasm and in patients with a high tumour burden on histological examination.

Results: Twenty-three patients were male and four were female. Median age was 44,6 years (range 32,2 - 60). All patients were affected by ESLD which was associated to HCC in 15 cases. All patients were preoperatively inside Milan Criteria. The median model for end-stage liver disease (MELD) was 19.9 points (range 11 - 34). The median CD4 T-cell count was 294.8/mmc (range 119 - 956). Conversion from CNI to Rapamycin occurred in eleven cases. HCV recurrence occurred in 15 of the 24 HCV-positive patients. No differences were observed between the group of patients under CNI and the one under Rapamycin as regards HCV and HCC recurrence, acute/chronic rejection, complications and survival. Median follow up was 26 months (range 0,9 - 91,3 months).

Conclusions: LT in HIV positive patients is a feasible procedure and the use of new immunosuppressive drugs has to be taken into account in this setting of patients.

MO-058 EFFECT OF PROLONGATION OF ANTIVIRAL TREATMENT BEYOND CONVENTIONAL TIME LIMITS ON SURVIVAL AND FIBROSIS PROGRESSION IN NON-RESPONDERS TO INTERFERON+RIBAVIRIN FOR HCV RECURRENCE AFTER LIVER TRANSPLANTATION

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The management of patients treated for hepatitis C (HCV) recurrence after liver transplantation (LT) and not achieving virological response following antiviral treatment (AVT) with interferon+ribavirin is controversial. A retrospective analysis of the outcomes of 71 non-responders to AVT after LT at a single Center was performed. Twenty-three patients (33%; Group A) were treated for <12 months and 47 patients (67%; Group B) for >12 months. Group A patients deceased due to HCV recurrence during AVT were excluded from the analysis. Survivals were computed starting from the initiation of AVT. The median follow-up was 54.3 months. Patient sex, age, body mass index, prevalence of hepatitis B co-infection, MELD score at transplant, donor age, prevalence of HCV-positive and of HBcAb-positive donors, viral genotype, type of immunosuppression, pre-treatment hepatitis staging score and time between LT and initiation of AVT were comparable between groups ($P>0.05$ for all comparisons). Median duration of AVT was 8.2 months in Group A and 32.3 months in Group B. AVT intolerance/toxicity and absence of response were the main causes of AVT discontinuation in group A and in Group B (43% and 62%, respectively). Overall discontinuation rate due to intolerance/toxicity was 20% (14 patients). Six-year survival was 53% in Group A and 79% in Group B (P=0.002). Mean fibrosis progression/year was 2.18 in Group A and 0.46 in Group B (P=0.01). Prolongation of AVT in non-responders to conventional treatment showed an overall beneficial effect and an acceptable tolerance rate.

MO-059 LACK OF INFLUENCE OF GRAFT ISCHEMIA ON REJECTION AND SURVIVAL IN INTESTINAL TRANSPLANTATION

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Background: Prolonged cold (CIT) and warm ischemia time (WIT) have been associated with graft dysfunction in liver and kidney transplantation. An increased rate of acute rejection (AR) has been attributed to prolonged CIT in kidney transplantation. This study was designed to try to find a correlation of ischemia times with AR and overall survival in a large series of intestinal transplantation.
Methods/Materials: Since 1994, 324 small bowel transplants, alone or as multivisceral transplantation, have been performed in 286 patients. Routine and surveillance biopsies were taken to rule out or confirm AR. Data for analysis of ischemia times and outcomes were available for 287 small bowel transplants.
Results: Average CIT was 7 hours and 11 min (431±98 min). Average WIT was 40±14 min. CIT up to over 10 hours did not increase the rate of AR (P=0.9). There were only 12 cases over 10 hours, and the longest CIT was 12h 28 m. The mortality rate was not different over 8 hours (P=0.2) and over 10 hours P was = 0.098 (not significant but even in favor of better survival). WIT over 60 min up to 90 minutes (10 cases) did not increase the rate of AR (P=0.5), nor the mortality rate (P=0.3). There were only 2 cases over that time. Other factors of ischemia like anoxia and hypotension in the donor, and impaired reperfusion of the graft during operation, did not show differences either in AR rate or mortality.
Conclusions: Adequate selection of donors and grafts, and an accurate surgical technique, with limitation of ischemic episodes and times of cold and warm ischemia in intestinal transplantation, avoid the complications attributed to graft anoxia in other organ transplants.

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Pancreas

MO-060 PANCREAS TRANSPLANTATION: DOES SURGERY RESULT IN HIGHER MORTALITY FOR DIABETICS?

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Background: Pancreas transplantation improves quality of life, stabilises complications and increases longevity when compared to other modalities for insulin dependent diabetes mellitus (IDDM). A mortality rate of 5-8% results in reticence among clinicians to refer suitable candidates, as patients have significant co-morbidity, particularly cardiovascular impairment. IDDM may result in high mortality rates even without transplantation. We aimed to establish the mortality rates of patients on our waiting list compared to post-transplantation.
Methods: A retrospective analysis of pancreas transplantation in our unit since 2001 was performed (SPK=148, PAK=33, PTA=11). This was compared with a control group accepted onto the waiting list for transplantation with a primary endpoint of mortality. Risk factors including diabetic complications, insulin requirements, age, type of transplant and waiting time were analysed.
Results: Mortality on the waiting list was 30% (36/119) compared to 9% (19/193) post-transplantation; ($p<0.001$) (8%(16/193) 1 year mortality) with no differences regarding cardiological risk (mean ejection fraction >60%; myoview and echo results); IDDM duration (21 and 24 years respectively; p=0.26) or dialysis requirements in patients with nephropathy (26 and 23 months respectively; p=0.73.) Age at death after surgery compared to the waiting list revealed no differences (46.7 vs. 43.7 respectively; p=0.31). Mean time from listing to death in the groups was comparable (537 and 582 days respectively; p=0.79). Younger patients had a shorter median survival from listing (<50) compared to older patients (525 vs. 933 days; $p<0.0001$.)
Conclusion: Mortality post-transplantation compares favourably to that awaiting surgery. The cohort of patients suitable for pancreatic transplantation has a high mortality risk even without surgery, representing young patients with aggressive disease. Transplantation offers a protective effect both against mortality and for risk modification, despite the concomitant risks of surgery and immunosuppression. In selected patients transplantation remains the benchmark treatment modality of IDDM.

MO-061 LAPAROSCOPIC ROBOT-ASSISTED PANCREAS TRANSPLANTATION

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Background: Surgical complications are a major disincentive to pancreas transplantation, despite the undisputed benefits of restored insulin independence. The da Vinci surgical system, a computer assisted electromechanical device, provides the unique opportunity to test whether laparoscopy can reduce the morbidity of pancreas transplantation.
Methods: Pancreas transplantation was performed by robot assisted laparoscopy in three patients. The first patient received a pancreas after kidney transplant, the second a simultaneous pancreas kidney transplantation, and the third a pancreas transplant alone. Operations were carried out through an 11 mm optic port, two 8 mm operative ports, and a 7 cm midline incision. The latter was used to introduce the grafts, handle vascular crossclamping, and create exocrine drainage into the jejunum.
Findings: The two solitary pancreas transplants lasted 3 and 5 hrs, respectively, the simultaenous pancreas kidney transplantation lasted 8 hrs. Mean warm ischemia time of the pancreas graft was 34 minutes. All pancreata functioned immediately, making their recipients insulin-independent. The kidney graft, revascularized after 35 minutes of warm ischemia, also functioned immediately and fully. No patient had complications during or after surgery; mean hospital stay was 25 days. After a mean follow-up period of 3.7 months, all recipients are alive with optimal graft function.
Interpretation: We have shown the feasibility of laparoscopic robot-assisted solitary pancreas and simultaneous pancreas and kidney transplantation. If the safety and feasibility of this procedure can be confirmed in larger series, laparoscopic robot assisted pancreas transplantation could become a new option for diabetics needing beta-cell replacement.

MO-062 USE OF COMPUTED TOMOGRAPHY (CT) IN PANCREAS TRANSPLANTATION

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Background: Imaging plays a vital role in the diagnostic investigation of graft dysfunction and surgical complications after pancreas transplantation. Ultrasound has several important limitations. For this reason, computed tomography (CT) has emerged as the primary imaging modality in these patients. The aims of this study were to evaluate the use of CT in pancreas transplantation and assess how imaging influenced patient management.
Methods: From January 2005 to August 2010, 99 pancreas transplants were performed at our centre. Indications, CT findings and whether imaging altered management (specifically; re-operation, further radiological investigations, commencement of antibiotics or anticoagulation) were determined by retrospective analysis.
Results: In the first 90 days post op, 178 CT scans were performed on 82 patients. The median number of days post op was 11 (range 1-88 days). The median number of CT scans was 2 (range 1-15 scans).
The most common indications for scanning were "? Collection" (37%), "High BM" (22%) and "Serum amylase and/or lipase high" (14%).
CT findings varied but commonly-reported abnormalities included: collections (15%); graft pancreatitis (7%); ileus (6%); portal or segmental thrombosis (5%); arterial thrombosis (3%). 25 CT scans (14%) were normal. The fre-

Table 1

Indication	Number of CT scans (%)	Change to management after CT (%)
? Collection	66	13 (20)
High BM	40	9 (23)
Serum amylase and/ or lipase high	25	5 (20)
Abdominal pain/ tenderness/ distension NOT obstruction	17	2 (12)
Bleeding	11	4 (36)
Other	11	3 (27)
Abdominal pain/ vomiting ? obstruction	7	4 (57)
Mass related to pancreas ? cause	1	0
Total	**178**	**40 (22%)**

quency of these findings were the same irrespective of the indication for scanning.
Notably, only 40 (22%) CT scans led to distinct changes in management; most commonly; re-operation (43%); followed by further radiological investigations (33%); commencement of antibiotics (18%), commenced on anticoagulation (15%).
Conclusion: This review highlights that multiple CT scans are performed in the post operative pancreas transplant recipients, but despite identifying a variety of abnormalities, relatively few alter management. A more selective approach to CT scanning is warranted.

MO-063 PERCUTANEOUS ULTRASOUND-GUIDED BIOPSY OF PANCREAS ALLOGRAFT: IT IS SAFE, ESSENTIAL AND DIAGNOSTIC

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Introduction: Monitoring a pancreatic allograft for rejection is difficult.Percutaneous US-guided biopsy is used patchily and there are few data on its safety and role.
Aim: The aim of this study was to assess the complications and diagnostic yield during a 2.5 year period from consecutive pancreatic allograft biopsies.
Results: 25 pancreas biopsies were performed on 15 patients between April 2008 and September 2010. Ten biopsies were from recipients of SPK transplants, 11 from PAK and 4 from PTA recipients. Of the 10 biopsies from SPK, 7 had concurrent renal biopsy. The indication for biopsy was hyperamylasaemia in 17 (68%) cases, hyperglycaemia in 5 (20%), renal dysfunction in 1 (4%), and protocol surveillance for high risk in 2 (8%). Median time to biopsy was 12 months (range 1-50) post transplant. One procedure was abandoned due to discomfort. Of the remaining 24, histologically satisfactory sample was achieved from 22 (92%). There was only one case of mild, self-limiting pancreatitis. Eight biopsies showed acute cell mediated rejection (ACMR, 6 Banff grade I, 4 Banff grade II), 3 showed antibody mediated rejection (AMR), 2 showed severe chronic rejection, 2 indeterminate, and 7 (28%) showed no rejection. Of the 7 cases with a concurrent renal biopsy, 3 showed histological discordance between the pancreatic and renal biopsies; in 2 cases the renal biopsy showed no rejection but the pancreatic showed ACMR, and the third case showed borderline rejection in the kidney but grade II ACMR in the pancreas. Three of the biopsies stained positively for C4d.
Discussion: In this series biopsy of pancreatic allografts achieved a high diagnostic yield without significant complications. Positive clinical information was identified in 70% of cases. Concurrent biopsy of both kidney and pancreas is essential in SPK recipients as histological discordance is common.

MO-064 LUMINEX SCREENING FOR DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN PANCREAS TRANSPLANT ALONE

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Background: The value of donor-specific anti-HLA antibodies (DSHA) at predicting graft failure has been established for many types of solid organ transplantations, but their role in pancreas transplant alone (PTA) has never been reported.
Methods: 83 PTAs were performed in Pisa since 2000 to 2010. Post-transplantation sera (median follow-up: 45 months;range 7-106) were available for 44 patients. Pre- and post-transplant recipient sera were screened for DSHA by Luminex (OneLambda, Canoga Park, CA). Using the HLA MatchMaker algorithm, we calculated the number of mismatched eplets for A+B loci for each transplant in order to assess whether a higher load of mismatched eplets for a given HLA locus could favor the onset of DSHAs.
Results: Among the 83 PTAs, the mean number of mismatched eplets was 15 (range 2-33). Among the 44 recipients with paired pre- and post-transplant sera, 14 recipients tested positive at baseline. At follow-up 13 of these 14 recipients remained sensitized, 1 seroreverted, and 6 more recipients seroconverted against class I antigens. There was no statistically significant difference in the mean number of mismatched eplets on A+B loci in these latter 6 recipients vs. recipients not developing de novo anti-HLA antibodies (median 16 vs. 15). After censoring for graft thrombosis and death with a functioning graft, only 5 of the 44 recipients had acute or chronic rejection and finally lose their grafts. Of them, 2 patients had pretransplant DSHA (MFIs: anti-A66 3900; anti-A32 5500, respectively) and rejected their PTA after 6 and 95 months, respectively. 3 more patients without pre-transplant DSHA seroconverted (MFIs: anti-B51 10679 + anti-A24 7960 + anti-DR1 1123; anti-A2 1708 + anti-DQ073417; anti-DQ06 2801) and all of them rejected within next year.
Conclusion: Luminex testing has the potential to predict PTA rejection.

MO-065 PANCREAS TRANSPLANTS AND REJECTION WITHIN ONE TRANSPLANT UNIT

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Background: Rejection is a worrying condition which can threaten graft survival.
Aim: To determine which factors played a role in development of rejection and subsequent graft survival within pancreas transplant patients from our centre.
Methods: Retrospective examination of clinical details of pancreas transplants performed between June 2001 and July 2010 to see if recipient or donor clinical details had an effect on pancreatic rejection and subsequent graft survival. Statistical analysis was made using Wilcoxon, Student's t-test and chi-square tests.
Results: 211 pancreas transplants were performed between 2001 and 2010. Median age was 41, IQ range 36-49. Male: Female ratio of patients was 128:83.
SPK transplants, (n=161), graft survival at one year was 78.9%, and 5 year graft survival was 72.7%.
PAK and PAT transplants n=50), revealed a one year graft survival of 64%, and 5 year of 48%.
One year and five year graft survival rates for SPK vs PAK and PAT group were found to be significant, P=0.02 and P=0.0007 respectively.
50 patients in total, suffered from 51 acute and 15 episodes of delayed rejection.
40 out of 50 patients treated for rejection, were treated with methylprednisolone (*MP*) alone. 27 patients, 67.5%, had a functioning graft in 5 years. Three were treated with anti-thrombocyte globulin (*ATG*) alone. All 3 had a functioning graft at 5 years. 7 patients were treated with MP and ATG, with 5 patients, 71%, still having a functioning graft at 5 years, P=0.0651.
Interestingly, no significant relationship was found between number of rejection episodes and graft or patient survival.
Cold ischaemic time and graft survival at 1 and 5 years, $<$720 mins and above), showed a trend towards significance, P=0.0521.
Conclusion: Different treatment therapies for rejection did not reveal any statistical significance on graft survival. No significant relationship revealed between number of rejection episodes and graft/patient survival.

MO-066 TRANSPLANT PANCREATITIS: TOWARDS DEFINING ALLOGRAFT FAILURE

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Background: Pancreas transplantation has evolved to become an effective long term treatment modality for complicated Insulin Dependent Diabetes Mellitus (IDDM). However, allograft failure or severe concomitant rejection remains an obstacle to successful transplant outcome, occurring in 21% of recipients within one year. The potential role of transplant pancreatitis in the process of failure and rejection has never been clearly delineated. This study aimed to define both quantitative and qualitative evidence of transplant pancreatitis in explanted pancreata.
Methods: Analysis was performed of a prospectively maintained database of 203 consecutive patients undergoing pancreas transplantation since the initiation of our programme (2001-2010; SPK=155, PAK=36, PTA=12). The histological reports (performed by experienced histopathologists) for explanted pancreata (44) were correlated against terms most commonly associated with acute and chronic pancreatitis as previously defined.
Results: 61% of patients with explanted allografts had histological evidence of pancreatitis. The most commonly described feature was fat necrosis (21/27, 83%), followed by inflammatory or neutrophil infiltrate (13/27, 48%). Specimens with evidence of pancreatitis had a similar rate of co-existing histologically confirmed vascular and cellular rejection and vascular thrombosis than those without. However, specimens demonstrating histological evidence of pancreatitis were significantly more likely to be explanted late ($>$7 days post-transplantation) than those without evidence of pancreatitis (65% (17/26) and 25% (4/16) respectively; p=0.02; Fisher's exact test).
Discussion: Pancreas transplantation has evolved as an effective treatment strategy for glycaemic control but allograft failure remains a considerable barrier. Pancreatitis appears to play an important contributing factor to this adverse sequence. It appears that transplant pancreatitis, a distinct entity from allograft rejection, may be an important feature in later failure of these grafts. Recognition of this complication may aid in successful salvage of these transplants thereby improving outcomes.

MO-067 AMYLASE AND LIPASE CONCENTRATION IN THE DRAINAGE FLUID BUT NOT IN THE SERUM INDICATE THE OCCURRENCE OF PANCREAS FISTULA FOLLOWING PANCREAS TRANSPLANTATION

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Background: Simultaneous pancreas kidney transplantation (SPK) is associated with a high postoperative morbidity with relaparotomy rates of up to 40%. As pancreas graft related complications are most common we evaluated parameters indicating the occurrence of pancreatic fistula.
Methods: From 1/04 to 1/11 53 pancreas grafts were transplanted, 51 SPK, 1 pancreas after kidney, 1 pancreas transplantation alone. The mean age was 42.2±7.6 years. All transplantations were performed using systemic-venous and enteric drainage.
Results: The incidence of clinically relevant pancreatic fistulas (PF) was 16/53 (30.2%). Eleven (68.8%) of those patients were treated conservatively by leaving the drainage in place. Five (31.2%) patients needed relaparotomy due to anastomotic leakage (n=2), pancreatitis (n=2) and acute hemorrhage (n=1). In one case the pancreas graft had to be removed.
Comparing the patients with (PF+) and without fistula (PF-) there was no significant difference in amylase or lipase serum concentration on day 1 to 7, peak-amylase (492.8±487.6 U/l versus 348.0±310.1 U/l) and peak-lipase (532.1±416.7 U/l versus 408.1±459.4 U/l). The lipase but not the amylase concentration in the drainage fluid was significantly higher in PF+ patients (3,661.4±3,474.8 U/l versus 821.8±1,293.7 U/l, p=0.006 and 1,747.3±3,346.7 U/l versus 265.3±254.9 U/l, p=0.097).
Overall pancreas graft survival was 41/53 (77.4%) after a mean observation time of 39.1 months. There was no significant difference in graft survival between the both groups (75.0% versus 78.4%).
Conclusion: There is a high incidence of PF following pancreas transplantation, but usually it can be treated conservatively and does not impair graft survival. Lipase concentrations in the drainage fluid but not amylase or lipase serum levels are significantly increased in patients with fistula.

MO-068 MYCOTIC ANEURYSMS FOLLOWING PANCREAS TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Background: Mycotic aneurysms following pancreas transplantation are rare but its clinical manifestations is dramatic and cause significant mortality.
Aim and Materials: Retrospective review of 215 consecutive pancreas transplants performed in a large centre (July 2001 to December 2010). Simultaneous Pancreas and Kidney SPK=166, Pancreas After Kidney PAK=37 and Pancreas Alone PA=12. We aimed to analyse the incidence, risk, contributing factors, treatment modalities and outcome in recipients who developed a major vessel mycotic haemorrhage following pancreas transplantation.
Results: 8 (4%) patients developed intra abdominal arterial perianastomotic mycotic infections following pancreas transplantation (SPK=6, PAK=1, PTA=1). All patients had organs transplanted from donors after brain death and no one was retransplant. 3 had bladder drained pancreas transplants and 5 were enterically drained. 7 out of 8 recipients who developed this complication died either due to mycotic infection or diabetic complication. The median time from transplant to death was 127 days (ranging from 40-1052). 2 patients died due to haemorrhagic shock caused by mycotic arterial rupture (40 and 95 days post transplant). The other 6 patients underwent pancreatectomy. The median time from transplant to pancreatectomy was 48 days (ranging from 14 to 194). 2 of these patients died within 90 days post transplant pancreatectomy. Donor and recipients demographics were not characteristic.
Summary: Perianastamotic arterial mycotic infection is a devastating complication with high mortality and morbidity in pancreas transplantation. Early and aggressive surgical approach is required for damage limitation. The number of patients in our study is small. A collaborative national or international approach with, collection of cases and root cause analysis of all intra abdominal mycotic infections may provide valuable data on management. This study highlights the stringent efforts and attention that must be paid to prevent intra-abdominal infection in pancreatic transplant recipients which can have devastating consequences.

MO-069 WHY ORGANS ARE TURNED DOWN – AN ANALYSIS OF REASONS GIVEN FOR REJECTING OFFERED PANCREATA FROM GERMANY

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Background: There is a high rate of discrepancy between offered and actually transplanted pancreata in organ allocation. Thorough analysis should shed light on the reasons for high non-utilization.
Material/Methods: We analysed the allocation protocols of all Eurotransplant-registered German whole pancreas donors offered to allocation in the period 2005-2009 (n=1769). Several reasons for rejection were analysed in detail and categorized according to their relevance for rejecting the organ for transplantation.
Results: 1113 (63%) of all offered pancreata were not transplanted. Of those, 239 pancreata were withdrawn from the allocation process following surgical inspection of the organ at the time of intended recovery. 128 were accepted, but not used due to recipient-related reasons (n=65), or because the organs were damaged or had anatomic abnormalities that precluded transplantation (n=63). In 738 cases the pancreata were offered to different centres, but repeatedly rejected and finally not transplanted. The reasons for rejecting an offer often differed between centres; a mean of 1,75 different turndown causes was given for each rejected pancreas. The most frequent reasons were “long ICU stay” (named for 176 organs), “resuscitation” (n=131), “age” (n=62) and “unfavourable lab results” (n=456).
Among the 293 organs with favourable P-PASS (< 15) and donor age (<30 years), 39% were discarded.
Discussion: The results enable better understanding of rejection reasons during the allocation process. Further studies are currently underway that attempt to analyse in detail the reasons for rejecting the offered organs, especially those with a favourable P-PASS.

Tissue injury / preservation

MO-070 LEVELS OF A CHOLANGIOCYTE-ABUNDANT microRNA IN LIVER GRAFTS PRIOR TO TRANSPLANTATION ARE PREDICTIVE FOR LONG-TERM GRAFT SURVIVAL

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Background: Initial ischemic biliary injury is a risk factor for graft survival after liver transplantation (LTx). Unfortunately, ischemic biliary injury cannot be sensitively diagnosed early after LTx by current means. MicroRNAs (miRNAs) modulate gene expression in response to tissue injury, and altered levels of hepatic miRNAs in serum can serve as sensitive and specific biomarkers for liver injury. The aim of this study is to identify high-risk liver allografts at the time of transplantation by analysis of miRNAs in graft biopsies.
Methods: Liver graft biopsies (n = 46) taken during LTx were analyzed for the expression of hepatocyte-abundant (miR-122 and miR-148a) and cholangiocyte-abundant (miR-30e and miR-296) miRNAs by quantitative real-time PCR.
Results: Expression levels of hepatocyte-abundant miRNAs were inversely correlated with the length of the graft’s warm ischemia time (WIT), with miR-148a levels being 33% lower in patients with WIT longer than 25 minutes ($P < 0.05$). Level of cholangiocyte-abundant miRNA, miR-296, was inversely correlated with the length of cold ischemia time (CIT) ($P < 0.05$), with an average of 59% lower levels in patients with CIT of more than 8 hours ($P < 0.005$). Levels of miR-296 were significantly reduced in grafts which required re-transplantation within 8 years due to biliary complications ($n = 4$, $P < 0.05$). ROC analysis showed that miR-296 tissue expression predicted the development of this type of graft loss with a sensitivity and specificity of respectively 100% and 75% (AUC > 0.80, $P < 0.05$).
Conclusion: Expression of cholangiocyte miRNA miR-296 in the liver graft during LTx is associated with graft survival after LTx, and may therefore represent a useful tool for the assessment of graft quality and long-term survival.

MO-071 HIGH BOX GROUP RELEASE IN FATTY LIVER GRAFTS PRESERVED IN IGL-1 SOLUTION: A ROLE FOR PPARgamma

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Antecedents: High mobility group box 1 protein (HMGB1), is an important inflammatory mediator involved in the pathogenesis of ischemia-reperfusion injury (IRI). Its role in fatty liver preservation was poorly understood. In this commmuncation, we evaluated the relationship of HMGB-1 with other potential factors markers implicated in the vulnerability of steatotic grafts against IRI, such as hemeoxygenase-1 and PPAR gamma, respectively.
Experimental: Steatotic and non-steatotic livers preserved in UW and IGL1 (24h; 4°C), respectively and the reperfused (2h; 37°C). HMGB1, PPARgamma and HO-1 were determined by western blot and correlated with oxidative stress, mitochondrial damage and apoptosis degree. Liver injury (AST/ALT), function (bile output, vascular resistance) and proteolysis were also evaluated.
Results: Major HMGB-1 levels were found in steatotic livers at 2 hours of reperfusion when compared to non steatotic ones. In any case, the liver HMGB1 protein levels were significantly lower in grafts preserved in IGL-1 solution than UW one ($p < 0.05$). This was concomitant with HO-1 increases which were more relevant for the steatotic grafts than non steatotic ones. However, this is not true for PPAR gamma expression which only was augmented in fatty livers. All changes in protein levels were consistent with a liver injury diminution (AST/ALT), proteolysis, as well as an ameliorated function of the grafts preserved in IGL-1 solution. Also, the oxidative (MDA) stress and mitochondrial damage (GLDH) and apoptosis were efficiently prevented by the IGL- 1 use.
Conclusions: IGL-1 solution prevented efficiently fatty liver proteolysis, as well as HMGB1 increases against IRI. The IGL-1 benefits mediated by HO-1 are due to PPAR gamma activation which explains the beneficial effects of IGL-1 on fatty liver preservation.

MO-072 PREVENTION OF ENDOPLASMIC RETICULUM STRESS BY KIDNEY GRAFT WASHOUT BEFORE TRANSPLANTATION

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Background: Ischemia reperfusion (I/R) injury remains a leading cause of acute kidney injury in both native and transplanted kidneys. This syndrome induces a variety of structural and functional damages including endoplasmic reticulum stress (ERS). As a consequence, a signal transduction cascade termed the unfolded protein response (UPR) is activated to repair protein synthesis disorder. However, when injury is excessive, the ERS causes cell death. The purpose of this study is to examine the effect of kidney graft washout with a rinse solution (RS) before transplantation on the ERS response in the rat.
Methods/Materials: 18 Wistar rats (180-250g) were randomly divided into 3 experimental groups (n=6, for each one): *Group 1:* rats were not subjected to kidney transplantation; *Group 2:* after 18 hours of preservation in cold (4°C) UW solution, kidneys were transplanted; *Group 3:* the same as group 2 but the grafts were washed-out before transplantation with RS ($CaCl_2.2H_2O$ (1.3 mM), KH_2PO4 (5 mM), NaH_2PO_4 (20 mM), $MgSO_4.7H_2O$ (5 mM), lactobionate (100 mM), rafinose (30 mM) and polyethyleneglycol-35 (5g/L) at pH 7.4). Tissue samples were collected to assess some ERS parameters: activating transcription factor-6 (ATF-6), phosphorylated and total protein Kinase RNA-like endoplasmic reticulum kinase (PERK), X-box binding protein-1 (XBP-1) and caspase-12 (Casp 12).
Results: We observed that ERS was markedly attenuated by graft rinse. A significant decrease in ATF-6, PERK and XBP-1 was observed in transplanted grafts previously washed with RS when compared to the second group. This was associated with an important reduction in Casp 12, main apoptosis inducer in the endoplasmic reticulum.
Conclusion: This work reveals that the washout of the renal grafts before transplantation contribute to disable the ERS response as well as the apoptosis.

MO-073 SUCCESSFUL TRANSPLANTATION OF RAT AND PIG AORTIC GRAFTS AFTER LONG TERM PRESERVATION IN DEHYDRATED SODIUM CHLORIDE

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Background: Infected artificial grafts are usually replaced by arterial allografts. The so far used cryopreserved or glutaraldehyde human allografts have limited longevity and are mechanically fragile. Moreover, the transplanted allogeneic arteries evoke host's immune reaction. A method for long-term preservation of arterial allografts with strong mechanical endurance and low antigenicity is desperately needed. The aim of our studies was to establish a method of successful preservation of arteries for months with unchanged morphological structure and low allogeneic reactivity.
Material/Methods: Fragments of rat aorta were preserved in anhydric NaCl powder and were stored at 4°C for 12 months and transplanted for 24 months. Fragments of pig abdominal aorta were preserved in the same way for up to 6 months and transplanted for up to 6 months.
Results: Rat aortic grafts pulsated 24 months after transplantation. H/E and trichrome staining showed preserved anatomical structure. There was not thrombosis, only some thickening of neo-intima. No differences between preserved transplanted and control syngeneic aortae stained for CD 31, CD 54, RECA-1 were observed. Electron microscopy revealed normal structure of elastin fibers, appearance of fibroblasts between elastin bundles and single endothelial-like cells. There was only slight infiltration by ED1, OX 6 and W3/13 cells around the allograft. Pig aortae preserved for 6 months remained patent, there were no aneurysms 6 months after grafting. Ultrastucture analysis did not show any significant changes compared to controls.
Conclusions: Rat and porcine aortae remained patent for 24 months and retained anatomical and molecular structure. Results of our studies suggest that preservation in pulverized NaCl could be a novel method for use of arterial allograft as av shunts and in infected ischemic areas. These observation justify clinical trials.

MO-074 CORONIN-1 DEFICIENCY CONTRIBUTES TO CARDIAC PROTECTION FROM COLD I/R INJURY IN MOUSE

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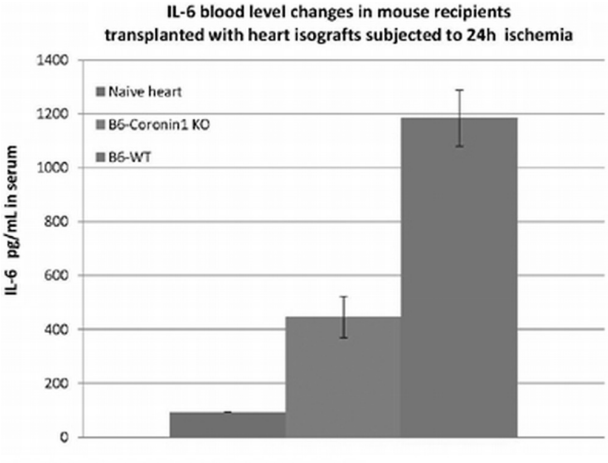
Background: Coronin-1 is a leukocyte specific protein recently proposed as a potential target in resolving inflammation. We therefore hypothesized that coronin-1 deficiency in mice could be protective against cardiac IRI through reduction of intra-myocardial inflammation.
Methods: According to our previous data, 24 hours of ischemia of mouse heart appeared still compatible with functional recovery of isografts. Hearts were harvested from CL57/B6, stored at 4°C in UW solution for 24 hrs before being heterotopically transplanted into coronin-1 KO mice or wildtype B6 mice (n=5 each). Upon revascularization, all heart isografts were blood-reperfused for 4 hrs.



Results: Measurements of tissue Myeloperoxidase (MPO) and inflammatory cytokines showed that increasing severity of heart isograft injury after 24 hrs ischemia was reduced in coronin-1 KO recipients.
1. IRI-induced increase of MPO in heart isografts was reduced by 28% in coronin-1 KO recipients, with similar Creatinine Kinase levels *vs* WT.
2. IRI-induced increase in serum IL-6 levels was reduced by about 65% in coronin-1 KO recipients ($p<0.05$; Fig1).
3. IRI-induced increase in mRNA expression of IL-6, IL-1β, IL-17F, TNFα, MCP-1 and TGFβ was reduced by 44%, 29%, 48%, 36% 35%, 10% respectively, in isografts of coronin-1 KO recipients.
4. IRI-induced infiltration of isografts by CD3+ lymphocytes and macrophages appeared similar in coronin-1 KO and WT recipients.
Conclusions: These results suggest for the first time that coronin-1 deficiency in mice could contribute to a reduction in IRI-induced inflammatory cytokines in tissues. Coronin-1 can therefore be considered as a potential target to achieve protection against IRI.

MO-075 A NEW PERSPECTIVE ON ORGAN PRESERVATION: THE PROTECTIVE EFFECTS OF BORON COMPOUNDS ON THE ISCHEMIA/REPERFUSION INJURIES

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Background: This study, is a featured prestudy to save the host and the tissue from ischemia/reperfusion injury which is an unwished result of the transplantations from cadaver organs and to increase the function of the graft organs with the addition of boron to the protective solutions.
In this study, boron compound, sodium metaborate ($NaBO_2$), was added to protective solutions and it's effects on renal perfusion pressure and the tissue oxidant and antioxidant systems were studied.
Methods/Materials: The kidneys of adult male Wistar-Albino rats were used. In the first step, the most appropriate concentration of $NaBO_2$ was determined as 50 μg/ml. In the second step, kidneys were kept in cold ischemia in the Krebs solution with or without 50mg/ml boron. After ischemia, contractile responses were obtained by phenylephrine. In the third step, contractile responses with phenylephrine were recorded. Then the second step was repeated. Besides, as an indicator of the oxidant stress, malonedialdehyde, an antioxidant glutatione, and nitric oxide levels were estimated.
Comparisons among groups were made with ANOVA followed by Mann Whitney U test, a p value of <0.05 was considered significant.
Results: Contractile responses by phenylephrine were increased in the present of $NaBO_2$. This increase was especially significant in cold ischemia group.
Moreover, $NaBO_2$ decreased malonedialdehyde and nitric oxide levels and increased glutatione levels in both cold ischemic and non-ischemic groups.
Conclusion: Increasing of the contractile responses by phenylephrine, sodium metaborate was seen as a factor that provides the continuation of the contrictile responses in the kidney vasculator especially after-ischemia. On the other hand, since $NaBO_2$ reinforces antioxidant protection and decreases oxidant stress, boron compounds might be added into preservation solutions for the protection the kidney and the other solid organs.

MO-076 THE BEST PEG FOR ORGAN PRESERVATION? A PRECLINICAL STUDY

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Background: Advances in organ preservation solutions development show that University of Wisconsin (UW), gold standard, is not the best strategy available and that polyethylene glycol (PEG such as found in SCOT, IGL-1 and Polysol) shows interesting benefits as a colloid. However doubts remains regarding which PEG provides the highest protection, and differences in solution formulations do not allow clear discrimination.
Methods: We tested similarly formulated preservation solutions containing either 15g/L or 20g/L PEG20kDa or 5, 15 and 30 g/L PEG35kDa. Performances were measured in vitro on kidney endothelial cells, ex vivo on preserved kidneys, and in vivo in a pig kidney autograft model.
Results: In vitro, all PEGs formulations provided superior preservation compared to UW in terms of cell survival, ATP production and allowing the cells to activate survival pathways early on (6h, versus 20h in UW).
Ex vivo, discrimination was possible between PEGs with slightly better tissue histology displayed in PEG20kDa preserved organs compared to either UW or PEG35kDa.
In vivo, function recovery was identical between UW and PEG35kDa groups, while PEG20kDa displayed swifter recovery. Three month follow up that PEG35kDa at 15 and 30 g/L-preserved graft had worse outcomes compared to UW, while 5g/L PEG35kDa provided identical level of fibrosis and function to UW. PEG20kDa preservation was superior to both UW and PEG35kDa in terms of function and fibrosis development, with lower activation levels of lesional pathways such as TGFb or HIF1a. PEG20kDa at 15g/L offered the highest level of protection.
Conclusion: We compared different PEG length and doses in identically formulated preservation solution, using highly reproducible models of ischemia reperfusion in transplantation. While in vitro models did not provide discriminating data, ex vivo and in vivo evaluation showed that all other parameters being equal, PEG20kDa offers a higher level of protection compared to PEG35kDa.

MO-077 ENDOTHELIAL TARGETED ANTICOAGULATION IN KIDNEY ALLOGRAFTS USING A PORCINE MACHINE PERFUSION THROMBOSIS MODEL

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Kidney transplantation is an established and successful solid organ transplant procedure. Allograft thrombosis is, however, implicated in 2-7% of early adult graft loss, and $\sim$35% in children; the pathogenesis related to preservation, recipient and donor factors with "marginal" kidneys at higher risk. The only preventative measure in place is systemic anti-coagulation, conferring bleeding risks. We have developed a porcine ex-vivo renal perfusion thrombosis model with autologous whole blood as perfusate. This model was used to test a series of novel endothelial binding hirudin-anticoagulant fusion proteins (FP). We hypothesise kidney pretreatment with FP will ameliorate deteriorations in perfusion seen in the thrombosis model. We report our preliminary results.
Methods: Fifteen kidneys were retrieved from cadaveric pigs at an abattoir, flushed with UW solution, and placed on ice (WIT=15mins, CIT=4-8h). Kidneys were then perfused on a modified Waters Medical (RM3) perfusion machine with 4°C UW solution (4h) then perfused (1.5h) with either HTK treated with FP (Protein-Test-Kidneys, PT,n=8) or unmodified HTK (Thrombosis-Controls, TC,n=7). All kidneys then underwent whole blood normothermic perfusion (6h) with perfusion parameters measured throughout.
Results: Kidneys demonstrated similar flow (29.4 vs. 26.8ml/min/100g), resistances (0.67 vs. 0.60mmHg/ml) and viable perfusion pressures (45.8 vs. 44.2mmHg);TC vs. PT kidneys respectively ($p>0.14$) during perfusion with UW solution. During perfusion with autologous normothermic blood PT kidneys demonstrated significantly less deterioration in perfusion dynamics compared to controls, with a decline in flow rates of 14.1% vs. 33.5%($p<0.03$).
Conclusion: Data demonstrates that kidney graft pre-treatment with novel anticoagulant proteins results in amelioration of deterioration in perfusion dynamics seen in ex-vivo thrombosis perfusion, with potential for development of an applicable strategy to provide local active anti-coagulant agents directly within the allograft; decrease the incidence of thrombosis, avoiding systematic anticoagulation. Work continues to delineate optimal dosage, protein pharmacokinetics, and histological outcomes.

MO-078 EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT FOR KIDNEYS FROM DONORS AFTER CIRCULATORY DEATH – DOES TEMPERATURE MATTER? A SYSTEMATIC REVIEW

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Background: Long term survival of kidneys from Donors after Circulatory Death (DCDs) and Donors after Brain Death (DBD) are comparable. However, rates of Delayed Graft Function (DGF) remain significantly higher in DCDs (uncontrolled>controlled) than in DBDs. Extracorporeal Membrane Oxygenation (ECMO) acts as a bridge between asystole and procurement thus reducing ischaemia mediated damage and DGF. This study evaluates the impact of temperature in reducing DGF in ECMO supported kidneys from DCDs.
Methods: MEDLINE, EMBASE and Cochrane databases were searched citing the MeSH terms "Extracorporeal Membrane Oxygenation" AND "Donors after Cardiac Death" (and their variants). Studies were grouped according to grades of temperature, and rates of DGF and Primary Non Function (PNF) compared.
Results: The search identified 59 articles of which 7 studies were eligible. In category II donors (2 studies, n=36), relative risks (RR) of DGF, when compared to normothermia (37°C, DGF 12.5%), was higher in moderate hypother-

mia (28-32°C, DGF 70%, RR 2.9167, p = 0.011) and profound hypothermia (DGF 75%, RR 3.5, p = 0.041). In category III donors (3 studies, n=80), RR of DGF, when compared to normothermia (DGF 8.3%), was higher at 4 °C (DGF 41.9%, RR 1.5787 p = 0.014) but similar in severe hypothermia (20-28°C, DGF 8%, RR 0.9964, p = 1). PNF was 0 in all category II and III groups. Catgeory I and IV donors (2 studies, n=320 and 34 respectively) were perfused at profound hypothermia (<20°C) only, with DGF rates of 60.9% and 85.3%, and PNF of 4.4% and 6.5% respectively.
Conclusion: Perfusion temperature significantly impacts DGF in ECMO supported kidneys. Normothermic ECMO is most beneficial in category II donors and may significantly reduce DGF related morbidity and cost.

MO-079 THE FINAL SHOWDOWN: PRECLINICAL COMPARISON BETWEEN PERFUSION MACHINES ORS Lifeport AND Waters RM3

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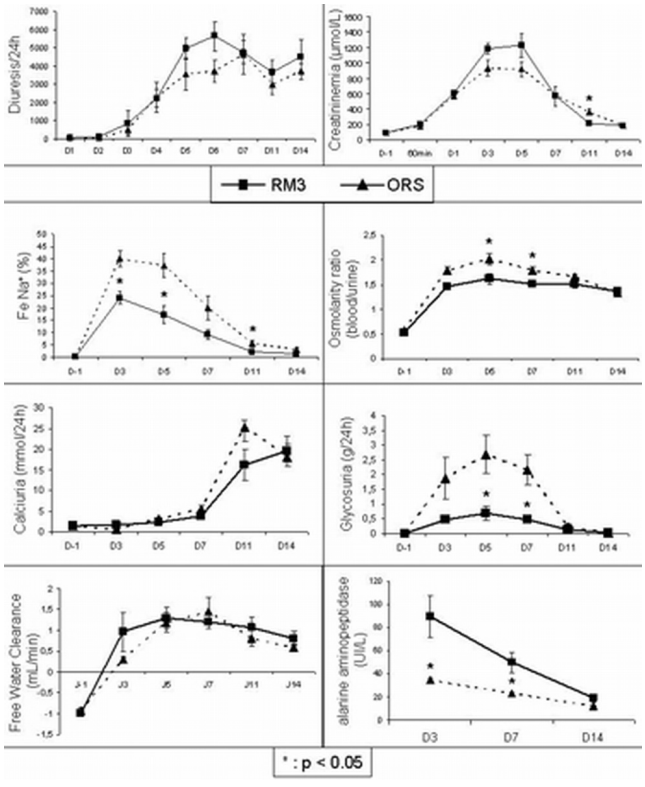
Background: Machine preservation has demonstrated clear benefits for organs in terms of reducing DGF rate and improving one year outcome. However, there is an ongoing debate about which perfusion technology provides the highest level of protection. We used a highly reproducible porcine kidney autotransplantation model to compare them.
Methods: Kidneys were subjected to 60 min warm ischemia prior to machine preservation on either the Waters RM3 (RM3 group) or the ORS Lifeport (ORS group). Perfusion parameters were identical to those used in the clinic. Pigs were followed for 2 weeks, endpoints were kidney function and urinary enzymes excretion.
Results (Fig 1): Kidney function recovery was identical between the 2 machines in terms of diuresis, creatininemia, calciuria and free water clearance. There was a slight superiority of the RM3 group compared to the ORS regarding sodium excretion, osmolarity ratio and glycosuria. However, the RM3 group displayed a higher level of urinary alanine aminoperoxydase at days 3 and 5 compared to the ORS group.



Conclusions: Our porcine autotransplantation model allows for a clear evaluation of the benefits of machine perfusion against ischemia reperfusion injury. The high reproducibility of the model permits us to state that all other parameters being equal, there were minimal differences between the two groups in terms of early recovery of function. However, these parameters are unlikely to keep their discriminating power in patients. Thus, both machines appear to perform at a similar level of quality in the first two weeks. Chronic evaluation is ongoing to evaluate the benefits of each technology on chronic inflammation and fibrosis.

Ethics, legal and psychosocial aspects of transplantation

MO-080 PRIORITY SETTING IN SWEDISH KIDNEY TRANSPLANTATION: ASSESSMENT FOR TRANSPLANT CANDIDACY AND ALLOCATION OF DECEASED DONOR KIDNEYS

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Background: Kidney transplantation is the established treatment of choice for end-stage renal disease; it increases survival, and quality of life, while being more cost effective than alternative tenements. It is, however, limited by the scarcity of kidneys. The aim of this paper was to investigate the fairness and legitimacy of the priority setting process underpinning access to kidney transplantation in Sweden using the accountability for reasonableness ethical framework, a leading paradigm in health policy. This is the first time this framework has been used to investigate the unique aspects related to kidney transplantation. To achieve this, two critical stages of the process with significant influence on access to transplantation were examined: (1) assessment for transplant candidacy, and (2) allocation of kidneys from deceased donors.
Methods: Semi-structured interviews were the main source of data collection. Fifteen Interviews were conducted with participants from all transplant centers and included transplant surgeons, nephrologists, and transplant coordinators for a comprehensive depiction of the priority setting process in kidney transplantation across Sweden. Thematic analysis was used in the analysis of interview transcripts.
Results and Discussion: Decision-making at both the assessment and allocation stages is based on clusters of factors that belong to one or other of three levels: patient, professional, and the institutional levels. The factors appeal to ethical values such as maximization of benefit, favoring the worst off, and equal treatment, which are traded off.
Conclusions: Overall, we believe that the priority setting process for kidney transplantation in Sweden can be considered fair and legitimate. However there is room for improvement. The presentation will highlight both best practices as well as areas for improvement in priority setting process for kidney transplantation in Sweden with reference to the accountability for reasonableness ethical framework.

MO-081 THE SOCIAL ORIGINS OF MORAL PERCEPTIONS AND PUBLIC POLICIES REGARDING THE BUYING, SELLING AND TRAFFICKING OF ORGANS

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Background: International norms have denounced and banned the trafficking of human organs for transplant. However, the practices of buying, selling and trafficking of organs are still widespread in different places. This paper suggests a model which emphasizes the importance of the intersection between local-particular worldviews and ideas from transnational sources in shaping the accepted domestic discourses and practices regarding the buying, selling and trafficking of organs. This paper demonstrates this model by exploring the case of Israel.
Methods/Materials: This paper is based on a multi-sited ethnography in Israel which includes: observations in fields such as courts and a parliamentary committee; in-depth, semi-structured interviews with relevant agents and stakeholders; and content analysis of various documents.
Results: The findings of this study suggest that the local moralities, discourses, practices and public policy decisions concerning organ commerce are affected by complex interactions between the following factors: fundamental moral attitudes, particularly deontological versus utilitarian approaches; the human rights discourse in its transnational as well as localized versions; deeply-rooted religious views; dominant socio-economic conceptions; and bodily perceptions. The balance between these factors explains the ways in which international ethical norms relating to organ trafficking are implemented, adapted or rejected in local settings. This paper examines how in the Israeli case, the equilibrium between these factors leads to a relative tolerance toward the buy-

ing and selling of organs amongst different stakeholders. This attitude, when in interaction with global norms and pressures, results in rather ambivalent public policies.
Conclusion: The proposed model may be useful in understanding and coping with the gap which frequently exists between the unequivocal international norms and the prevalent moralities, practices and public policies in diverse local settings regarding the buying, selling and trafficking of organs.

MO-082 INFORMED CONSENT, DECISIONAL CONFLICT, ANXIETY, AND PREPAREDNESS IN LIVING KIDNEY DONOR CANDIDATES

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Background: Psychosocial factors may undermine living kidney donor (LKD) candidates' preparedness and comprehension essential for informed consent. We assessed LKDs candidates' decisional conflict, anxiety, and preparedness for donating.
Methods: LKD candidates were surveyed by telephone after they began the second phase of donation evaluation according to standardized institutional protocols at our transplant center between July 2010-February 2011. Measures included the: Decisional Conflict Scale (DCS), Spielberger State-Trait Anxiety Inventory (STAI) short form Y-6, and the Preoperative Preparedness Scale (PPS).
Results: Forty-four LKD candidates participated in an interview (75% participation rate). The average age was 40 years, 52% were female, 71% were white, 57% were married/partnered, and 98% had completed high school. Nearly half of all candidates experienced decisional conflict regarding donating (Table 1). Candidates had moderate to high levels of anxiety (mean=9.25). Greater anxiety was associated with less certainty (r=0.42, p=0.004) or support (r=0.37, p=0.015) in decision-making. While 19% of candidates felt prepared overall to donate, 58% felt that clinicians have not spent enough time preparing them for surgery.
Conclusions: The results suggest that many LKD candidates in the early stage of evaluation are moderately uncertain and anxious about their decision to donate, and require greater preparation for donation. Future interventions are needed to facilitate candidate-clinician communication to ensure adequate informed consent.

MO-083 NEW WAYS OF DYING CREATE NEW ETHICAL CHALLENGES FOR THE SPANISH MODEL OF ORGAN DONATION

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Background: Spanish organ donation rates dropped from 34.4 in 2009 to 32 donors per million population in 2010. (Lago, M. BMJ 2011; 342: d242) This paper identifies some factors that explain this phenomenon and discusses a number of new ethical challenges the Spanish Model of organ donation will need to face as a result of new dying patterns and new ways of managing end-of-life (EOL) care of potential donors.
Methods: A descriptive and normative assessment of the Spanish 2010 rates of organ donation has been carried out.
Results: The drop in donations in Spain is related to a fall of brain deaths in the ICU. Reduction of traffic and labour accidents, improved management of cerebral infarctions and a shift in public attitudes towards EOL decision-making are playing an important role in Spanish statistics. These societal changes are likely to confront the Spanish Model to new ethical dilemmas if Spain is willing to maintain its rates in organ donation. Future ethical challenges for the Spanish Model include the following: 1. Withdrawal of life support resulting in fewer brain-dead donors may generate the need to turn to controlled donation after circulatory death, (so far rejected in Spain due to ethical and pragmatic reasons) 2. Alternatively, not withdrawing futile life support in order to maintain the possibility of brain death may introduce the temptation of discussing with families the donation options before potential donors are declared dead. This strategy may involve patient's instrumentalization, family coercion and professionals' conflicts of interest.
Conclusion: Some adjustments to traditional methods in the way families are approached for donation in Spain might be necessary. The nature of these adjustments requires ethical discussion before they are implemented.

MO-084 INTRODUCTION OF AN EARLY EDUCATIONAL PROGRAMME TO PROMOTE INFORMED DECISION MAKING REGARDING INITIAL RENAL REPLACEMENT THERAPY

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Introduction: Pre-emptive kidney transplantation offers optimal graft, patient survival, and quality of life. Currently however, over half of living donor transplants in the Netherlands are performed after dialysis. To improve early education on renal replacement therapy (RRT) options, including living donor transplantation, we initiated a multi-centre home-based education programme (van Kooij et al 2009; Rodrigue et al 2008). This abstract describes the first experiences among 5 pilot patients and recommendation for implementation.
Methods: After referral by the nephrologist, patients eligible for transplantation with an indication for RRT within 1 year are invited to participate. Participants are randomly assigned to group 1 (education) or 2 (care as usual). In group 1, patients and their social network are educated on RRT options and the impact on quality of life.
Findings: Participants appreciated the patient-centred home-based approach and the information provided. The education generated greater understanding and support for the patient and some attendees considered kidney donation. An intake interview with the patient is essential to explain the goal of the meeting and to provide support in inviting their family and friends. Further, it is important to involve nephrologists, nursing staff and educators when developing the programme content and procedures. It is a challenge to create an unified approach which complements the existing educational efforts. A website can assist communication and standardization of procedures across centres.
Recommendations: Patients as well as their social networks should be informed in a timely fashion about RRT possibilities. Close collaboration between nephrologists, nursing staff and educators is essential. Programme effectiveness will be investigated in a multi-centre randomized control trial with knowledge and communication about RRT options as primary outcomes and type of initial RRT as secondary outcome.

MO-085 LIVING KIDNEY DONATION AMONG ETHNIC MINORITIES: A DUTCH QUALITATIVE STUDY ON ATTITUDES, COMMUNICATION AND KNOWLEDGE OF KIDNEY PATIENTS

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Introduction: Living donor kidney transplantation (LDKT) has proven to be a better treatment alternative compared to deceased donor kidney transplantation, e.g. in terms of waiting time and survival rates. However, we observed a significant inequality in the number of LDKT performed between the non-European and the Dutch patients in our center. It has been suggested that such inequality relates to differences in psychosocial and cultural factors.
We set out to investigate whether attitudes, communication patterns and knowledge relate to inequalities in LDKT rates between Dutch and non-European patients.
Methods: Focus group discussions and in-depth interviews were conducted among 50 kidney patients, most of who were being treated with dialysis and were on the deceased donor waiting list. Analysis was conducted according to "grounded theory" using Atlas.ti.
Results: We found nearly all patients to be in favour of LDKT (96%). However, multiple prohibiting and interrelated factors played a role in considering LDKT. We propose a model which addresses these factors as barriers to LDKT in our non-European patients. These barriers are: 1) a perceived gap in information 2) cognitions and emotions 3) social interference 4) and non-communication with family and friends. Additionally, we found that our patients held a wel-

Abstract MO-082 – Table 1. Decisional Conflict Scores

Level of Decisional Conflict	Uncertainty Subscale N (%)	Informed Subscale N (%)	Values Clarity Subscale N (%)	Support Subscale N (%)	Effective Decision-Making Subscale* N (%)	Total Decisional Conflict Score* N (%)
Low (<25)	19 (43)	25 (57)	21 (48)	15 (34)	22 (50)	24 (55)
Medium (25-37.5)	10 (23)	10 (23)	10 (23)	15 (34)	20 (45)	10 (23)
High (>37.5)	15 (34)	9 (20)	13 (29)	14 (32)	1 (2)	9 (20)

*Lower conflict means less uncertainty. Percentages do not round to 100 due to participant refusal to answer questions in one subset (n=1).

coming attitude towards tailored education program, for instance a home-based education.
Conclusion: This study has identified modifiable factors that contributed to the ethnic disparity in our LDKT program. As these factors appear modifiable, and because patients are open to education, we argued that a home-based educational intervention suits the complexity of these factors and our patients' personal needs. We have recently developed such a home-based intervention program.

MO-086 WHICH INTERVENTIONS ARE USED BY HEALTH CARE PROFESSIONALS TO ENHANCE MEDICATION ADHERENCE IN TRANSPLANT PATIENTS? A SURVEY OF CURRENT CLINICAL PRACTICE

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Purpose: Organ transplant (Tx) requires medication intake lifelong. Non-adherence (NA), which is associated with serious complications, is prevalent among Tx recipients. Different interventions to improve patients' medication adherence can be implemented in clinical practice. This study aims are to assess which strategies Tx healthcare professionals (HCP) utilize to 1) assess patient's medication NA, and 2) enhance medication adherence (educational/cognitive, counseling/behavioral and psychological/affective interventions). Third, we assessed the perceived effectiveness of used interventions.
Methods: A 46-item questionnaire to determine adherence assessment and interventional strategies utilized by Tx HCP in daily practice was distributed to the attendants of an European meeting of transplant nurses in Germany in June 2010. Respondents not in direct clinical practice were excluded. Descriptive statistics were used to describe the practice patterns.
Results: Of 141 distributed questionnaires, 94 (67%) were returned. Eight (9%) were excluded because of no direct patient contact. The most frequently used assessment strategy in 86 HCP was questioning patients about NA during follow-up visits (61% n=52). Participants reported using on average 47% of the educational/cognitive interventions, 44% of the counselling/behavioural and 42% psychological/affective interventions listed. The most frequent interventions used were providing reading materials and training patients during inpatient recovery (70% n=68) followed by providing printed instructions (69% n=59).
Using reports from electronic monitoring devices for feedback was least frequently used. Most used combination of interventions (90% n=77). The intervention which was perceived by the HCP as the most effective was training patients during inpatient recovery how to take medications.
Conclusions: Despite evidence that shows they are less effective, educational interventions were mostly used in this sample to enhance adherence. Further, enabling HCP to deliver effective interventions that optimize adherence will require training in health behavior modification strategies.

MO-087 THE LIVING DONOR STUDY CONCEPTS AND FRAMES OF LIVING KIDNEY DONORS

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Background: Living kidney donation represents between 40-45% of renal transplantation in Queensland, Australia. The number of patients awaiting transplantation are rising and commensurate increases in individuals who volunteer or are recruited as living donors have been noted. Using transcript analysis and (*Leximancer*) text-mining software, living donor concepts and frames of their pre-donation experience and assessment are examined.
Method: Queensland Renal Transplant Service is the only renal transplant centre in Queensland and largest in Australia. Living donors are assessed within a multi-disciplinary team to determine suitability. As part of PhD research, 10 living donors representing 25% of Queensland's annual living donor cohort were consented for participation in the Living Donor Study. Preliminary interviews were conducted to determine donor understanding and knowledge of process. Audio recordings between donors, the social worker, renal physicians and surgeons were collected, transcribed and analysed.
Transcripts input into software quantitatively identified and illustrated concepts within the dialogue.
Common themes were explored.
Results: Qualitative and quantitative themes included:
– 90% of living donors derived information from the internet.
– Living donors considered donation well before assessment. Many declared that their donation decision was made before transplant centre contact.

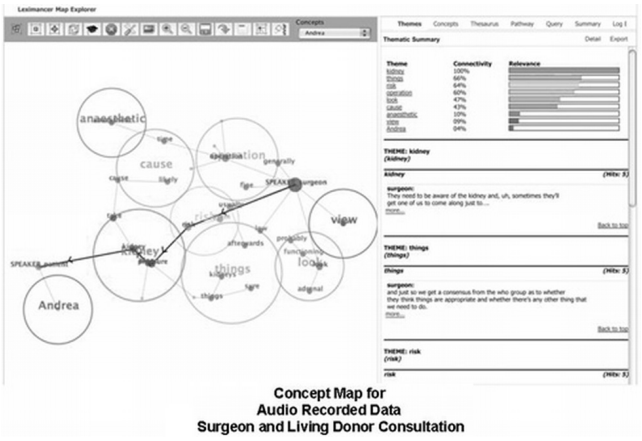

Figure 1

– Living donors hold strong beliefs and expectations of their donation experience. Elements like surgical complications or long-term risk played a lesser role in patient framing than logistical and financial concerns.
– Information received from the internet, literature or peer-to-peer reporting notably impacted their ability to hear and interpret messages conveyed during multi-disciplinary assessments.
Conclusion: The living donor's desire to donate reflects elements of "auto-coercion" [1], gift-giving and a strong sense of bond-obligation. Using common living donor frames, transplant experts can continue to identify areas requiring additional attention and clarification. This ensures donors remain suitably informed and appropriately represented within multi-disciplinary teams.
Reference:
1. Aeder, M. et al. Case Surgery 2008, 131.

MO-088 UNSPECIFIED AND SPECIFIED LIVING KIDNEY DONATION TO UNRELATED RECIPIENTS

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Background: In unspecified living kidney donation, formerly known as Good Samaritan, altruistic or anonymous donation to a stranger, the recipient is not specified by the donor. There is no emotional relationship between them and there is no material benefit for the donor.
Methods: Over the last 10 years we have been approached by 168 individuals with the intention to donate a kidney to an emotionally and genetically unrelated patient.
Results: A minority 16/168 did specify a recipient and 12 donated either directly to their intended recipient (n=10) or in kidney exchange procedures (n=2). The vast majority, 152/168 were potential unspecified living kidney donors. 57 of them have donated thus far (see table): 19 directly to the wait list and 38 in domino-paired procedures in which 46 incompatible couples participated. This has in total resulted in 103 kidney transplants: 57 in patients on the wait list and 46 in recipients of incompatible couples.

Overview

Performed	N	Total TXP	Unspecified donor	INC couple	Waitlist recipient
Doublet	31	62	31	31	31
Triplet	6	18	6	12	6
Quartet	1	4	1	3	1
TOTAL	38	84	38	46	38
Single	19	19	19	0	19
TOTAL	57	103	57	46	57

Conclusion: We conclude that most altruistic donors to emotionally and genetically unrelated patients do not specify an intended recipient. Both wait list patients and recipients of incompatible couples profit from unspecified living kidney donation.

MO-089 ORGAN TRANSPLANTATION BETWEEN ALTRUISM AND JURIDICAL REGULATION

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In order to investigate the ways in which the Romanian population relates to the problematic of organ transplantation, we built a 42-item questionnaire with the following dimensions: attitude towards organ transplantation, perceived legitimacy of organ donating and recovery in relation to the type of consent, personal willingness (behavioral intention) to donate one's organs in various situations, information sources about the topic, as well as social and demographic information. The instrument was administered to 250 participants, of various ages and social categories from three districts belonging to different Romanian geographic regions.

Regarding the manner in which Romanians would express their consent for organ donation, results suggest a few formulas of consent which would prove acceptable for the population. 69% of participants agree with the necessity of a legal frame of manifesting their option, and the same percent approve the introduction of a donor's card. On the other hand, 54% believe that consent should be expressed in front of one's family doctor, suggesting that organ donation is perceived as having a stronger medical than juridical connotation. Although most respondents identified themselves as Christians, only 54% believe that organ donation could be an altruist gesture and the expression of one's love for his/her kind, 15% affirming that it's only sometimes that it can express feelings defined as values and virtues in the Christian ethics, and only 55% would donate their organs to a family member while in a state of clinical death. Also, results indicate various significant associations between the dimensions under scrutiny, in relationship to some demographic variables as well. Generally, they suggest the insufficiency of a medical discourse which would support the necessity of organ donation, and the importance of psycho-social and religious issues in this respect.