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Kidney I

RO-001

MMF AND RITUXIMAB HAD GREAT BENEFICIAL EFFECTS ON IMPROVING ABO INCOMPATIBLE KIDNEY TRANSPLANTATION

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Purpose: The purpose of this study was to compare the prognosis and the titers of anti-donor blood group antibody between different immunosuppressant protocols in ABO incompatible kidney transplantation (ABOiKTx).
Method: One hundred twenty two recipients, who had ABOiKTx between March 1989 and January 2011, were enrolled in this study. 62 patients received azathioprine (AZA) with splenectomy (Spx) (AZA group), and 31 received mycophenolate mofetil (MMF) with Spx (MMF group), and 29 patients received MMF and rituximab (RIT) without splenectomy (RIT group). Graft survival and status of anti-donor blood group antibody were compared among three groups.
Results: Overall graft survival rates were 90.3%, 100% and 95.7% at one year, 88.7%, 100% and 89.7 at three years, 78.6%, 96.6% and 89.7% at five years for AZA, MMF and RIT, respectively. MMF significantly improved graft survival (p=0.014).

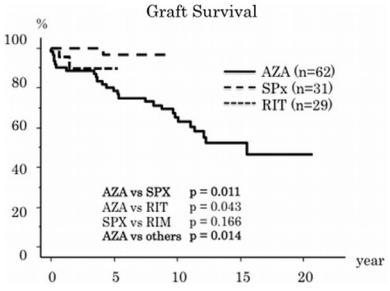

Figure 1

Anti-donor blood group antibodies were suppressed after Tx in all groups, compared to those before Tx Furthermore, RIT significantly suppressed anti-donor blood group antibody at one, two and four weeks and one month after Tx despite of non-Spx, compared to other two groups.

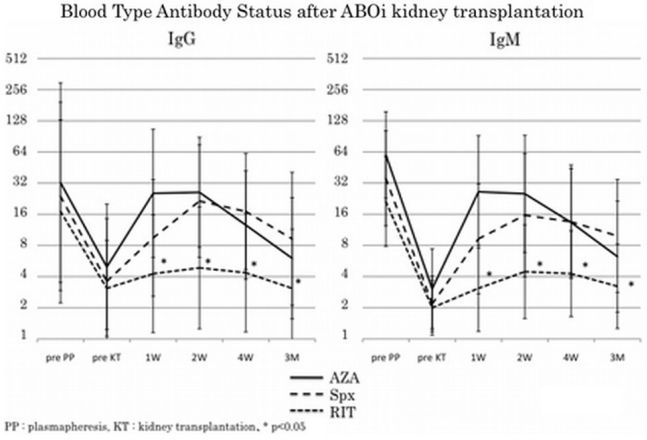

Figure 2

Conclusion: MMF and RIT had beneficial effects on improving outcomes of ABOi KTx. MMF improved graft survival, and RIT inhibited donor specific anti-donor blood group antibody production after ABOi KTx.

RO-002

INITIAL RESISTANCE INDEX EVALUATED BY DOPPLER SONOGRAPHY AND THE RISK OF DEATH IN KIDNEY TRANSPLANT RECIPIENTS – A PAIRED KIDNEY ANALYSIS

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Background: Doppler flow spectrum, quantified in the segmental arteries of the graft early after kidney transplantation (KTx), reflects mostly the exacerbation of interstitial oedema, but numerous donor- and recipient-dependent factors may also influence the values of resistance parameters. To evaluate the prognostic significance of initial resistance index (RI) values for patients' outcome, we analysed the mortality of kidney graft recipients, transplanted with organs harvested from the same donor, in whom the initial RI values substantially differed.
Material and methods: Doppler sonography was performed in 689 consecutive recipients between 2 and 3 days after KTx. Patients with primary graft nonfunction were excluded. We identified 128 pairs (256 patients) who received their kidney grafts from the same donor and their initial RI values differed of more than 0.1.
Results: Mean follow-up after KTx was 57±38 months. The groups of paired patients with higher RI (0.88±0.07) and lower RI (0.72±0.08) did not differ significantly in respect to their age, BMI, HLA class I and II mismatches, cold ischemia time, and the duration of dialysis therapy prior to transplant. Survival analysis revealed significantly higher mortality among patients with higher initial RI values (14.1% *vs.* 6.3%, log rank=0.026). The frequency of the cardiovascular deaths (myocardial infarction, stroke, aneurysm) in the higher RI group was of borderline significancy (7.03% *vs.* 1.56%, p=0.06).
Conclusion: Higher RI value estimated during the first days after KTx is associated with the increased risk of death in the long-term observation.

RO-003

SHOULD KIDNEY TRANSPLANT RECIPIENTS RECEIVE CHILDREN AFTER TRANSPLANTATION?

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Introduction: Most young women with ESRD appeared to be infertile. One of the benefits of kidney transplantation is restored fertility and a chance to become pregnant. In this study we focus on the long-term outcomes of renal transplant recipients after pregnancy.
Methods: Medical records of all women $\leq$ 45 years transplanted in the Erasmus Medical Centre between January 1971 and December 2010 were studied. Pregnancies $\geq$ 6 months were included in our study.
Results: 450 female patients were included. 7% (30/450) gave birth to one or more children after kidney transplantation. These 30 women gave birth to 42 live births and one stillborn. Women had a median age of 30 years when they gave birth (range 19 - 40). The median transplant-to-delivery interval was 7 years (range 1- 17 years). 28% (12/43) of these pregnancies were complicated by preeclampsia and two developed HELLP syndrome. One patient lost her graft in the first year after delivery due to chronic transplant failure. Five females died during our follow-up. One female died within a year after delivery of a cerebro-vascular event, the others died 3, 5, 17 and 18 years after their delivery. Causes of dead in these women were cardio- or cerebro-vascular events and one B-cell non-Hodgekin lymphoma. Twenty years after transplantation 78% of the patients who delivered a baby is still alive. Of the 420 transplanted women of 45 years or younger who did not gave birth to a child, only 40% lived 20 years or more after their transplantation.
Discussion: Only a small proportion of women delivered a baby after transplantation. One third of these pregnancies were complicated with preeclampsia. Although patient survival was excellent in the group of women who delivered a baby, still 13% died before their children reached adulthood.

RO-004

RENAL OUTCOMES AFTER LIVE KIDNEY TRANSPLANTATION FROM ELDERLY DONORS ARE ACCEPTABLE

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Introduction and Objectives: The recent outcome studies suggest that the

overall survival and risk of end-stage renal disease in renal transplant donors are similar to the general population. Although the long-term safety is justified, the outcome study focused on the elderly donors themselves is lacking. This study was conducted to elucidate the residual renal function of the donors and the graft function of the recipients in the longitudinal observation.
Methods: Eighty-eight pairs of donor and recipient were eligible for the study, and 20 of the 88 (22.7%) were donated from elderly donors over than 65 years old. Functional parameters were compared between younger and elderly donors, between recipients with and without diabetes, and their combinations. The median follow-up period was 35.5 months.
Results: Perioperative characteristics did not significantly differ among groups. Percent estimated glomerular filtration rate (eGFR) of its pre-donation value in the younger donors improved up to 13%, whereas the elderly donors remained unchanged below 2% until three years post-donation. The graft function of the recipients with diabetes did not show uniform results, and the combination of elderly donor and diabetic recipient showed poorer graft function in the three years post-transplantation: the average creatinine value over than 2.5mg/dl.
Conclusions: The tolerable difference in recovery of renal function following kidney donation was noted according to age. Low GFR itself does not necessarily indicate a bad prognosis unless it is accompanied by risk of progression such as albuminuria and hypertension. Therefore, elderly donors need careful evaluation before kidney donation to confirm that they are competent as donors. The future evaluation based on a larger donor series may provide a conclusion for the continued use of kidneys from elderly donors, but the combination of elderly donor and diabetic recipient should be avoided.

RO-005 INFLAMMATION AND PRO-FIBROSIS IN BIOPSIES FROM DECEASED BRAIN DEAD DONORS AND LIVING KIDNEY DONORS: ASSOCIATIONS WITH POST-TRANSPLANT RENAL FUNCTION

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Background: Kidneys retrieved from living donors provide better function and a longer half-life after transplantation than kidneys from deceased brain death donors (DBD). In this study, we evaluated whether the presence of pro-inflammatory and pre-fibrotic changes in renal biopsies of DBD and living donor (LD) kidneys prior to transplantation are correlated with post-transplant function and outcome.
Methods: We evaluated 38 DBD and 72 LD kidney donors. GFR (^{125}I-iothalamate) and ERPF (^{131}I-hippuran) were measured pre-donation in LD and 3 months and 1 year post-transplantation in recipients. Biopsies were taken at the end of cold storage. Sections were immunohistochemically stained for inflammation (macrophages; anti-CD68) and pre-fibrosis (α-smooth muscle actin (α-SMA)). Macrophages were manually counted in the interstitium; interstitial α-SMA was quantified using computerized morphometry. The number of interstitial macrophages and the extent of interstitial α-SMA were corrected for biopsy surface area.
Results: Kidneys from DBD show approximately two-fold increased pre-existing damage compared to LD. In recipients of DBD kidneys, short and long term renal function is impaired compared with LD recipients. Interestingly, in LD kidneys, interstitial pre-fibrosis was positively correlated to donor age and MAP, and negatively to pre-donation GFR and ERPF (R 0.24, -0.32 and -0.37 respectively, all $p<0.05$), as well as recipient short term ERPF (R-0.31, $p<0.01$). In kidneys of DBD donors, the number of macrophages correlated negatively to short term recipient GFR (R -0.37, $p<0.05$).
Conclusion: Renal biopsies of DBD have more inflammatory and pre-fibrotic changes compared with biopsies of LD kidney donors. This pre-existing renal damage is associated with inferior early renal graft function and outcome at one year post transplant. Evaluation of donor biopsies may therefore be of value for the choice of renoprotective therapy following transplantation.

Donor characteristics and recipient short term and 1 year outcome

	Living Donors	Heart Beating Deceased Donors	p
Donor (n=110), N (% female)	72 (44)	38 (72)	<0.01
Age (year)	52±10	50±12	0.25
MAP (mmHg)	94±8	–	–
GFR (ml/min)	121±25	–	–
ERPF (ml/min)	445±88	–	–
FF (%)	27±3	–	–
Interstitial α-SMA	1.9±2.5	4.5±4.5	<0.01
Interstitial Macrophages	0.09±0.06	0.15±0.09	<0.01
Recipient short term (n=110), N (% female)	72 (43)	38 (60)	0.16
Age (year)	46±14	56±11	<0.01
MAP (mmHg)	104±12	108±11	0.10
GFR (ml/min)	62±18	50±16	<0.01
ERPF (ml/min)	244±62	194±55	<0.01
FF (%)	27±5	27±5	0.38
Recipient 1 year (n=93), N (% female)	65 (42)	28 (61)	
MAP (mmHg)	106±13	107±15	0.90
GFR (ml/min)	69±36	51±21	<0.01
ERPF (ml/min)	230±75	185±63	<0.01
FF (%)	35±5	27±5	0.43

Values represent mean ± SD.

RO-006 CIRCULATING AST, H-FABP, AND NGAL ARE EARLY AND ACCURATE BIOMARKERS OF GRAFT INJURY AND DYSFUNCTION IN A PRECLINICAL MODEL OF KIDNEY TRANSPLANTATION

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Background: Injury endured by kidney grafts early post-transplant determines their outcome. No biomarker able to quantify this injury has been validated. Creatinine (clearance) is a poor surrogate of tissue injury. Use of urinary biomarkers is limited by graft-anuria or persistent native kidney diuresis. We investigated circulating biomarkers in a porcine kidney transplant model.
Methods: Minimally injured grafts (n=6) were cold stored (18h) and autotransplanted. Moderately (n=6) and severely injured grafts (n=7) were exposed to 30 min or 60 min warm ischemia, cold stored (18h) and autotransplanted. Four biomarkers [aspartate transaminase (AST), heart-type fatty acid binding protein (H-FABP), neutrophil gelatinase-associated lipocalin (NGAL), N-acetyl-β-glucosaminidase (NAG)] were measured post-transplant and compared with creatinine (clearance) and histology.
Results: Diuresis was delayed in moderately [2.5d (2-3)] and severely injured grafts [4d (4-5)] vs. minimally injured grafts (p=0.0003). Creatinine peaked later than AST, H-FABP, and NGAL [4d (3-5) vs. 3h (3-6), 6h (6-24), 2d (1-3), respectively] and only differentiated minimally from severely injured grafts. Peak AST, H-FABP distinguished all injury grades. NGAL discriminated increasing initial graft injury 2d post-transplant. Peak AST, H-FABP, and NGAL correlated with peak creatinine [Pearson's coefficients: 0.70 (p=0.001), 0.85 ($p<0.0001$), 0.80 ($p<0.0001$)]. NAG was not different between groups. Decreased clearance accounted for a small percentage of the H-FABP, NGAL increase. Histology was not different among transplanted groups.
Conclusion: Plasma AST, H-FABP and NGAL reflect the severity of initial kidney graft injury and predict graft dysfunction earlier and more accurately than creatinine (clearance) and histology. They represent promising tools to improve patient care after kidney transplantation.

RO-007 OESOPHAGEAL DOPPLER MONITORING OF HAEMODYNAMIC CHANGES DURING LIVE DONOR KIDNEY TRANSPLANTATION

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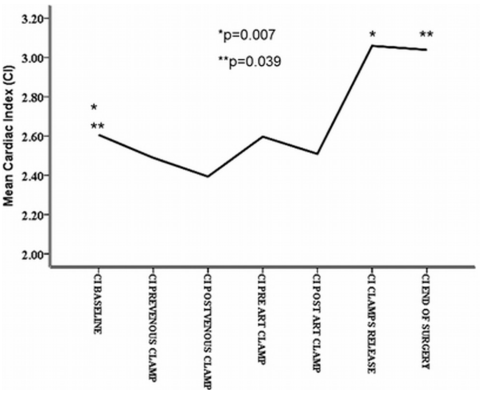
Background: Haemodynamic changes may occur during kidney transplantation (KT), where intraoperative fluid management is crucial to renal perfusion. Moreover, new, less invasive haemodynamic monitoring tools are increasingly replacing traditional intravascular monitoring. In this study we used oesophageal Doppler (OD) in live donor kidney transplantation (LDKT) recipients, to test its feasibility and safety profile and monitor any acute haemodynamic changes.
Methods: We consecutively monitored with OD 65 LDKT recipients under a general anaesthetic standardised protocol. Data and trends derived from OD guided intraoperative fluid management.
Results: There were no perioperative, OD probe-related complications. No significant changes in monitored haemodynamic parameters occurred post venous- or prior to arterial clamping. After reperfusion, a significant increase in both cardiac output (CO) and cardiac index (CI) compared to baseline (2-tailed T-test, p=0.004 for CO and p=0.007 for CI) were observed. These changes were still significant at the end of surgery (p=0.017 for CO and p=0.039 for CI). Similar changes were observed in stroke volume (SV) (p=0.034 and p=0.018) and peak velocity (PV) (p=0.006 and p=0.002) at clamps release and at the end of surgery compared to baseline, respectively. There was no significant effect of gender, hypertension, β-blocker use, age, mode of dialysis and presence of polycystic kidney disease on the mentioned parameters. However, there was a significant difference in CO between pre-emptive and haemodialysis groups at clamps release compared to baseline (p=0.032).



Conclusion: In this study, OD was safely used for haemodynamic monitoring during LDKT. At reperfusion, there was a significant increase in cardiac performance parameters; this was still significant at the end of surgery. Further studies are needed to ascertain whether the transplanted kidney plays a role in this phenomenon, whether this change occurs in cadaveric KT as well and whether it is permanent in nature.

RO-008 EXPANSION OF THE KIDNEY DONOR POOL BY USING CARDIAC DEATH DONORS WITH PROLONGED TIME TO CARDIORESPIRATORY ARREST

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Donation after Cardiac Death (DCD) is an increasingly important source of kidney transplants, but because of concerns of ischaemic injury during the agonal phase, many centres abandon donation if cardiorespiratory arrest has not occurred within one hour of controlled withdrawal of life-supporting treatment (WLST). We report the impact on donor numbers and transplant function using instead a minimum “cut-off” time of four hours.
The agonal phase of 173 potential DCD donors was characterised according to the presence or absence of: acidaemia; lactic acidosis; prolonged (>30 minutes) hypotension, hypoxia or oliguria, and the impact of these characteristics on three and twelve-month transplant outcome evaluated by multivariable regression analysis.
Of the 117 referrals who became donors, 27 (23.1%) arrested more than one hour after WLST. Longer agonal-phase times were associated with greater donor instability, but surprisingly neither agonal-phase instability nor its duration influenced transplant outcome. In contrast, three and twelve month eGFR in the 190 transplanted kidneys was influenced independently by donor age, and 3-month eGFR by cold ischaemic time.
DCD kidney numbers are increased by 30%, without compromising transplant outcome, by lengthening the minimum waiting time after WLST from one to four hours.

RO-009 COST ANALYSIS OF RENAL REPLACEMENT THERAPY BY TRANSPLANT IN A SYSTEM OF BUNDLED PAYMENT OF DIALYSIS

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Renal replacement therapies (RRT) for patients with end stage renal failure represent a high burden on European countries health care budget.
Our purpose was to report and compare the costs of RRT by haemodialysis (HD) or peritoneal dialysis (PD) and renal transplant (RT) after introduction of a bundled payment system of dialysis.
We analyzed average annual cost of RT in a public national health system hospital - surgical/anaesthesiologist team and material, costs of induction therapy and hospital stay, diagnostic exams (DE), unitary cost of post transplant office visits (including DE). Maintenance immunossupression as well as antiviral prophylaxis was evaluated in 90 patients with an average RT time of 365±111,8 days.
Annual cost of HD or PD was estimated by bundled payment established in Dispatch n.19109/2010 published in December 27th of Portuguese DiárioRepública, 2nd series – N.° 249-537,25 €/week.

Average costs of RT (euros)

	Average costs (€)
Initial admission	38182,67
Office visits (unitary)	204,52
Average monthly medication (first semester / second semester	506,4 / 441,6

Average number of office visits in the first year was 26 and from the second year forward 6.
Total first year cost or RT is 49174,27 € and from the second year forth 543,86 €/month. Dialysis costs 28033,71 €/year, that is 2336,14 €/month.
Break-even point for costs is at 2 years and from there on RT is less expensive.
With an average graft life of 10 years, RT saves 172426,05 €/patient.
RT confers better survival than RRT by dialysis with lower costs to Portuguese health system.Development of strategies to increase RT including optimization of live donor organs areneaded.

RO-010 EXPANDING THE ENVELOPE: OLDER AGE AND ITS IMPACT ON PERIOPERATIVE AND LONG-TERM OUTCOMES FOLLOWING LIVING-DONOR NEPHRECTOMY

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Introduction: High demand for live-donor kidneys, coupled with national trends towards an increasingly elderly population, make it important to consider the expansion of the donor pool to include older donors. Controversy arises from the higher incidence of co-morbidity and concerns with advancing age and greater risk of post-operative complications. This study aims to delineate whether older donors face a greater risk of perioperative and long-term complications with nephrectomy.
Methods: Data from 386 living-donor nephrectomies, utilizing the “mini-open” technique, were collected over five years at one of the United Kingdom’s largest renal transplant units. Donors were stratified by age into 3 groups (18-50, 60-64, >65) with 65 donors being >60 years of age. Extensive post-donation metabolic and renal function data, collected at 6-12 monthly intervals over a 5-year follow-up period, were analysed and compared to pre-operative data. Perioperative endpoints and surgical complications were also reported.
Results: Older age was shown not to impact significantly on intra-operative endpoints including mean operative time, and estimated blood loss. Post-operative complication rates were also not significantly different, with pneumonia and wound infection constituting the commonest complications across the age ranges. Long-term follow-up showed renal function and propensity towards hypertension, cardiovascular events and diabetes not to be significantly different between groups. Major surgical complications, readmission, and re-operation rates were comparably low across age categories.
Conclusion: Our unit’s experience is that donor nephrectomy is safe in elderly donors and does not result in higher rates of major perioperative complications. Long-term follow-up data show good outcomes for donors of older age. It would be prudent to re-evaluate age’s position as an exclusion criterion if we are to successfully expand the organ pool.

RO-011 CHIMERISM OF BLOOD TYPE ANTIGENS ON THE VESSEL ENDOTHELIUM IN PATIENTS WITH ANTIBODY-MEDIATED REJECTION

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Background;: Few studies have investigated the changes in the blood type antigenicities of the transplanted organs after renal transplantation.
Material and methods;: The subjects included six recipients without any rejections, six recipients with T cell mediated rejection (TMR) and six recipients with antibody mediated rejection (AMR), who had received allografts from living donors at our institution between 2000 and 2010. We examined, by immunohistochemical assay, the changes in expression of the blood-type antigens on the transplanted kidneys after ABO-incompatible kidney transplantation (A to B or B to A).
Results;: All six recipients with AMR due to the presence of donor specific antibodies (DSA) demonstrated complete establishment of endothelium chimerism, while reciepients without any rejection or with TMR did not do it. Morover, The titer for anti-blood type prior to transplantation was not associated with chimerism, however, the presence of DSA was srongly associated with chimerism.
Conclusion;: Establishment of antigenic chimerism on the graft endothelium could be one of the hallmarks of the immunological reaction associated with antibody-mediated rejection.

RO-012 RECURRENCE OF FSGS AMONG ADULT TRANSPLANT RECIPIENTS: A LONGITUDENAL STUDY

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Focal segmental glomerular sclerosis (FSGS) is known to recur after kidney transplantation mainly among the young patient population. We sought to determine the recurrence rate among our adult population and evaluate the efficacy of plasmapheresis (PP) treatment.
Material and Methods: We reviewed our database to identify adult patients ($>$ 18 y) who underwent kidney transplantation between 1/2000- 12/2009 with diagnosis of FSGS based on biopsy results prior to transplant (n=31). Diagnosis of recurrence was based on hitology and electron microscopy of biopsies associated with proteinuria $>$ 3 gr/24hr. We analyzed rate and interval to recurrence and the efficacy of treatment by PP as determined by reduction of proteinuria $<$ 500mg/24 hr. Overall patient and graft survival rates were also calculated.
Results: Of the 31 patients in the study, eight (25.8%) fulfilled criteria for recurrent FSGS. Recurrence rate was 35.7% in deceased- donor recipients and 17.6% in living-donor recipients (p=ns). In six patients recurrence occurred within the first 2-weeks after transplant. Seven patients underwent PP (1-156 sessions) and three received also Mabtera. Four patients had a complete response and maintain long-term good graft function. Three patients failed treatment and two of them lost their graft at 652 and 1099 days post-transplant. Another 61 y/o patient who showed a partial response following Mabtera died of pneumonia six weeks after the injection. The overall patient and graft survival rates were 93.5% and 83.8%, respectively.
Conclusions: Recurrent FSGS occurs in about 25% of adult kidney transplant recipients. Plasmapheresis is an effective treatment in about half of the patients. Mabtera should be carefully considered in the non-responders.

RO-013 KILLER-CELL IMMUNOGLOBULIN-LIKE RECEPTOR GENES AND LIGANDS IN KIDNEY TRANSPLANT

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Background: Innate immunity represents a new frontier in the field of transplantation. It is the first line of defense and involves a number of different mechanisms in response to attack by foreign agents, such as natural killer (NK) cells, neutrophils and macrophages, the complement system, cytokines and other soluble proteins. NK cells in particular have a role as a bridge between the innate and adaptive immunity. Killer-cell immunoglobulin-like receptors (KIRs) belong to a polymorphic family of activating and inhibitory receptors expressed on the surface of NK cells and recognize human leukocyte antigen (HLA) class I ligands. The aim of this study was to investigate if KIR/HLA compatibility affects renal allograft survival on the long term.
Methods: We studied 113 patients who received kidney transplant between 1999 and 2005. Eighty-six kidney recipients had a stable renal function, while 26 showed a decrease by 20% of renal function after 5 years from transplantation. Patients in the two groups were matched for sex, donor and recipient age, time on dialysis, cold ischemia time and therapy. All patients were typed using HLA and KIR SSO genotyping test. For all patients we analyzed the presence of single KIR genes and haplotypes in relation to the decrease of renal function by 20%. Finally we examined all the possible matches/mismatches between KIR genes and known HLA ligands in donor/recipient pairs.
Results: The presence of KIR2DS3 showed a significant association with a worse serum creatinine and MDRD trend (p=0.02). The analysis of the gene in the presence of its ligand HLA-C1 on donor DNA showed a worse serum creatinine and MDRD trend (p=0.03).
Conclusions: Our data suggest that KIR genes may influence long-term graft outcome after renal transplantation.

RO-014 EXTENDING THE ANATOMICAL BARRIERS TO A RIGHT SIDED LAPAROSCOPIC LIVE DONOR NEPHRECTOMY (LLDN)

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Background: Right sided LLDN is now widely accepted when complex anatomy is encountered on the left side. The aim of this study was to analyse the effects of right sided complex LLDN; defined as the bifurcation of a right renal artery behind the inferior vena cava (IVC).
Methods: This retrospective review involved 59 cases out of 303 LLDN in a single centre from 01/2001 to04/2010 [Group 1: simple (n=48); Group 2: complex (n=11)]. The impact of donor right kidney on operative time, warm ischaemia, graft function, and donor and recipient complications were analysed.
Results: There was no difference in donor age, recipient age, operative time, warm ischaemia between groups. There was no difference in eGFR or serum creatinine (μmol/L) at 1 week, 3 and 6 months.[eGFR (6/12): 49$\pm$15 vs. 60$\pm$9; P=0.087 and Serum creatinine (6/12): 159$\pm$116 vs.120$\pm$25; P=0.356]. No cases of DGF were reported and none of the grafts encountered vascular thrombosis. The cumulative eGFR at 6/12 was 51$\pm$15. Two cases of conversion to open surgery were reported in Group 1.
In the complex group with a retro-caval dissection, 8 kidneys were retrieved with a single artery while 3 had multiple vessels (2$\times$2 vessels and 1$\times$3 vessels) (anastomotic time: 26$\pm$6 minutes)
Conclusion: Complex vasculature in right sided donation should not be considered as a contraindication, as kidneys procured had an excellent function compared with single vasculature with no increase in conversion or vasculature thrombosis.

RO-014A IMPACT OF HEPATITIS B AND HEPATITIS C VIRUSES ON GRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Chronic liver disease due to hepatitis B (HBV) and hepatitis C (HCV) viruses infections has emerged as a major concern in kidney transplant recipients in the last decay. Our aim was to evaluate the impact of HBV and HCV on kidney transplant recipients.
Patients and Methods: We retrospectively compared the outcome among 413 kidney transplant recipients who had been operated upon between February 1998 and October 2003 in three centers in Egypt.The patients have been divided into three groups; group I: 36 patients who were HBsAg and received lameviodin and/or adivovir till they all become HBsAg negative. Group II: 216 patients who were HCV antibodies positive. Group III: 161 patients who were all negative for both markers.
Results: Between all groups, no significant differences were observed regarding acute allograft rejection rate at 12 months (mean GFR in 12 months in the HBV group was 72.3 ml/min.; in the HCV group was 73.6 ml/min. and in the third group was 75.1 ml/min.); or at 5 years post transplantation (mean glomeriolar filtration rate in 5 years in the hepatitis B group was 56.4 ml/min.; in the hepatitis C group was 57.2 ml/min. and in the non-B non-C group was 59.1 ml/min.).No significant progressive elevation in ALT, AST or serum bilirubin were noted during the 5-years observation period between all groups.
Conclusion: HBV or HCV are not contraindications in kidney transplantation. Kidney functions and liver functions at 5 years post transplantation did not differ significantly between hepatitis B virus patients; hepatitis C virus patients and non-B non-C virus kidney transplant recipients.

Kidney II

RO-015 LONG TERM FOLLOW-UP OF OVERWEIGHT AND OBESE LIVING KIDNEY DONORS

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Background: Due to donor organ shortage, living kidney donor selection has become more liberal with acceptation of overweight and obese donors. We found that early after donation overweight donors have a higher risk for impaired GFR and lower renal reserve. Whether this results in a worse long term outcome is unknown.
Methods/Materials: We evaluated short term and 5 year outcome in 100 donors who donated at our center. All had GFR (^{125}I-iothalamate) and ERPF (^{131}I-hippuran) measured 4 months prior, and 2 months and 5.4$\pm$1.1 year after donation. Filtration fraction was calculated as [GFR/ERPF*100]. Delta GFR from "single kidney status" was calculated as [GFR long term (pre-donation GFR/2)]. For analysis, donors were divided according a pre-donation Body Mass Index (BMI) $\leq$ 25 or $>$ 25 kg/m^2.
Results: Results are shown in the table, with a break-up for pre-donation BMI. Values represent mean$\pm$SD or median [IQR]. Of the 64 donors with a BMI $>$25, 18 (28%) had a BMI $>$ 30. Overweight donors were older, and had higher mean arterial pressure (MAP) and FF pre-donation and higher FF long term post-donation. On regression analysis ΔGFR to long term was associated negatively with pre-donation age (R^2 0.15, p$<$0.01), but not with BMI.

Long term blood pressure was positively related to age and BMI (R^2 0.08 and 0.04, $p<0.05$).

		BMI ≤ 25	BMI > 25	p
Pre-Unx	N (% female)	36 (61)	64 (56)	–
	Age (years)	46±13	51±9	0.03
	BMI (kg/m^2)	23±2	29±3	by default
	MAP (mmHg)	88±9	92±8	0.04
	GFR (ml/min)	112±15	117±21	NS
	ERPF (ml/min)	433±80	429±74	NS
	FF (%)	26±2	27±3	0.05
Early post-Unx	MAP (mmHg)	91±9	94±9	NS
	GFR (ml/min)	73±12	75±13	NS
	ERPF (ml/min)	289±58	288±44	NS
	FF (%)	26±3	26±3	NS
Long term post-Unx	MAP (mmHg)	91±9	95±9	NS
	GFR (ml/min)	80±15	83±14	NS
	ERPF (ml/min)	282±61	278±48	NS
	FF (%)	28±5	30±4	0.03
	ΔGFR (ml/min)	24±10	24±8	NS
	UPE (g/24h)	0.1 [0.0–0.2]	0.1 [0.0–0.2]	NS

Unx: Nephrectomy; UPE: urinary protein exretion; NS: not significant.

Conclusion: In conclusion, in this small population overweight donors have higher blood pressure and FF prior and higher FF long term post-donation. However, long term course of renal function is equal to lean donors and not determined by BMI. We want to emphasize that although these overweight donors perform well, close long term monitoring and adequate blood pressure treatment remains necessary.

RO-016 NEUROCOGNITIVE OUTCOMES ONE YEAR AFTER KIDNEY TRANSPLANTATION (KTx): A LONGITUDINAL CONTROLLED STUDY

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Objective: Dialyzed patients with end-stage renal disease (ESRD) often present with impaired neuropsychological performance. However, it remains unclear, whether cognitive deficits associated with ESRD and/or dialysis are reversible after successful KTx. The aim of this study was to longitudinally compare the cognitive performance of adequately dialyzed patients before and after successful KTx.
Methods: Twenty-seven dialyzed patients - 17 on hemodialysis (HD), 10 on peritoneal dialysis (PD) who subsequently received kidney transplant, 18 dialyzed patients (12 on HD, 6 on PD) still waiting on transplant wait list, and 30 matched controls were the participants for this study. All individuals completed a battery of standardized neuropsychological tests on the following longitudinal schedule: baseline, 8 and 20 months.
Results: Overall, the results of a series of repeated measures ANOVA, with significance level set at $p<0.002$, demonstrated improvement in neuropsychological performance of patients who underwent KTx. Significant improvement on the measures of psychomotor speed/executive function and abstract reasoning was already seen shortly after KTx and these effects were still present during the second follow-up. Additionally during the 2nd follow-up in transplanted patients a marked improvement on most memory tests was noted. Cognitive performance of dialyzed patients being still on waiting list was often below that of individuals without renal disease and declined slowly over time.
Conclusions: 1. KTx leads to a significant improvement and relatively long-lasting of cognitive performance of previously dialyzed patients. 2. The cognitive performance of patients remaining on adequate dialysis tends to decline over a time period of approximately 20 months.

RO-017 ELEVATED TROPONIN I AND NT-proBNP AT TIME OF RENAL TRANSPLANTATION MAY PREDICT AN ACUTE CARDIAC EVENT IN THE EARLY POST-OPERATIVE PHASE

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Background: Elderly patients with end-stage renal disease accepted for kidney transplantation often carry a high cardiovascular (CV) co-morbidity. Despite thorough pre-transplant cardiovascular work-up some patients experience major adverse cardiac event (MACE) in the early post-operative period. Improved pre-transplant selection process is warranted.
Methods: We performed a retrospective, single center study and identified all patients with early post operative cardiac infarction from January 1st 2008 to December 31st 2009. Each index patient was matched with four control patients with respect to known pre-transplant cardio-vascular risk factors. Blood samples collected on the day of admittance for transplantation were analyzed for the following cardiac biomarkers: Troponin I, Troponin T and NT-proBNP.
Results: During the given time-period 559 adult kidney transplantations were performed at our center. Seven patients (6 males/1 female) developed MACE. Four died. Seven patients, mean age 69 (60-75) and 28 controls, mean age 67 (59-81) were thus included in this pilot study. At time of transplantation median (interquartile range) Troponin I and NT-proBNP in recipients whom developed post-operative infarction were significantly higher compared to controls (Troponin I: 31.9 (26.3-37.9) ng/L vs 13.6 (9.4-21.2) ng/L, p=0.035 and NT-proBNP 751 (492-2592) pmol/L vs. 49 (34-60) pmol/L, p=0.013). Troponin T did not show a statistically significant difference between groups.
Conclusion: Elevated Troponin I and NT-proBNP at time of transplantation may represent a useful pre-operative biochemical marker identifying patients at risk of developing MACE. Routine use may aid the clinician in selecting kidney recipients for transplantation.

RO-018 DETECTION OF RENAL SCARS BY TRANSPLANT RENAL ULTRASOUNDS AND DMSA SCANS AFTER URINARY TRACT INFECTIONS IN PEDIATRIC RENAL TRANSPLLANT RECIPIENTS

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Aims: To study the clinical features and compare the accuracy of transplant renal ultrasound (TRUS) and dimercaptosuccinic-acid (DMSA) scans in the detection of scars following urinary tract infection (UTI) in paediatric renal transplant recipients (RTR).
Methods: Clinical notes of RTR who underwent TRUS and DMSA following UTI were reviewed for presence of bladder dysfunction, clinical presentation and episodes of culture positive UTI. The presence or absence of cortical thinning on TRUS and the severity of scarring (focal or multiple) detected on DMSA was noted.
Results: 44 RTR, with age at RTR between 1.5 to 16.6 (median 6.3) years were recruited. 25 (57%) patients had bladder abnormalities. 11 (25%) patients required hospital admission for intravenous antibiotics with 33 (75%) culture positive UTI with single or multiple pathogens. Only 12 (27%) patients had afebrile UTI and 59% of these had hostile bladders who had statistically higher incidence of renal scarring 17 (68%) vs 7 (36%) with normal bladders; p = 0.04). TRUS were performed in all children during or after UTI episode. Abnormal DMSA scans were noted in 27 (61%) patients, of whom 17 (63%) had multiple and 10 (37%) had focal defects. TRUS could delineate only 3 (12%) of the 27 patients who had a defect on DMSA. DMSA is considered the gold-standard in detecting renal scarring and the calculated sensitivity of TRUS in this study was only 11%.
Conclusion: UTI commonly occur in paediatric RTR with hostile bladders. Prompt treatment of UTI is required for RTR to prevent transplant renal scarring and preserve renal allograft function. TRUS is easily available but has a low sensitivity when compared to DMSA scans in detecting areas of scarring in transplant kidneys in paediatric RTR following UTI.

RO-019 SIROLIMUS THERAPY EXACERBATES NEW ONSET DIABETES MELLITUS AFTER RENAL TRANSPLANTATION: A LONG TERM ANALYSIS OF VARIOUS TREATMENT REGIMENS

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Objective: This retrospective analysis evaluated the impacts of sirolimus (SRL), cyclosporine (CsA) and steroids (S) on the occurrence, treatment and complications of new onset diabetes after transplant (NODAT).
Methods: We compared four groups: Group 1, SRL treated plus full exposures CsA/S (n=118); Group 2, full exposure CsA/S/no SRL ± antiproliferative drug (n=141); Group 3, SRL plus reduced CsA exposure/S (n=212) or no SRL/full exposure CsA/S ± antiproliferative drug, Group 4 (n=43). Uni- and multivariate analyzes were used.
Results: NODAT rates reflected the level of CsA exposure; at ten years 54% vs 30% for Group 1 vs 2 (p=0.0001); whereas at five years 30% vs 21% for Group 3 vs Group 4 (p=0.3); 81% of overall cases were detected within 1 year. The lower NODAT rate in Group 3 reflected a benefit of reduced CsA exposure (p=0.02; HR=1.006). Group 1 vs 3 showed higher CsA (p=0.0001) and lower SRL concentrations (p=0.016). CsA exposure closely correlating with NODAT

among Group 1 (p=0.0001) was the major difference between Groups 1 and 3 (p=0.04; HR=0.97). Differences in steroid treatment did not play a significant role in NODAT. Comparing Group 1 to 2, SRL was an independent risk factor for NODAT (p=0.004; HR=3.5).
Conclusion: This analysis based on a 10 year single center experience, revealed SRL to be an etiologic agent for NODAT with interactive effects with concomitant CsA treatment.

RO-020 SERUM ERYTHROPOIETIN LEVEL AND MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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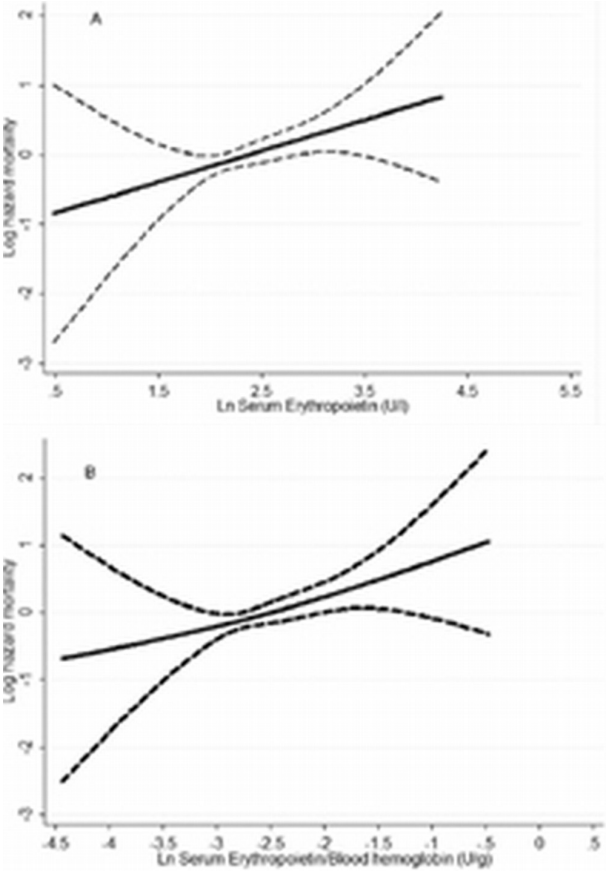
Background: Post-transplant anemia is frequently reported in kidney transplant recipients and is associated with worse patient survival. Similarly to high erythropoesis stimulating agent requirements, resistance to endogenous erythropoietin may be associated with worse clinical outcomes in patients with end stage renal disease.
Methods: We collected socio-demographic, clinical, medical and transplant history and laboratory data at baseline in 886 prevalent kidney transplant recipients. A solid-phase chemiluminescent immunometric assay was used to measure serum erythropoietin. Cox proportional hazards regression was employed to model the association between baseline serum erythropoietin levels and all-cause mortality risk.
Results: During the median 39 months follow-up, 99 subjects died. The mortality rate was significantly higher in patients with higher erythropoietin levels (crude mortality rate [95%CI] in the highest to lowest erythropoietin tertiles were 51.7 [38.6–69.3], 35.5 [25-50] and 24.0 [15.8-36.4] per 1,000 patient-years, respectively (p=0.008)). In unadjusted and also in adjusted Cox models each SD higher serum erythropoietin level significantly predicted all-cause mortality (HR and 95%CI): $HR_{1\ SD\ increase}$ 1.22 (1.12-1.33) and 1.28 (1.02-1.62), respectively. In adjusted Cox models each SD higher serum erythropoietin/blood hemoglobin ratio also significantly predicted all-cause mortality: $HR_{1\ SD\ increase}$ 1.32 (1.05-1.67). The association of serum erythropoietin level (A) and serum erythropoietin level/blood hemoglobin ratio (B) with mortality was monotonously up-going when modeled as a continous variable and using fractional polynomials and cubic splines.
Conclusions: In this sample of stable prevalent kidney transplant recipients, higher serum erythropoietin levels were associated with increased mortality.



RO-021 INFLUENCE OF VIRAL REPLICATION AT THE TIME OF RENAL TRANSPLANTATION ON THE LONG-TERM OUTCOME OF PATIENTS WITH POSITIVE SEROLOGY FOR HEPATITIS C VIRUS

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Background: Seropositivity for hepatitis C virus (HCV) results in lower patient and graft survival after renal transplantation (RT). However, the influence of viral replication at the time of transplantation on long-term outcome remains to be determined.
Methods/Materials: This was a retrospective study conducted in 4 Spanish hospitals. Data were collected for all patients with RT from 1997-2006 (excluding combined), HCV+ (ELISA), and negative viremia at the RT (by PCR, spontaneous or after antiviral treatment) (NEG group). For each NEG patient enrolled, data from the two patients with RT nearest in time, HCV+ and positive viremia (POS group) were also collected. Patient and graft survival were analyzed using Cox regression models.
Results: A total of 41 patients in the NEG group [mean age (SD) 46 (12) years, 54% women] and 78 in the POS group [age 47 (13), 47% women], mean time since transplantation of 6.8 (3.4) and 6.4 (3.4) years, respectively, were included. The POS group patients had a higher incidence of chronic liver disease (56% vs 24%, p=0.0009) and cytolysis (38% vs 7%, p=0.0003), and worse renal function [serum creatinine 3.0 (2.7) vs 1.9 (1.6) mg/dl, p=0.032, glomerular filtration rate 44 (22) vs 57 (28) ml/min, p=0.075]. Active viral replication at the time of RT and dialysis in the first week remained as independent predictors of lower graft survival (death censored): HR 3.11 (95%CI 1.34-7.19, p=0.009) and HR 3.13 (95%CI 1.53-6.37, p=0.002). The main independent predictors of death were recipient age (HR 1.04, 95%CI 1.01-1.07, p=0.012) and diabetes mellitus (HR 3.00, 95%CI 1.45-6.21, p=0.003).
Conclusion: Active viral replication at the time of transplantation is an independent risk factor for graft failure in patients with positive serology for HCV virus.

RO-022 THE ROLE OF NEUTROPENIA, CMV INFECTION AND MMF DOSE REDUCTION IN ACUTE KIDNEY GRAFT REJECTION

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Background: Cytomegalovirus (CMV) infection, neutropenia occurence and mycophenolate (MMF) dose reduction are linked with an increased risk of acute kidney graft rejection. The aim of this retrospective study was to evaluate the linking of acute rejection episodes with MMF dose reduction succeding neutropenia of anti-CMV prophylactic therapy with gancyclovir or valgancyclovir and/or CMV infection in renal transplant patients.
Methods: 161 patients transplanted from January 2005 till December 2010, who received anti-CD25 antibodies induction, MMF, calcineurin inhibitor and steroids, were retrospectively analysed for the incidence of neutropenia (leucocyte count $<4.0\times10^6$/mL), CMV viremia (number of virus copies/mL detected by polymerase chain reaction), MMF dose modification, granulocyte colony-stimulating factor (G-CSF) therapy and rejection episodes.
Results: Neutropenia was experienced in 47 (29.2%)patients It was associated with CMV viremia ($p<0.0001$)but not with CMV prophylactic therapy. MMF dose was reduced due to neutropenia in 32 patients (69.6%). Acute rejection occured in 7 (15.2%) neutropenic patients after MMF dose reduction. The average reduction of MMF dose in these patients was 31% from the starting dose. All neutropenic patients with rejection had CMV infection, 57% of them before rejection. There was a positive but statistically nonsignificant correlation between MMF reduction, CMV infection and rejection (p = 0.06). G-CSF was

used in 10 severely neutropenic patients. No significant correlation was found between G-CSF use and occurence of acute rejection.
Conclusion: CMV infection was important cause of neutropenia, that resulted in MMF dose reduction and consequently increased rate of acute graft rejection. G-CSF therapy could possibly be an alternative therapeutic approach in neutropenic patients, that enables the maintenance of optimal therapeutic dose of MMF and possibly prevents acute rejection episode.

RO-023 SELECTIVE PROLIFERATION OF HUMAN CD28NULL EFFECTOR MEMORY T-CELLS INDUCED BY PRIMARY RENAL TUBULAR EPITHELAILC CELLS

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Introduction: Tubulitis, the hallmark of rejection, is a consequence of T-cell alloreactivity. Memory T-cell repertoire can result in clinically relevant allospecific effector responses. The current prescribed immunosuppressive agents exert relatively less impact on memory T-cells. We hypothesize that tubular epithelial cells (TEC) of the donor stimulate recipient memory T-cells.
Materials and Methods: TEC cell lines (n=3) were cultured from cortex tissue of human donor kidneys obtained during transplantation. For TEC/PBMC coculture, allogeneic PBMCs were cultured with irradiated TEC. Transwell experiments were performed in parallel. Proliferation was analyzed by 3H-thymidine incorporation and flow cytometry using PKH at day 7. PBMCs were analyzed for CD3, CD4, CD8, CD28, CD45RO and CCR7. In addition, the effect of tacrolimus (20 ng/ml) was studied on the TEC/PBMC coculture.
Results: TEC/PBMC coculture resulted in a proliferative response. In simultaneously performed transwell experiments no proliferation was found. MACS isolated memory and not naïve $CD4^+$ T-cells grew upon stimulation by TECs. Flow cytometric analysis of the coculture experiments showed that 6% of the $CD4^+$ T-cells and 10% of the $CD8^+$ T-cells proliferated, which was again the result of memory $CD45RO^+$ T-cells. Of the proliferating $CD4^+$ T-cells, 23% expressed the central memory phenotype, 22% effector memory (EM) and 48% effector memory RA. Of the proliferating $CD8^+$ T-cells 89% was EM. In addition, 70% of the proliferating population was CD28null, a phenotype associated with known high proinflammatory and tissue-damaging properties. While tacrolimus (20ng/ml) inhibited the mixed lymphocyte reaction by 80%, the TEC/PBMC coculture was suppressed by 20% only.
Conclusion: Primary renal tubular epithelial cells induce a selective cell-cell contact dependent proliferation of human CD28null effector memory T-cells. This TEC induced memory T-cell response is, to a great extent, resistant for inhibition by tacrolimus.

RO-024 CMV INFECTION MAY BE AN INDEPENDENT RISK AFFECTING LONG-TERM ALLOGRAFT FUNCTION

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Introduction: Cytomegalovirus (CMV) infection has been reported as a potential risk factor for allograft prognosis in renal transplantation. This study aims to examine the impact of CMV infection on renal graft function and histological changes in pediatric renal transplant recipients.
Methods: Fifty-nine renal transplant recipients were recruited in this study. To detect subclinical CMV infection, an antigenemia test (pp65 antigen) was done every week until 2 months, and every 2 weeks thereafter. Prophylactic oral gancyclovir was not given in all patients. Sequential protocol biopsies of the renal allograft were performed at 4 month, 1, 2 and 3 years after transplantation. Biopsy specimens were examined according to Banff 2003 criteria. Estimated GFR (eGFR) at the time of protocol biopsy was calculated by Schwartz formula. All cases were divided into two groups (CMV-positive group and CMV-negative group) by CMV infection within the first 100 days posttrasplant. Histological findings and eGFR were investigated in both groups at 4 month, 1, 2 and 3years after transplantation.
Results: Twenty-one (35.6%) of 59 patients had CMV Infection at 46.3 (24-93) days posttransplant. Protocol biopsy studies revealed that subclinical acute rejection (SAR) was found in 23.8%, 38.1%, and 33.3% in CMV-positive group, while 13.5%, 29.7%, and 37.8% in CMV-negative group at 4 month, 1, and 3 years after transplantation. SAR was more prevalent in CMV-positive group at 4-month and 1-year biopsy. Moreover, eGFR in CMV-positive group was significantly lower than that in CMV-negative group at 4 month, 1 and 3 years after transplantation, although there was no significant difference in the frequency of SAR after 2nd year biopsy.
Conclusion: CMV infection was associated with the occurrence of SAR in the early phase posttransplant. Furthermore, it may be an independent risk affecting long-term allograft function.

Comparison of eGFR between CMV-positive group and CMV-negative group

	CMV-positive group	CMV-negative group	p
eGFR at 4month-Bx (mL/min)	64.0±22.4	76.7±19.1	0.026
eGFR at 1year-Bx (mL/min)	61.0±20.6	72.7±20.6	0.041
eGFR at 2year-Bx (mL/min)	59.0±16.5	67.8±17.6	0.067
eGFR at 3year-Bx (mL/min)	53.8±19.6	65.6±16.8	0.019

Bx, biopsy.

RO-025 VARIATIONS IN DURATION OF MACHINE PERFUSION AND OTHER PARAMETERS MAY AFFECT GRAFT FUNCTION IN NON HEART-BEATING RENAL TRANSPLANTATION

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Background: Hypothermic machine perfusion (MP) has been used to prepare kidneys pre-transplantation. Evidence suggests that the incidence of delayed graft function (DGF) can be reduced with MP in Non Heart-Beating Donor (NHBD) kidneys. Little data is available regarding optimum perfusion times and parameters with relation to patient outcome.
Methods: MP data from NHBD renal transplants performed over an 18 month period (n=36) was analysed retrospectively at a single-centre. The Lifeport system was used in all cases and routine protocol for immunosuppression of recipients was applied (Alemtuzumab, Tacrolimus, Mycophenolate). Variables collated included duration of MP (used to divide cohorts), dynamic resistance and flow rate. Graft function was assessed by Serum Creatinine (Cr) at days 0 to 7 and 30. Incidence of functional DGF (<10% drop in Cr on 3 consecutive days within week one post- operatively) was recorded. Biopsy results were also noted. Subject end points were at day 30.
Results: Patient outcomes were most favourable in the 5-10 hr group, with the greatest percentage decrease in Cr (72.4%) and lowest incidence of fDGF (55%). A greater percentage reduction in resistance was also noted in this group (53.5%). Smaller reductions in both Creatinine and resistance, and a higher incidence of fDGF was noted in MP under 5 hours and between 10 and 15 hours.
Conclusion: Our results, though limited by sample size suggest that there may be an optimum duration for MP correlating to improved recipient graft function. This may be associated with greater reductions in machine-measured resistance. More detailed analysis is planned in order to characterise these findings further.

RO-026 OBESITY AND VASCULAR ANOMALIES IN RENAL TRANSPLANTATION – EFFECTS ON GRAFT OUTCOME?

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Background: Obesity lacks established best practice within the transplant community. Increasingly, patients with raised body mass index (BMI) are being accepted for transplantation. Outcomes are suboptimal but reports have refuted this with graft survival better than initially accepted. Multiple vessels are also known to increase risk of adverse outcome. We aimed to stratify raised BMI risk and establish the cumulative outcome risk of obesity and multiple vessels.
Methods: Patients undergoing renal transplantation over a 67 month period (Jan 2004 to July 2009) were analysed using graft survival, 3 month and 1 year Creatinine as primary endpoints. Secondary endpoints included wound infections, lymphocoeles and urological complications. Sub-group analysis was performed on patients with multiple vessels.
Results: 576 patients (M = 328; F = 248; Live = 228; Cadaveric = 289; NHBD = 59; aberrant anatomy =166; mean age = 44.3±0.6) underwent renal transplantation with a mean BMI of 26.5±0.2 (<20: 37 patients; 20-25: 208 patients; 25-30: 200 patients; 30-35: 105 patients; >35: 26 patients) Graft survival was 91%, best in the BMI 25-30 group (92.5%) and worst in the highest BMI group (80%). Aberrant anatomy resulted in graft survival of 83%, worst in the BMI>30 group (71%; $p<0.0001$) In surviving grafts, Creatinines at 3 months or 1 year were equivalent. Increased BMI also resulted in increased wound infections (15% compared to 8% respectively; $p<0.01$) with aberrant anatomy patients having a 19% rate (p=0.03.)
Conclusion: In an era of increasing donor organ scarcity, utilitarian decisions are required to optimise outcomes. Decisions with regards to undertaking transplantation in patients with raised BMI combined with vascular anomalies are required to prevent sub-optimal outcomes. Patients with raised BMI should preferentially receive the anatomically "normal" kidney from the donor pair.

RO-027 OPTIMIZATION OF CARDIAC PRELOAD USING OESOPHAGEAL DOPPLER MONITORING (ODM) AND ITS EFFECTS ON EARLY GRAFT FUNCTION FOLLOWING RENAL TRANSPLANTATION

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Background: Optimal volume maintenance is essential to prevent acute renal failure during major surgery and to ensure graft function after renal transplantation. We report the use of ODM to optimize flow related haemodynamic variables during peri-operative management of renal transplantation.
Methods: 21 consecutive patients undergoing renal transplantation were analysed with an OD probe in addition to central-venous-pressure (CVP) and blood-pressure (BP). The aim was to maintain a descending aortic corrected flow time (FTc) of $\geq$ 375 ms
Results: The patient group included the following demographics; age 48±11, BMI 25±4, Hb 11.2±1.8, M:F 12:9, Hypertension 16, while all received Methyl prednisolone 500mg and were from ASA III. The FTc at start (S) of operation was 370±27, reperfusion (R) 379±37 and end of surgery (E) 405±89 which resulted in a significant improvement of the cardiac-output (CO) [S (5.6±1.5); R (6.5±1.9); E (7.3±2) (p=0.016)]. The CVP [S (9±3); R (13±2); E (13±3)] and systolic BP [S (100±17); R (111±16; E (121±18)] also significantly improved.
The patient median stay was 9 days, while none developed delayed-graft-function (DGF) or pulmonary oedema. The eGFR on day 11 was 58±18 compared to a pre-op of 9.8±4 and similarly the serum creatinine was 124±54 compared to 602±253.
Conclusions: Oesophageal Doppler monitoring can be used to non-invasively optimise the cardiac pre-load and thus quantifies a randomised controlled study to assess its effects with just CVP and BP peri-operative monitoring during renal transplantation.

RO-028 ALTERED CARDIAC HIGH ENERGY PHOSPHATE METABOLISM IN ESRD PATIENTS BEING ASSESSED FOR RENAL TRANSPLANTATION

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Background: Premature cardiovascular (CV) death is the commonest cause of death in waitlisted and renal transplants recipients and associated with uraemic cardiomyopathy (comprising of left ventricular hypertrophy (LVH), systolic dysfunction (LVSD) and LV dilation). High energy phosphate (HEP) metabolism, quantified using phosphorus magnetic resonance spectroscopy, is reduced in patients with diabetes and heart failure. We compared resting HEP metabolism between transplant wait listed patients and hypertensive LVH patients with normal renal function and assessed associations of HEP levels with abnormalities of uraemic cardiomyopathy.
Methods: 53 end stage renal disease (ESRD) and 30 hypertensive patients with LVH and normal renal function (LVH only) underwent cardiac MRI and phosphorus magnetic resonance spectroscopy of their LV. Left ventricular dimensions were measured and corrected for body surface area. PCr:ATP ratios were calculated from 31 P-MR spectra obtained from the left ventricle. No spectra were obtained from areas of reduced/absent LV motion.
Results: There were no significant differences in age, LV mass, chamber sizes and ejection fraction between patient groups. PCr: ATP was significantly higher in LVH patient compared to ESRD patients (1.6 SD 0.4 vs, 1.3 SD 0.5 respectively; p=0.007). In the ESRD group, PCr:ATP was significantly lower in patients with LV systolic dysfunction (n=10; no LVSD 2.0 SD 0.5vs LVSD 1.2 SD 0.2; p=0.05) and LV dilation (n=16; no LV Dilation 1.79 SD 0.4 vs LV Dilation 0.98 SD 0.8; p=0.01). LVH was not associated with significant difference in PCr: ATP.
Conclusion: Despite similar myocardial mass, ESRD patients have lower HEP metabolism compared to LVH patients. Lower PCr:ATP ratio, indicating reduced myocardial metabolic function, may predict risk of peri-operative or post renal transplantation CV events.

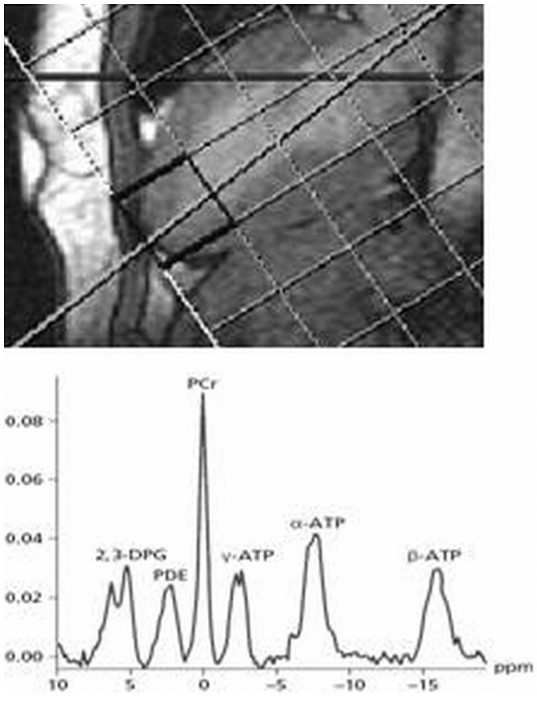

Figure 1. Acquisition of 31P-MR spectra.

RO-029 COMPENSATORY RENAL HYPERTROPHY FOLLOWING LAPAROSCOPIC LIVE KIDNEY DONATION: NO REDUCTION COMPARED WITH OPEN TECHNIQUES

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Introduction: Compensatory renal hypertrophy (CRH) is the ability of the kidney to increase its GFR in response to renal mass loss. Assumptions of its average magnitude are in-built to most guidelines regarding suitability to be a live kidney donor. Laparoscopic donor nephrectomy (LDN) has now overtaken open surgical techniques (ODN) as the procedure of choice for live kidney donation but this procedure entails additional potential stresses to the kidney in the form of extreme position, pneumoperitoneum etc. Our study investigated whethter these processes affect the magnitude of CRH observed.
Methods: Between Jan. 2005 and Oct. 2010, 152 patients underwent donor nephrectomy. From June 2009, donors were offered hand-assisted LDN. Clinical and biochemical data were obtained from a prospectively collected electronic database, (SERPR), supplemented by clinical record review. All donors underwent measured isotope GFR. Using this data it is possible to quantify the level of CRH as a percentage of original function using the following formula:
GFR = Pre-op Isotope GFR x (Serum Cr (pre op)/serum Cr (post op)) as well by eGFR comparison.
The effects of LDN versus ODN on magnitude of CRH were assessed by univariate analysis and in a multivariate model with other key independent variables (e.g. sex, age, BMI etc.)
Results: Of 152 patients, 20 had LDN and 132 underwent ODN. Median age of LDN was 46 and ODN was 45.5 years. Mean pre op isotope GFR was equivalent 89.5 ml/min/1.73m^2 LDN v 97 ml/min/1.73m^2 ODN.
Direct comparison of LDN and ODN shows that at 3 months following the procedure the results are equivalent 74% vs 75% of baseline. (p=0.497 T-test).
Discussion: Early results suggest that LDN is associated with equivalent levels of CRH to open techniques. This should reassure clinicians that GFR thresholds for donation, developed in ODN, are valid for LDN.

Liver I

RO-030 CADAVERIC LEFT LIVER REDUCED OR SPLIT LIVER TRANSPLANTATION

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The lack of size-matched cadaveric livers for transplanting (LTx) paediatric recipients has led to the development of liver splitting/reduction. By transecting the liver through the main hepatic fissure, a left lobe (segments I to IV) is obtained, providing grafts of small/medium size. The technical and surgical challenges were analised focusing on graft loss, vascular and biliary complications. We performed a retrospective outcome analysis of our cadaveric left lobe (LL) LTx.

Donor data assessement included brain death, macroscopic liver appearance, 5 ICU days, stable hemodynamics and liver function tests < twice normal. The liver division technique was performed using Kelly forceps crush clamping, one centimetre to the right of Cantlie's line after retrograde cholecystectomy. No cholangiogram was performed on the bench and segment I was usually removed. Biliary anastomosis was performed as duct-to-duct (with or without T-Tube insertion) or Roux-en-Y hepatico-jejunostomy.
From 1989 to 2010, 161 LL LTx were performed. Tables 1 and 2 show donor and recipient characteristics. 2 patients were lost in follow up, 59 died and 74 grafts failed.

Table 1. Donor characteristics

Gender	Female / Male	61 (38.1%) / 99 (61.9%)
Age (years)		20 (1–74)
ICU days		2 (1–14)
Inotropes	Yes / No	107 (66.9%) / 53 (33.1%)
Cause of death	ICB	58 (36.3%)
	HBI	13 (8.1%)
	NT	59 (36.1%)
	Others	14 (8.8%)
BMI		19.7 (9–29.7)
Na+ (mmol/L)		148 (129–175)
AST (IU/L)		38 (8–612)
BIL (umol/L)		10 (2–63)
Liver macroscopical assessment	Optimal	8 (5%)
	Non optimal	135 (84.4%)
	N/A	17 (10.6%)

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	92 (57.5%) / 68 (42.5%)
Age (years)		7 (0–64)
Age group	Adult / Paed	25 (15.6%) / 135 (84.4%)
Disease	Toxic	10 (6.3%)
	Viral	6 (3.8%)
	Autoimmune	3 (1.9%)
	Neoplasm	6 (3.8%)
	Congenital cholestatic	43 (26.9%)
	Other	55 (34.3%)
	N/A	37 (23.1%)
Presentation	ALF / CLD	48 (30%) / 112 (70%)
CP	A	29 (18.1%)
	B	55 (34.4%)
MELD Score		19 (7–64)
CIT (hours)		11.7 (2.4–21)
GRWR		3.2 (1.3–6.7)
Post AST Peak (IU/L)		832 (286–3741)
Day 5 INR		1.83 (0.9–15)
Day 5 BIL (umol/L)		117 (14–616)

ALF: Acute Liver Failure; CLD: Chronic Liver Disease; CP: Child Pugh; 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).

Patient and graft actuarial survival at 3 months, 1, 5 years were 82.3%, 74%, 66.6% and 75.9%, 65.7%, 59%. Complications included 13 (8.1%) primary non function, 11 (7.2%) arterial thrombosis, 9 (5.6%) biliary complications, of which 5 (3.1%) were bile leaks.
Cadaveric LL LTx is a relatively uncommon operation. Outcome after living donor and full split right/left has been less successful than left lateral segments and right lobes. Our experience shows that LL cadaveric grafts can be used successfully but the incidence of complications resulting in graft loss is higher than with whole livers. Biliary complications were less common reflecting the use of the intact common hepatic for hepatico-jejunostomy.

RO-031 SPLIT LIVER TRANSPLANTATION WITH EXTENDED RIGHT GRAFTS. SINGLE CENTER MATCHED-PAIR OUTCOME ANALYSIS

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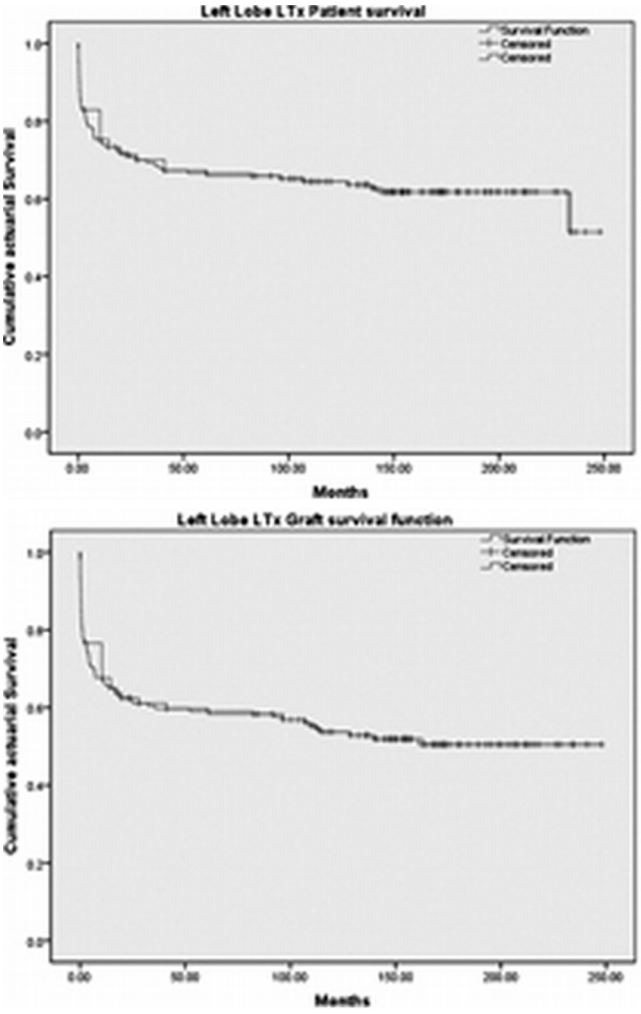
Objective: Scepticism remains about the use of extended right (ER) split graft or adult liver transplantation (LT). We compared the outcome after transplantation of the ER liver lobe with whole liver transplantation (WLT) using a matched pair analysis.
Methods: Between November 1996 and December 2009, 44 ER LT were matched with 44 WLT. Matching criteria were: 1) indication for transplantation, 2) United Network for Organ Sharing (UNOS) status, 3) recipient Model for End Stage Liver Disease (MELD), 4) recipient age, 5) donor age, 6) cold ischemic time and 7)year of transplantation. All splitting procedure were performed in situ and in all cases celiac axis stayed on the left. The outcome was analyzed retrospectively.
Results: Median follow up was 72 months (range: 1-156). Actuarial 1 and 5 years patient and graft survival after ER LT were 89%/84% and 84%/81% versus 93%/90% after WLT. ER LT is not associated with an increased risk of vascular complications (p=0.5, HR=1.5, IC 95%: 0.43-5.00). Number of artery complications were significantly higher if an interposition graft was used (p=0.05). In spite of ER graft seems to be a risk factor for biliary complications (p=0.04; HR 3.00, IC 95%: 1.9-8.63), the higher incidence of these between split liver grafts, 30% vs 11% in WLT, didn't reach statistically significance (p=0.06). We did not observe significant differences between the groups in term of short term and long term morbidity.
Conclusion: ER LT provides a safe and efficient procedure in adult patients. In attempt to decrease the incidence of hepatic artery thrombosis an increasing collaboration among transplant teams about where to maintain celiac trunk, is advisable.



Abstract RO-030 – Figure

RO-032 OUTCOME AFTER LIVER TRANSPLANTATION USING DONATION AFTER CARDIAC DEATH DONORS: A SINGLE-CENTER EXPERIENCE

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Introduction: Donation after Cardiac Death (DCD) donors are increasingly used to expand the donor pool for Liver Transplantation (LTx) but are considered -based on multi-center data- a risk factor for poorer graft survival. We reviewed short/long-term outcome after DCD-LTx at our center.

Patients&Methods: Between 2003-2010, 30 DCD-LTx were performed (6% of all LTx). Donor demographics, LTx indications, post-LTx peak transaminase (AST),%biliary complications and%graft rejection were analyzed. Patient/graft survival were analyzed and compared to outcome using Donation after Brain Death (DBD) donors.
Results: Mean donor age was 47.3 yr (range:13-69). Warm ischemia time (stop ventilation to cold perfusion) was 23±11'. Cold ischemia time was 415±104'. Recipient age was 58 yr (range:24-71). Mean labMELD was 17 (range:8-31). LTx indications were cirrhosis related to post-ethyl (13), HCV (4), NASH (3), unknown (4), PBC (1), PSC (1), acute liver failure (1), congenital disorder (1) or HCC without cirrhosis (2). Eleven recipients (37%) had an associated HCC. Post-LTx AST peak was 1712 IU/L. Reasons for graft loss were: hepatic artery thrombosis (1), ductopenic rejection (1) and diffuse intrahepatic biliary strictures (1). Ten patients (33%) developed non-anastomotic biliary complications requiring conservative treatment (2), endoscopic interventions (7) and re-LTx (1). Three recipients had acute rejection: 2 responded to steroids and 1 developed ductopenic rejection. Follow-up ranged from 1-93 months. Actuarial 1, 3, and 5-yr patient/graft survival after DCD-LTx was 92, 83 and 83%, and 89, 79, and 79%, respectively and was similar after DBD-LTx (1, 3 and 5-yr patient/graft survival of 90, 82 and 75%, p=0.846 and p=0.707, respectively).
Conclusion: Unlike in registry data and despite substantial ischemic injury (high peak-AST), short/long-term survival after DCD-LTx was comparable to DBD-LTx. Rapid donor surgery by experienced surgeons, careful donor/recipient selection, short warm/cold ischemia times are key factors to optimize outcome after DCD-LTx. However, strategies to reduce biliary complications are warranted.

RO-033 EFFEKT OF Cilostazol® ON HEPATIC MICROCIRCULATION AND LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN A RAT MODEL

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Introduction: Major liver resection has the risk of postoperative liver failure. So far no efficient treatment was established to improve patient outcome after extended liver resections. The aim of our study was to elucidate if pretreatment with Cilostazol®, a selective phosphodiesterase (PDE)-III-Inhibitor, was capable to improve hepatic perfusion and liver regeneration after major hepatectomy.
Materials and Methods: Sprague-Dawley rats (n=64) were pretreated with Cilostazol® (5mg/kg KG) or glucose solution for 5 days. After 70% liver resection on day 0 as well as on 1., 3. and 6. postoperative day hepatic arterial and portal venous blood flow were analyzed by ultrasonic flow measurement and microvascular blood flow by laser-Doppler-flowmetrie (LDF). Hepatic function and liver regeneration were characterized by bile excretion and liver histology (PCNA). Cilostazol® or placebo was given until end of experiment. Additional animals (n=16) received PDE-III-inhibitor or placebo and no liver resection. Mean values ± SEM, $p < 0{,}05$.
Results: Pretreatment with the PDE-III-Inhibitor resulted in a significantly impaired portal venous blood flow (2.00±0.07 vs. 1.56±0.11 ml/g*min; $p<0.05$) and improved hepatic microcirculation (642.9±41.1 vs. 493.8±25.0 aU; $p<0.05$) when no liver resection was performed. Portal blood flow and hepatic microcirculation were increased 77% and 32% respectively after 70% hepatectomy, whereas hepatoarterial blood flow was found unchanged. Cilostazol treatement improved hepatic blood flow and microcirculation. Interestingly liver regeneration was found enhanced by cilostazol over the whole observation period, with a maximum on the first day after liver resection (32±4 vs. 20±2 PCNA +cells/HPF $p<0.05$).
Conclusion: We could demonstrate that preconditional PDE-III inhibition can improve hepatic perfusion and liver regeneration after 70% hepatectomy. Thus, PDE-III inhibitors may represent an efficient drug therapy to ameliorate liver regeneration and hepatic function after extended liver resection.

RO-034 TRENDS OF USAGE IN STEATOTIC LIVER GRAFTS FOR ORTHOTOPIC LIVER TRANSPLANTATION OVER A TEN YEAR PERIOD IN A SINGLE INSTITUTION

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Introduction: Macrovesicular steatosis is associated with poor peri-operative and long term outcome after liver transplantation (LT). This study was designed to evaluate the trends of steatosis in transplanted grafts at a single institution.
Patients and methods: Graft steatosis was semi-quantitatively assessed in biopsies after immediate reperfusion (t0), and trends in graft steatosis of a historical control (group A;2001–2005) were compared with those obtained in the recent past (group B;2006 –2011). Outcomes were compared between groups with relevance to the degree of steatosis. Significance was assigned at $p<0.05$ using χ^2, Kruskal-Wallis and Mann-Whitney U tests.
Results: Total of 586 t0 biopsies were available from 1172 LT performed during the study period. (Group A, n=211 (36%); group B, n=374 (64%)). The donor age in groups A and B were 53.1 (16.6–72.1)years vs. 54.1 (18.0–73.4) years (p=0.71) and BMI was 25.7kg/m^2(16.5–50.8kg/m^2) and 25.9kg/m^2(14.7–48.0kg/m^2) respectively (p=0.81). The incidence of moderate (MS) and severe steatosis (SS) was 36 (17.1%) and 10 (4.7%) compared to 53 (14.2%) and 3 (0.8%) in group B respectively (p=0.001;OR=1.21;95%CI,0.63-2.33). For the entire cohort, the peri-operative morbidity for no steatosis, MS and SS was 48 (10%), 14 (16%) and 4 (31%) respectively (p=0.02), and the peri-operative mortality was 28 (6%), 9 (10%) and 4 (31%) respectively (p=0.001).The peri-operative morbidity was 26 (14.0%) and 40 (10.0%) respectively (p=0.16). The incidence of peri-operative mortality in group A was 17 (9.1%) compared with 24 (6.0%) in group B (p=0.12).
Conclusion: There has been a significant trend towards reduced use of steatotic grafts for LT due to the significantly increased peri-operative risk. Novel strategies to increase the safe use of steatotic grafts should be explored.

RO-035 LIPOCALIN-2, A PROMISING INFLAMMATORY MARKER IN ACUTE ALLOGRAFT REJECTION?

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Purpose: Lipocalin-2 (Lcn-2) is associated with ischemia/reperfusion injury (IRI) in different organs. Data on Lcn-2 expression during allograft rejection have been missing so far. The main focus of this study was to analyze the possible implication of Lcn-2 during acute rejection following liver transplantation.
Material and Methods: Serum of 68 patients undergoing orthotopic liver transplantation was collected preoperatively and postoperatively from day 1 to 15. Lcn-2 was analyzed by ELISA and expression levels were correlated with parameters of allograft rejection.
Results: Six patients (8.8%) experienced acute graft rejection within and 12 patients (17.7%) were diagnosed rejection beyond 20 days post transplantation. Serum levels of Lcn-2 following liver transplantation were elevated 3 to 7-fold immediately after transplantation due to IRI and also increased prior to clinically apparent acute rejection closely related to elevated routine markers (e.g. AST, ALT). Dynamic correlations could be observed between Lcn-2 expression and posttransplant renal function and immunosuppression regimens.
Conclusion: Lcn-2 is an inflammatory marker upregulated during acute graft rejection and its expression prior to clinical parameters of acute rejection might help to identify possible targets for therapeutic intervention. Lcn-2 expression correlates with posttransplant renal function (e.g. delayed graft function) and various immunosuppression regimens and is therefore proposed a monitoring marker in the early posttransplant period.

RO-036 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER RESECTION: WHY DENY THIS CHANCE OF CURE?

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Introduction: Liver Transplantation (LT) after Liver Resection (LR) for Hepatocellular Carcinoma recurrence may be associated with poor patients long term results and higher peri-operative patients morbidity and mortality. Despite that, some studies published later have demonstrated opposite results, emphasizing the absence of different outcome between primary LT or LT secondary to prior LR.Thisstudy focused on short- and long-term outcomes of LT recipients due to HCC recurrence after LR in asingle-institution cohort as well as inhighly comparablecase-matched subgroups.
Methods: From 2000 to 2009, 570 consecutive patients with documented HCC were treated our Institute by LR (n = 355, 62.2%) or LT (n = 215, 37.8%). The case-matched analysis between two groups: Group A1, LT recipients whom have received a previous LR (n = 26); Group B1, LT recipients whom have not received a previous LR (n = 26).
Results: Patients morbidity resulted higher among the A1 Group in term of packed red blood cells units transfused (respectively, 4.9 and 2.5 for Group A1 and B1: P-value=.008), fresh frozen plasma units transfused (respectively, 2.0 and 1.3 for Group A1 and B1: P-value=.035), median operative time (respectively, 430 min vs 366 min for Group A1 and B1: P-value=.04), post-operative

bleeding occurred (16% vs 7.6%for Group A1 and B1, P-value=.05), post-operative re-operations (respectively, 23.6% vs 7.6%for Group A1 and B1: P-value=.005). No differences were detected in term of patient mortality, patients survival and patients recurrence free survival at the univariate and multivariate analysis.
Conclusions: Although LT among previous liver resected patients is associated with higher risk of patient morbidity, the patients long term survival and recurrence free survival resulted not impaired. Therefore, from our experience, there isn't valid reason to deny the chance of LT to the patients before underwent LR.

RO-037 PATIENTS WITH 18F-FDG NON-AVID HCC BEYOND MILAN BURDEN ACHIEVE EXCELLENT RECURRENCE-FREE LONG-TERM SURVIVAL AFTER LIVER TRANSPLANTATION

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Background: The introduction of the Milan criteria has significantly improved outcome after liver transplantation (LT) for hepatocellular carcinoma (HCC). However, there is increasing evidence that a significant number of patients with HCC beyond the Milan burden may as well benefit from LT. The aim of this trial was to identify prognostic variables predicting long-term survival in this special population.
Patients: Ninety-one patients with HCC were included in this study. Listing for LT was based on Milan criteria. Biological tumor progression, such as macrovascular invasion, extrahepatic tumor spread or tumor-related symptoms, resulted in patient drop out. The impact of clinical (age, Child, MELD, immunosuppression, tumor macromorpholpogy) and biological (AFP-level, grading, microvascular invasion, lymphovascular invasion, 18F-FDG-uptake on PET) variables on tumor recurrence rate and long-term survival were determined.
Results: The current follow-up post-LT was ranging between 5 and 165 months. Final clinical staging pre-LT demonstrated HCC meeting the Milan criteria in 57 patients (Milan In; 62,6%), while 34 patients revealed HCC beyond the Milan burden limit (Milan Out; 37,4%). Five-year recurrence-free survival rates were 86% and 47% in Milan In and Milan Out recipients, respectively ($P < 0,001$). In the Milan Out population, only FDG tumor uptake on PET (odds ratio 6,4) and poor tumor differentiation (odds ratio 4,6) were identified as independent variables predicting long-term outcome. Five-year recurrence-free survival rates in the Milan Out population were 70% in patients with well/moderate tumor differentiation (versus 0%; $P < 0,001$) and 81% in patients with 18F-FDG non-avid HCC (versus 21%; $P < 0,001$).
Conclusions: Patients with 18F-FDG non-avid HCC beyond the Milan burden have an excellent prognosis after LT. Pretransplant assessment of glucose metabolism by PET may result in a useful extension of selection criteria in liver transplant candidates with HCC.

RO-038 TACE BEFORE LIVER TRANSPLANTATION: RESPONSE TO BRIDGING PREDICTS HCC RECURRENCE

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Background: Bridging the waiting time to liver transplantation (LT) in patients with hepatocellular carcinoma (HCC) is a clinical challenge and the most effective therapy still needs to be defined. Based on our recent results, we advocate repeatedly performed transarterial chemoembolization (rTACE).
Patients and Methods: Between 1998 and 2010, LT for HCC after rTACE was performed in 129 patients. Lipiodol and Mitomycin was used for rTACE, the median number of rTACE was 5 (2-14). Progress during TACE was defined as any increase in size or number of lesions.
The impact on tumor recurrence was scrutinized for 15 different potential predictors such as T and G classification, angioinvasion, number and size of lesions, Milan criteria (MC), progress during rTACE, etc.
Results: Five and ten-year survival was 68 and 52%, the respective figures for absence of recurrence were 76 and 73%. Thirty-nine patients died within this period, 23 of them from recurrence. According to initial imaging, 57 and 72 patients met and exceeded the Milan criteria, according to the assessment of the surgical specimen the respective numbers were 79 and 50. Including factors significant in the univariate analysis, the multivariate Cox analysis resulted in two independent predictors: grading ($p=0.022$, hazard ratio 0.37, confidence interval 0.15-0.86) and progress during rTACE ($p<0.001$, hazard ratio 18.0, confidence interval 6.1 – 53.0). Factors such as Milan, San Francisco and Up-to-Seven criteria lost their influence on recurrence.
Conclusion: This update of our patients pre-treated by rTACE corroborates our former results: after rTACE, accepted predictors for tumor recurrence lose their importance whereas biological factors such as tumor grading and the selection criteria "progress during rTACE" gain influence on results after LT for HCC.

RO-039 ASSESSMENT OF ETHYL GLUCURONIDE IN HAIR IMPROVES EVALUATION OF LONG-TERM ALCOHOL ABSTENTION IN LIVER TRANSPLANT CANDIDATES WITH ALCOHOLIC LIVER DISEASE

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Background: To assess long-term alcohol abstention prior to listing patients for liver transplantation (OLT) the diagnostic value of ethyl glucuronide in hair (hEtG) was evaluated.
Methods: In OLT candidates with alcoholic liver disease hEtG was quantitatively assessed in a 0-3cm and, if available, a 3-6cm hair segment, reflecting alcohol consumption within the last 0-3m or 3-6m. Cut offs were: >30pg/mg (>60g ethanol/day), 7-30pg/mg (>10-40g ethanol/day) and <7pg/mg (teetotallers/rare drinking). In parallel, a psychological evaluation – blinded to the alcohol test results - was done.
Additionally, results of alcohol marker testing, done within the last 3-6m prior to hair sampling, were retrospectively collected: ethanol (EtOH), methanol (MeOH), carbohydrate-deficient transferrin (CDT), and urinary EtG (uEtG).
Results: Thirty-seven patients (m/f: 22/15; median age: 56y, range: 39-67y) were included. hEtG was positive in 43.2% of patients. Assessed by psychological evaluation 24.3% of patients admitted, 70.3% negated alcohol consumption within the last 3-6m. However, in 26.9% denying alcohol consumption hEtG was elevated.
In addition, in 33 patients alcohol markers completing hEtG testing were available. In 60.6% of patients at least one alcohol marker was elevated. hEtG was the only positive marker in 35% of these patients. Yet, in 20% alcohol consumption was not detected by hEtG, but by uEtG and/or CDT. In these cases, blood/urine analysis was done not later than 4-28 days after hair sampling, indicating a diagnostic time gap for hEtG.
Conclusion: hEtG analysis considerably improved detection of alcohol consumption compared to psychological evaluation as well as blood/urine alcohol tests. However, in 20% alcohol intake was not revealed by hEtG, but uEtG and/or CDT. Therefore, hEtG is recommended in addition to uEtG and CDT for evaluating long-term alcohol abstention in OLT candidates.

RO-040 RECURRENT HEPATITIS C AND BILE DUCT COMPLICATIONS AFTER LIVER TRANSPLANTATION

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Complications that affect the extrahepatic bile duct are an important cause of morbidity after liver transplantation (LT). A possible association between hepatits C virus (HCV) and biliary complications (BC) has been suggested in recent reports.
To assess the possible causes of biliary complications (BC) and ascertain whether a relationship between hepatitis C and BC exists, the record of 163 consecutive liver transplants performed on 159 patients between August 2005 and April 2010 was reviewed.
Forty-six patients were excluded from the analysis for the following reasons: follow-up shorter than 6 months (27 cases), retransplantation (4), HIV positivity (7), hepatic artery stenosis (2), Roux-en-Y hepaticojejunostomy at LT (6).
The influence of the following variables on the development of bile duct complications was assessed: cold ischemic time (CIT), recipient age and MELD score, donor age, HCV serology before LT (HCV-positive versus HCV - negative), histological recurrence of hepatitis C, episodes of acute rejection and CMV infection.
Overall, 37 of 117 (31,6%) patients developed BC that included 31 (83,8%) anastomotic and 6 (16,2%) non-anastomotic strictures; median time of the diagnosis of BC after LT was of 132 (33-1272) days.
BC developed in 19 of 68 (27,9%) HCV-negative recipients and in 18 of 49 (36,7%) HCV-positive recipients (P=0.41).

Among the 49 HCV-positive recipients in this study, 34 developed a histologically-proven recurrent hepatitis C: BC were observed in 16 of these 34 patients (47,1%) while only 2 of those 15 (13,3%) HCV-positive recipients who did not experience recurrent hepatitis experienced these complications (P=0,028).
Recurrent hepatitis C was the only parameter significantly associated with BC at univariate analysis of possible risk factors (P=0,037).
This study seems to indicate a strong relationship between recurrent hepatitis C and BC after LT.

RO-041 CORRELATION OF MAJOR SURGICAL COMPLICATIONS AFTER LIVER TRANSPLANTATION FOR HEPATITIS-B AND -C AND HEPATITIS RE-INFECTION RATE

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Background: It is hypothesized that postoperative complications have a negative interference with the immune system. The aim of this study was to evaluate the impact of postoperative complications after liver transplantation on the re-infection rate of Hepatitis B or C.
Methods: The records of all patients who underwent a liver transplantation for Hepatitis B or/and C liver cirrhosIs between 2004 and 2008 were retrospectively reviewed. Postoperative complications were graded using the Clavien Classification system, and scored from minor (Grade I) through the most serious (Grade IV). Major complications were defined as Clavien Grade $\geq$IIIb.
Results: The study population consisted of 186 patients with a median age of 54 years. All patients underwent an orthotopic liver transplantation. There were no intraoperative complications. Postoperative complications were seen in 135 patients (72%). Complications were Clavien grade I-IIIa in 43 patients (23%) and grade IIIb or IV in 92 (49%). There were no significant differences in median age, co-morbidities and the severity of the cirrhosis between patients with and without complications. Of these 186 patients, 34 patients (18%) died during the hospital stay within the first month after transplantation and were excluded from further analyses. Of the remaining 58 patients with major complications, 29 (50%) had a re-infection in a median time of 14 month and of the 94 patients with none or minor complications, 10 (11%) had a re-infection after a median time of 26 month (50% vs. 11%, $p<0.0001$).
Conclusion: The results of our study show that major postoperative complications after liver transplantation for Hepatitis B or C are associated with a significantly higher rate of re-infection.

RO-042 ANTITHROMBIN III AS A PART OF THE ANTICOAGULANT PROTOCOL IN THE EARLY POSTOPERATIVE PEDIATRIC LIVER TRANSPLANTATION: A PROSPECTIVE STUDY

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Background: Early postoperative arterial thrombosis remains a significant cause of graft loss following paediatric liver transplantation (LT). The highest incidence occurs in recipients under the age of 3 years. Our study aimed to analyse the effect of the anticoagulation protocol including Antithombin III (ATIII) in preventing early hepatic arterial thrombosis post-LT.
Patients and Methods: We monitored the coagulation status by daily determinations of International Normalized Ratio (INR), Activated Partial Thromboplastin Time (APTT), fibrinogen, platelets and ATIII levels. Anticoagulation therapy consisted of LMWH, ATIII and dipyridamol. LMWH was started at 1 mg/Kg/day subcutaneously (once daily) when, on two consecutive blood tests, platelet count was higher than 50,000$\times$10E9/L, INR was higher than 2 and no active bleeding was detected. ATIII concentrates were administered if its activity was under 60%. Finally, dipyridamol was started at a dose of 1 mg/Kg (three times a day) when the platelet count was higher than 80,000$\times$10E9/L. Doppler Ultrasound was performed every morning during the first five postoperative days or whenever vascular thrombosis was suspected.
Results: From October 2007 to September 2009, 23 transplants were performed in our centre. The median age was 51 months (r:6-196) with a median weight of 18 Kg (r:8-49). Eight of them (34%) were partial grafts (5 living donors, 1 split liver and 2 reduced grafts). During the first 3 days post-LT, ATIII activity was under 60% in 13 patients. In those patients, ATIII concentrates were administered to achieve normal levels. Patent arterial flow was present in all 23 LT during the first 5 postoperative days.
Conclusion: In conclusion, the use of AT-III as part of an anticoagulant protocol may be useful to prevent arterial thrombosis post-LT, and might be considered particularly in paediatric population.

RO-043 PREOPERATIVE PORTAL VEIN THROMBOSIS DOES NOT INFLUENCE MORBIDITY AND MORTALITY AFTER LIVER TRANSPLANTATION

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Introduction: Portal vein thrombosis (PVT) is a well recognized complication of chronic liver disease with a prevalence ranging from 1% to 16% of patients. In the past PVT was considered an absolute contraindication to liver transplantation (LT), whereas nowadays thanks to the improvement of surgical techniques it is considered a relative contraindication. Aim of the present study is to evaluate the impact of pre-existing PVT on the surgical procedure, perioperative complications, patients and graft survival.
Materials and Methods: A retrospective review of 447 consecutive patients who underwent first LT between 10-2000 and 12-2010 was performed. Fourty-eight recipients (10.7%) with preoperative PVT (PVT group) were compared with 399 (89.3%) recipients without PVT (No PVT Group).
Results: In the PVT Group, 44 cases had partial thrombosis and 4 complete thrombosis. In all cases, a tromboendovenectomy followed by T-T anastomosis was performed. In 6 cases the portal anastomosis was performed at the confluence of the superior mesenteric vein and in 1 case with venous graft interposition.
The only pre-operative characteristics that resulted statistically different were the recipient age (57.1$\pm$7.2 vs 52.3$\pm$10.7, p=0.003) and the presence of TIPS (18.8% vs 6.8%, p=0.009) in PVT and no PVT Groups, respectively.
The warm ischemia time was higher in PVT group (47.2$\pm$23 min vs 39.3$\pm$15; p=0.04), as RBC transfusion (1889$\pm$1833.5 cc vs 1387$\pm$1354.6; p=0.03).
The ICU stay was longer in PVT group (5.8$\pm$11.7 days vs 3.6$\pm$3.9; p=0.02). However, there was no differences in the postoperative morbidity. The PNF and PVT recurrence were similar in both group.
The patient survival at 5 years resulted similar in PVT and no PVT Group, respectively (67.8% vs 68.6%; p=0.9).
Conclusion: PVT is associated with greater operative complexity, but has no influence on postoperative complication and overall survival.

RO-044 ACUTE KIDNEY INJURY (AKI) AFTER OLT USING AKIN CRITERIA

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AKI after OLT impacts on medium and long term outcome.
Methods: According to AKIN, we retrospectively evaluated the incidence of postoperative AKI in 90 pts who underwent OLT at our Institution. Median age was 52 y, median MELD 16. Data included intraoperative hemodynamics, fluid management, transfusion requirements, pressors use, renal function and urine output (UO).
Results: 1 year mortality rate was 3.4%. VVBP was never used. Basal pCreatinine was 0,95$\pm$0,92 mg/dL, GFR 114$\pm$46,5 ml/min. Blood losses were 2335$\pm$3370 mL, median transfusion requirements being PRC 5 U and FFP 15 U; median total crystalloid infusion was 3000 ml, UO 2835$\pm$1200 mL. Furosemide continuous infusion was used at 0.002 mg/kg/h throughout surgery, lasting 487$\pm$112 mins. Renal function showed significant impairment during the anhepatic phase (piggyback technique). Early postoperative AKI was recorded in 26 pts (29.5%): stage 1, 16 pts, (61%); stage 2, 7 pts; stage 3, 3 pts. On POD 1, pCreat was 1,1$\pm$0,44 mg/dL, GFR 89,5$\pm$34 ml/min (*p 0.001 vs baseline*); on POD 3, pCreat was 1,1$\pm$0,57 mg/dL and GFR 91$\pm$47 ml/min (*p 0.001 vs baseline*). 3 patients (3.4%) needed CRRT. pCreat and GFR were 0,92$\pm$0,48 mg/dL (*ns vs baseline*) and 84$\pm$35 mL/min (*p< 0.001 vs baseline)* at ICU discharge and 0,98$\pm$0,31 mg/dL and 90,4$\pm$34 mL/min at Hospital discharge *p< 0.002 vs baseline).*
Conclusions: Incidence of AKI was among the lowest reported in the literature, large part of the AKI pts being in stage 1: strict hemodynamic control, volume optimization and renal perfusion pressure defense might have positively impacted on renal function after OLT.

Liver II

RO-045 LEVEL OF ACUTE RENAL DYSFUNCTION IN LIVER TRANSPLANTATION: RELATION WITH PRE- AND POST-TRANSPLANT HEPATIC FUNCTION

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Aim of the study is to evaluate the incidence of acute renal disease (ARD) post liver transplantation (LT) and its association with pre and post-LT hepatic dysfunction.
Methods: Single centre study of 54 patients who underwent LT 08/2008-01/2011. Pre-LT hepatic function was evaluated by bilirubin, INR, albumin, and MELD. Bilirubin, INR, GOT and GPT were recorded to assess immediate graft function. Indexes of renal function included serum creatinine (sCr), MDRD4 and natremia. ARD was defined and classified by RIFLE criteria in 3 levels of renal dysfunction: Risk (ARD-R), Injury (ARD-I) and Failure (ARD-F), on the basis of the degree to which sCr or GFR change from baseline. Parameters were monitored since the immediate pre-LT for 1 week after LT.
Results: the incidence of ARD was 53.7% (29/54 patients); of these 55.2% developed ARD-R, 27.6% ARD-I and 17.2% ARD-F.
Pre-LT MELD, bilirubin, sCr and MDRD4 were significantly different in ARD-F group compared to no ARD-F group: among ARD-F group, MELD and bilirubin were higher, while sCr and MDRD were abnormally low and high, respectively. Bilirubin and GOT were significantly higher in ARD-F group to the 4th and 5th day post-LT respectively (see table).

	ARD-F group	no ARD-F group	p
Pre-LT			
MELD	24 (18–28)	16.1 (8–39)	0.024
sCr (mg/dl)	0.3 (0.0–0.9)	0.9 (0.3–3.4)	0.005
MDRD4 (ml/min)	238 (79–940)	93 (15–371)	0.024
Bilirubin (mg/dl)	10 (1.65–37.3)	2.9 (0.47–32)	0.034
Post-LT			
GOT (mg/dl)	265 (150–422)	70 (21–269)	0.004
Bilirubin (mg/dl)	7.9 (4.7–30.5)	3.25 (0.64–35)	0.048

Conclusion: Development of ARD post-LT is multifactorial and concerned more than half of patients in our study.
ARD-F was associated with a worse pre- and post-LT hepatic function. The abnormal sCr and GFR may result from the reduced creatine hepatic synthesis in these patients with end stage liver disease.
High post-LT bilirubin and GOT levels are associated with ARD-F, in grafts showing a slow recovery of function.
The worst degree of ARD post LT seems to be influenced by the poor pre-LT hepatic function as well as early graft dysfunction.

RO-046 XEROSTOMIA AND BURNING MOUTH SYNDROME ARE COMMON ORAL SIDE EFFECTS IN LIVER TRANSPLANT PATIENTS

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Background: Few data exist on oral side effects after liver transplantation (LT). Transplant patients have immunosuppressive and also many other medications which may predispose oral side effects. We investigated the prevalence and possible risk factors of subjective oral symptoms in a group of post-LT patients.
Methods: Patients were recruited for a prospective study (n=77; 26 women, 51 men) to have a dental examination in connection of an outpatient clinic. A structured questionnaire was used to record oral symptoms and saliva samples were taken. Variables entered on multivariate logistic regression analysis (SPSS) included gender, age, post-LT follow-up time, socioeconomic status, smoking, alcohol use, diabetes, number of medications, systemic corticosteroid, type of calcineurin inhibitor (CyA/Tacro), oral health status, and resting and stimulated salivary flow rates.
Results: The median age of the patients was 55.9 (range 24.6-70.9) and the median time after LT was 5.0 years (range 2-10). Chronic liver disease (CLD) was the main etiology (74%) and majority of patients had cholestatic liver disease; either primary sclerosing cholangitis or primary biliary cirrhosis. Median number of medications was 7 (range 2-11). Xerostomia was recorded in 42.9% of the patients with dryness of mouth mainly at night. Risk factors for xerostomia were retirement, number of medications, and alcohol use. Burning mouth syndrome (BMS) was recorded in 15.6% of the patients most typical site being the tongue. Main risk factors for BMS were dry mouth and age.

Risk factors for xerostomia and BMS

Risk factor	OR	95% CI lower	95%CI upper	Sign.
Xerostomia				
Retirement	1.51	1.14	1.99	0.004
No. of medications	1.20	0.91	1.57	n.s.
Alcohol use	2.58	0.73	9.07	n.s.
BMS				
Dry mouth	5.09	0.97	26.84	0.055
Age	1.07	0.97	1.19	n.s.

BMS = burning mouth syndrome.

CLD patients had lower resting salivary flow rates than acute patients (0.34 ml/min vs. 0.53 ml/min, p= 0.032, t-test).
Conclusions: Number of medications and alcohol use correlated with xerostomia which was also a risk factor for BMS. CLD patients had significantly lower salivary flow rates than acute liver disease patients.

RO-047 APURINIC APYRIMIDINIC ENDONUCLEASE/REDOX EFFECTOR FACTOR 1 IMMUNOREACTIVITY IN HEPATOCELLULAR CARCINOMA RISK OF RELAPSE AFTER LIVER TRANSPLANTATION

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The risk of HCC recurrence after LT is related to the number and dimensions of the tumours and to their biological characteristics. Investigation of the biology of HCC might better define the risk of relapse after resection or transplantation. Apurinic apyrimidinic endonuclease (APE1)/redox effector factor 1 (Ref-1), a multifunction protein involved in transcriptional regulation of gene expression during cellular responses to oxidative stress and in the base excision repair pathway of DNA lesions due to oxidant-damage, contributes to genome stability. APE1/Ref-1 is localized in the nucleus; cytoplasmic localization has been correlated with a poor prognosis. Of 98 patients subjected to LT for HCC over a 10 years period within the Milan criteria, 13 (13.2%) had microvascular invasion (MVI) at explant; of those 8 were positive for APE1/Ref-1 (62%). The overall incidence of HCC recurrence was 10,2%; 8 (80%) were APE1/Ref-1 positive, 5 (50%) had MVI and 5 (50%) had combined MVI and positivity for APE1/Ref-1. Three of the 5 (60%) HCC recurrences without MVI were APE1/Ref-1 positive. Of a total of 18 patients with HCC recurrence or MVI, 11 (61%) were positive for APE1/Ref-1; of those 8 (73%) died for HCC recurrence. Overall morality for HCC recurrence was 90%. Five of the eight patients (63%) with both MVI and APE1/Ref-1 positivity died for HCC recurrence. Five out of 13 patients (38%) with MVI at explant died for HCC relapse. Although retrospective and limited in numbers our results on APE1/Ref-1 cytoplasmic localization in HCC explant after LT might support the hypothesis of a predictive role of this protein for HCC risk of relapse after LT. The determination of APE1/Ref-1 cytoplasmic localization by analysis of a pretransplant needle biopsy should aid the decision making for LT.

RO-048 EFFECT OF LOW MOLECULAR WEIGHT HEPARIN (LMWH) ON THROMBIN GENERATION (TG) IN CIRRHOTIC PATIENTS

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Introduction: Cirrhotics, including patients awaiting liver transplantation, may present thrombotic complications such as portal vein thrombosis, that warrant anticoagulation therapy to prevent extension into the splanchnic vessels, which can jeopardize transplantation. However, due to the reset hemostatic balance in cirrhotics, the anticoagulant effect of LMWH could differ from the one expected.
Aim: To evaluate in vitro the effect of LMWH on TG in cirrhotics at different stages of liver disease with respect to antithrombinIII (ATIII) levels.
Methods: Thirty cirrhotics (10 ChildA, 10 ChildB, 10 ChildC) without HCC or known thrombophylic genetic defects, 10 type1-ATIII-defect patients, and 10 healthy subjects were included in the study. ATIII activity was determined for every subject. TG on PPP, with determination of endogenous thrombin potential (ETP), was performed at basal conditions and with enoxaparin at

0.35UI/mL anti-Xa activity. The effect of LMWH was expressed in terms of ETP ratio at 0.35UI/ML (0.35ETP ratio), and was calculated by dividing ETP with LMWH by ETP in native plasma.
Results: Mean±SD ATIII activity levels in cirrhotics were 75±25%, 55.3±22%, and 41.1±13.6%, for Child A, B, and C patients, respectively, in contrast with 51±6.8% for ATIII-defect patients. The decrease in ATIII activity was statistically significant in all cirrhotics compared to controls (104.9±8.6%,p<.001). 0,35ETP ratio was significantly lower in cirrhotic patients compared to controls (0.26±0.1 vs 0.48±0.1,p<.001), reduced parallel to increasing disease severity. There was a direct correlation between 0.35ETPratio and ATIII (r=.64,p=.001).
Conclusions: Cirrhotic patients show an increasing response to LMWH parallel to increasing severity of liver disease, despite a decreasing level of ATIII. Clinically, LMWH dose adjustment should be considered in cirrhotic patients according to the Child class.

RO-049 EARLY SWITCHING TO INTRAMUSCULAR ANTI-HBs IMMUNOGLOBULINS (Igantibe™) AFTER LIVER TRANSPLANTATION: FEASIBILITY, EFFICACY, AND SAFETY

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We present the results of a single-center trial on early switching from i.v. to i.m. anti-HBs immunoglobulins (HBIG) in adult (≥18 years) liver transplantation (LT). Inclusion criteria called for HBsAg positivity; undetectable HBV-DNA at transplantation; no HCV or HIV co-infection. Patients were administered 30,000 IU i.v. HBIG perioperatively and re-boosted with 4,000 IU if necessary to achieve an anti-HBs titre ≥150 mIU/mL by day 14. Switching to i.m. HBIG (Igantibe™) was allowed for patients with a functioning graft, no systemic infection, no need for renal replacement therapy, and discharged home ≤ day 28 post-transplantation. On the first outpatient visit within one week from discharge, patients were administered 2,000 IU Igantibe™ followed by 2,000 IU every second week. A total of 55 patients were enrolled (males 39; mean age 50.2±10.4 years). Fifty-one patients (92.8%) were on lamivudine, 2 (3.6%) on lamivudine and adefovir, and 2 (3.6%) on entecavir. Fifty-four patients (98.2%) were switched to Igantibe™ at a mean of 24.3±3.2 days after LT. One patient (1.8%) could not be switched due to primary non function of the graft. Six months after switching, 48 patients (87.3%) were on i.m HBIG, while 6 (10.9%) were on i.v. HBIG due to anticoagulation in 2 cases (3.6%), and non-anastomotic biliary strictures in 4 (7.3%). No HBV breakthrough was observed. A protective titre was achieved throughout the study period (mean baseline 211.4±46.7 mIU/mL; mean at 3 months 254.7±78.9 mIU/ml; mean at 6 months 211.2±54.7 mIU/ml). Complications were reported by 4 patients (7.4%) and consisted of pain in 2 cases (3.7%), itching and bleeding in one each (1.8%). Early switching from i.v. to i.m. HBIG is feasible in 87.3% of patients and allows for protective titres 6 months after conversion with no HBV breakthrough.

RO-050 A SURGICAL MODEL OF ACUTE LIVER FAILURE FOR TESTING A BIOARTIFICIAL LIVER

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Acute liver failure is characterized by jaundice, coagulopathy and encephalopathy and relates to hepatocellular injury or necrosis. The developments of artificial hepatic-support devices has been restricted due to the lack of suitable liver failure models. In this study we describe a surgical model of acute liver failures in pigs.
Large white X Landrace pigs weighing between 20 and 30kg were anaesthetized with Ketamine, Sodium thiopentone and Isoflurane and subjected to a midline laparotomy. The ligamentous attachments of the liver were divided. The common bile duct and the branches of the hepatic artery were ligated and excised in the hilum of the liver. A side-to-side portacaval shunt was created, and the liver rendered totally ischaemic by ligation of the portal vein in the hilum of the liver. Venous cannulae were inserted into the splenic vein and the external jugular vein for attachment to the Bioartificial Liver (BAL).
Twenty six animals were included in the study. There was an increase in intracranial pressure and a decrease in brain tissue oxygenation. The animals developed a coagulopathy and became acidotic. There was also an increase in bilirubin. All animals were killed within 13 hours because of haemodynamic instability.
Thus a surgical model of acute liver failure has been established and can be used to study artificial liver-support devices. A limitation of the model is that it is irreversible, but the advantage is 100% mortality without treatment thereby being appropriate for a real test of BAL function.

RO-051 PRE-TRANSPLANT PARAMETERS PREDICT SURVIVAL DURING AND AFTER LIVER TRANSPLANTATION

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Background: Prediction of survival in patients after liver transplantation (LT) remains challenging. Several models and parameters have been suggested, all with different cut-off values or points of measurement. Most studies include parameters up to 1-month before transplantation and focus on 1-year survival. Patients however are more interested in staying alive with or without transplantation. In this study we aim at identifying factors that predict survival during LT and post-LT survival.
Methods: Patients transplanted at our center between 2004 and 2008 were analyzed for post-LT survival. The last available routine blood laboratory tests before LT were collected. Blood samples had to be taken in the previous 24 hours before LT to be eligible for analysis. Comparison of means was done with student's t-test. Correlation analysis was done with Spearman's non-parametric test. Survival was assessed using Kaplan-Meier analysis. Multivariate analysis was performed with Cox regression analysis.
Results: In total 220 consecutive patients were transplanted and included for analysis. Univariate analysis showed a correlation between overall survival and the following pre-LT parameters: urea (P = 0.042), Hb (P = 0.007), Ht (P = 0.026), APTT (P = 0.012), patient height (P = 0.026), serum sodium (P = 0.032), albumin (P = 0.043), and creatinin (P = 0.04). Multivariate analysis with all pre-LT laboratory parameters showed that serum sodium, INR, PT and APTT were independent predictors of overall survival after transplantation.
In this cohort 5 patients (2.3%) died on the day of transplantation. Creatinine levels were significantly higher in these patients (P = 0.003). No other pre-LT parameters were correlated with intraoperative mortality.
Conclusion: Pre-transplant serum sodium and coagulation factors, mainly APTT, are independent predictors of post-LT survival but not of mortality during transplantation. High serum creatinine is a risk factor for mortality during transplantation.

RO-052 IS PLASMA DISAPPEARANCE RATE OF INDOCYANINE GREEN (PDR_{ICG}) AFTER LIVER TRANSPLANTATION (OLT) ALWAYS A RELIABLE TOOL TO ASSESS EARLY GRAFT FUNCTION AND OUTCOME ?

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Early graft dysfunction (EAD) after OLT is associated with increased morbidity and mortality. PDR_{ICG} is used to assess functional recovery of the graft, values <10%/min predicting poor graft and patient outcomes.
Methods: We prospectively evaluated PDR on POD 1 and 2 in 71 patients who underwent OLT to evaluate its correlation with EAD, liver function tests, lactate clearance, graft and patient outcomes. Statistical analysis included Anova, Spearman and Wald's tests, ROC analysis for the influence of bilirubin on PDR.
Results: 3 mo survival rate was 94.5% for pts and 90,2% for grafts. 7 grafts were lost, 3 for GNF (2 early PGNF, 1 late hepatitis). 13 pts (17%) had EAD: no pt died, 2 had early PGNF. PDR values were widely and randomly distributed between functioning and dysfunctioning grafts. Among the 36 pts (48%) with PDR < 16% (11±4%), 8 pts had EAD. Of the 15 pts (20%) with PDR < 10% (7.2±1.9%), 5 pts had EAD. Among the 26 pts without EAD,12 had PDR < 10%. In patients with PDR < 10%, PT on POD 7 was normal. On POD1, PDR < 10% or PDR < 16% did not correlate with graft or pt outcomes and did not impact on ICU LOS or MOF. A possible explanation may reside in the competition of ICG with bilirubin for the same carrier (bilirubin > 6.2 mg/dl increased the odds to find PDR < 10% $p = 0.011$).
Conclusion: In our study low PDR seems to overestimate the incidence of graft dysfunction, possibly reflecting a competition of ICG with bilirubin for the same carrier.

RO-053 TECHNICAL ASPECTS OF HEPATIC ARTERY RECONSTRUCTION IN LIVING DONOR LIVER TRANSPLANTATION

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Background: In living donor liver transplantation (LDLTx) hepatic artery (HA) anastomosis still remain a challenge. Indeed arterial reconstruction using a microscope has been advocated to decrease the incidence of hepatic artery thrombosis (HAT). However microscope itself is not considered compulsory by

many surgeons. We herein describe our experience of arterial reconstruction without the microscope.
Methods: From March 2001 to December 2008, 49 LDLTx were performed at our institution using the right graft without the middle hepatic vein. All the arterial anastomosis were performed using the "parachute " technique, after an arteriotomy on both arterial stumps, with one running 7/0 prolene suture using 2.5X surgical loupe magnification. Arterial flow is re-established before the suture is tied to allow further expansion at the anastomosis site. The arterial anastomosis was performed with the right hepatic artery in 22 cases and with the proper hepatic artery in 27 cases. In 2 cases an interposition arterial conduit was used.
Results: Data have been retrospectively analyzed. HAT occurred in 2 patients (4%).One of them has been retransplanted while the second one underwent an urgent surgical revision within 8 hours after transplantation. A thrombectomy and a new anastomosis using an aortic conduit have been performed. The HA developed a new thrombosis. Four months after transplantation an intra hepatic biloma has been drained. Patient is alive with a biliary stent in place and normal liver function tests.
Conclusion: Our results show an overall arterial complication rate of 4%. These data are comparable to other previous published series that report a negative arterial complication rate between 1.6% and 22% using a microscope. Although the use of microscope allows more precise and easy arterial anastomosis in LDLTx, an accurate surgical technique using 2.5X surgical loupe magnification can assure remarkable results.

RO-054 USE OF FUNCTIONAL IMAGING IN THE INVESTIGATION OF PATIENTS WITH SUSPECTED SEPSIS FOLLOWING MULTI-VISCERAL TRANSPLANTATION

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Introduction: Radiolabelled leucocyte scintigraphy using 111In-labelled leucocytes (LS) and 18F- FDG PET (PET) are useful functional imaging modalities for investigating patients with fever/occult sepsis where conventional imaging methods may fail to establish a cause. The present study examined the usefulness of LS and PET in evaluating multi-visceral transplant (MVT) patients with suspected sepsis.
Patients And Methods: Six consecutive patients underwent MVT between Dec 2007 and Feb 2009. Post-operatively, they presented with prolonged pyrexia and a rise in inflammatory markers. All of them had serial ultrasound and CT examinations. LS was undertaken as no definite cause of pyrexia was identified following these investigations. Two patients also had 18F-FDG PET studies.
Results: Out of 6 patients who had LS studies, two showed increased uptake in the small bowel, one had normal uptake, one showed uptake related to the surgical stoma, one had increased uptake in the surgical wound and one had abnormal uptake in the mid and upper abdomen corresponding to small fluid collections around the pancreas. The patients who had uniform uptake in the entire small bowel had treatment with methyl prednisolone and subsequent LS showed no abnormal uptake in the small bowel, which suggested rejection despite a negative small bowel mucosal biopsy. Two patients who had PET and LS imaging showed concordant abnormal findings.
Conclusion: Although our experience is limited, LS and PET imaging appears to be useful in evaluating the complex clinical problems associated with MVT.

RO-055 PREDICTING SURVIVAL AFTER LIVER TRANSPLANTATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA USING EXPANDED MILAN CRITERIA AFTER 10th YEAR

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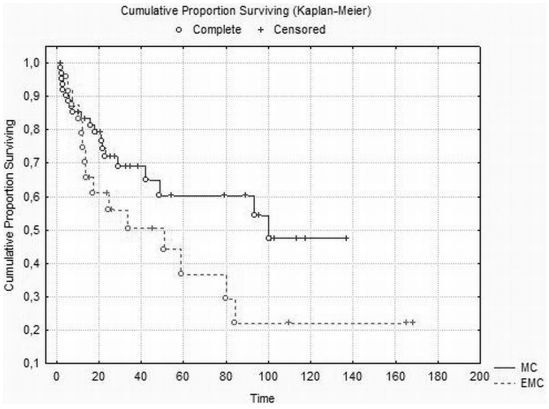
Introduction: Liver transplantation represents a controversy in management of early-stage hepatocellular carcinoma (HCC). Expansion beyond the Milan criteria for liver transplantation remains controversial. Survival for patients with cancers that exceed these criteria remains unpredictable.
Aim: To study the survival of patients with tumors that exceed the Milan criteria in HCC pacients who underwent liver transplantation.
Method: Between 1996 and 2010, we analyzed 121 cases of HCC patients who underwent liver transplantation distributed in two groups according to explant histology inside Milan criteria (MC) or expanded Milan Criteria (EMC).
Result: The survival rates after 10th year can be seen in Figure 1.
Whereas MC patients had better survival than EMC patients a long-term following (log-rank test; P=0.008).
Conclusion: Long-term follow up showed best survival to patients within Milan criteria.



Abstract RO-055 – Figure 1

RO-056 SOMATOSTATIN IMPROVES HEPATIC HEMODYNAMICS, INJURY, AND OUTCOME IN "SMALL-FOR-SIZE" LIVER TRANSPLANT

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Portal hyperperfusion and hypertension are early events in "small-for-size" liver transplant that lead to significant sinusoidal endothelial cell (SEC) destruction and graft failure. We hypothesized that perioperative somatostatin treatment would improve postreperfusion hepatic hemodynamics, SEC injury, and graft outcome in a clinically relevant model.
Methods: Weanling pigs (15-20 kg) underwent 70% hepatectomy. Livers were stored at 4 °C for 5 h and transplanted into recipients (30-35 kg). Two groups were performed: 1) SFS (n=18), no treatment; 2) SST (n=12), somatostatin bolus during the anhepatic phase followed by continuous postoperative infusion.
Results: Cold ischemia was 332 (283-340) and 323 (303-345) min, and grafts were 23.5 (19.4-26.2) and 22.2% (18.7-24.7) of recipients' standard liver volume in SFS and SST, respectively. Immediately after reperfusion, portal vein flow (PVF) and venous pressure gradient (PVPG) were lower and hepatic artery flow (HAF) significantly higher in SST versus SFS (TABLE). Peak serum levels of endothelin-1, a marker of SEC injury, were lower in the SST group versus SFS: 2.69 (1.67-2.72) *vs* 3.72 (3.08-5.19) at 3 hours after reperfusion, *P*=0.030. Hepatic function was also improved in somatostatin-treated animals, as evident by significantly lower AST levels in SST versus SFS recipients on post-operative days 2-5. Furthermore, five-day survival was 28% in SFS, whereas perioperative treatment with somatostatin led to 83% survival in SST (*P*=0.028).

Hepatic hemodynamics

		SFS (N=18)	SST (N=12)	*P*
PVPG	Baseline	2 (2–3)	1 (1–2)	NS
	PR	9 (8–10)	6 (5–6)	<0.001
PVF	Baseline	989 (686–1315)	1042 (912–1244)	NS
	PR	3418 (2547–3742)	2488 (2120–2826)	0.013
HAF	Baseline	332 (275–506)	300 (256–547)	NS
	PR	185 (119–237)	280 (211–330)	0.029

PVPG in mmHg, PVF and HAF in mL/min/kg hepatic tissue. Values represent mean (25–75% interquartile range). PR, post-reperfusion.

Conclusions: Somatostatin attenuates postreperfusion portal hyperperfusion and hypertension and improves HAF, SEC injury, and outcome in "small-for-size" liver grafts. Unlike surgical portal inflow modification, which is reversed only through invasive means, somatostatin may be applied during the acute phase of "small-for-size" liver injury and then withdrawn, making it an attractive therapeutic option for the clinical setting.

RO-057 LIVER AND LIVER PANCREAS TRANSPLANTATION IN THE TWO STAGE TREATMENT OF LIVER METASTASIZED NEUROENDOCRINE TUMORS OF THE PANCREAS: ABOUT THREE CASES

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Liver transplantation is an accepted treatment in liver metastasized neuroen-

docrine tumors. However, in most series recurrent disease is frequent. Therefore, the accurate patient selection for this aggressive treatment option is necessary.
We report on 3 cases who underwent a two staged pancreatic resection and liver or liver pancreas transplantation.
We also report on the selection criteria published in the recent literature.
Conclusion: Liver transplantation can offer a chance of cure in highly selected patients. The poor results of liver transplantation for liver metastasized NET's can be explained by 1. incomplete tumor clearance when the resection of the primary and the transplantation are performed in one stage, and 2. older patients not supporting this extensive surgery.
Therefore, based upon the recently published selection criteria and risk factors for recurrence (Fig. 1), we adopted a two stage treatment modality for NET's with diffuse liver metastases: 1. radical resection of the primary before the transplantation (stage 1); 2. a waiting period to observe the natural behaviour of the tumor and to exclude residual or recurrent extrahepatic disease; 3.orthotopic liver or cluster liver pancreas transplantation to treat the liver metastases and the pancreatic insufficiency (stage 2).We reserve this aggressive approach for patients under 50 who can endure this extensive surgery and NET's with low Ki 67 index.

	Mazzaferro [1,2]	Le Treut [3,4]	Rosenau [5]	Van Vilsteren [6]	Olausson [7,8]	Frilling [9]	Florman [10]	Lehnert [11]
Age over 50 years	+	–	–	–	–	–		+
Symptomatic tumor	+	–	–	–	–	–	+	
Primary pancreatic tumor	+	+if massive liver involvement	–	(+)	–			
Non-carcinoid tumor	+	(+)	–					
Primary tumor not drained by portal vein	+		–	+	–			
Ki 67 index (%) Aberrant E-Cadherin	<16		<>30	Probably <>2	<>10	<>10		
Liver involvement >50% of standard liver volume	+	+if pancreatic tumor			–	–		
Extrahepatic lymph node involvement		–	–	–	–	–	–	
Extrahepatic spread	+	(+)	+	+	(+)	(+)		
Primary tumor not resected pre-transplantation	+	(+)	+	+	(+)	(+)	+	+
Period of stable disease pre-transplantation (months)	<6	(+)		<6		<6		
Multivisceral transplant	+	+	+		+	(+)		

Figure 1

To transplant within these criteria is, in our opinion, the key to success for longstandig disease free survival.
References: Coppa Transpl Proc. 2001; Mazzaferro J Hepatol. 2007; Le Treut Ann Surg 1997; Le Treut Am J Transplant 2008; Rosenau Transplantation 2002; Van Vilsteren Liver Transpl 2006; Olausson World J Surg 2002; Olausson Liver Transpl 2007; Frilling Liver Transpl 2006; Florman J Gastrointest Surg 2004; Lehnert Transplantation 1998; Bonaccorsi-Riani Transpl Int. 2010.

RO-058 USE OF NHBD IN RECIPIENTS WITH HCV CIRRHOSIS: INFLUENCE OVER PATIENT SURVIVAL

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Introduccion: The scarcity of organs for transplantation from brain death donors (BDD), as well as the increase in mortality of patients in waiting list, determines us to look for alternatives to achive more organs, being graft from non heart beating donors (NHBD) the most attractive source. Our aim is to compare the neccesity of hemoderivates usion BDD or NHBD for orthotopic liver transplantation (OLT).
Material and Methods: This comparative study comprise a sample of 243 patients who underwent OLT: 200 patients were transplanted with BDD and 43 with NHBD, between January 2006 and December 2010.
Results: We compare a series of 25 HCV patients who received liver grafts from NHBD with a mean age of 57,5+10,29 years versus 18 non HCV patients who received liver grafts from NHBD too with a mean age of 59,17+7,98 years. No significant differences were found also with respect to pretransplantation laboratory parameters, hemoderivates requirements during the transplantation and preoperative CHILD and MELD scores in patients of both groups. We found worse, but not statistically significant, patient survival in patients who received liver graft from NHBD: 80%, 52,7% and 52,7% at 1, 3 and 5 years respectively in the HCV group, versus 88,5%, 81,7% and 68% at 1, 3 and 5 years respectively in the non HCV group (p=0,15). This tendences was also found with with respect to graft survival rates, which were 67%, 48,9% and 32,6% at 1, 3 and 5 years in the HCV group, while in the non HCV group they were 65,8%, 59,2% and 47,4% (p=0,20).
Conclusion: There seems to be a worse evolution of HCV patients who received liver grafts from NHBD. If this is confirmed, the use of grafts from these kind of donors in HCV patients should be reconsidered.

RO-059 COMBINED "EN BLOC" LIVER-PANCREAS TRANSPLANTATION USING WHOLE SIZE AND SPLIT LIVER GRAFTS

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Combined en bloc liver pancreas transplantation (EBLPTx) has been rarely performed. In all reported cases a whole size liver graft was used. We report 1 case of EBLPTx using a split liver graft combined with a kidney transplant and 1 case using a whole size graft.
Case 1: A 46 year old man affected by HCV related liver cirrhosis, type 1 diabetes with chronic renal failure on haemodialysis, diabetic retinopathy underwent EBLPTx combined with a kidney. The extended right graft was harvest en bloc with the pancreas after an in situ split. A left Kidney was procured as well. The EBLPTx was performed using the piggyback technique for the vena cava anastomosis. Arterial anastomosis was performed between a y iliac arterial graft (sutured on the back table to the celiac trunk of the graft and to the superior mesenteric artery) and the common hepatic artery of the recipient. The recipient's portal vein was anastomosed in an end to side fashion to the portal vein of the graft. A double layer end to side duodeno-duodenostomy was performed. The kidney was transplanted extraperitoneally into the left iliac fossa. Immunosauppression was based on basiliximab, tacrolimus and steroids.
Case 2: A 40 year old man affected by hepatocellular carcinoma on an HCV-alcohol related cirrhosis and type 1 diabetes with related retinopathy and polineuronopathy underwent EBLPTx with an whole size liver graft. Surgical technique and immunosuppression were the same as in case 1.
Results: Both patients are alive and well and have achieved a permanent euglicemic status soon after EBLPTx.
Conclusion: EBLPTx is an effective surgical option to cure diabetic patients with end stage liver disease. A split liver graft can safely be used en bloc with the pancreas.

Donation / retrieval

RO-060 HEPARIN DOES NOT IMPROVE GRAFT FUNCTION IN NON-HEART BEATING LUNG DONATION. AN EXPERIMENTAL STUDY IN PIGS

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Background: Non-heart beating donation (NHBD) has the potential to increase the number of patients treated with lung transplantation. We investigated, with a simulated clinical situation in the uncontrolled NHBD setting, whether or not heparin after death affects the donor lung function.
Material and Methods: Twelve Swedish domestic pigs underwent ventricular fibrillation and were left untouched for 7 minutes followed by cardiopulmonary resuscitation with mechanical compressions during 20 min. The animals were declared dead after a hands off period of 10 min and randomised to injection of heparin or placebo given into a central venous catheter. In the animals receiving heparin 2 more min of chest compression followed. Intrapleural cooling was initiated 1h after death, and prevailed for 2h. Lungs were explanted and Ex vivo lung perfusion (EVLP)performed with the Vivoline® system. Lung function was evaluated with blood gases, pulmonary vascular resistance (PVR), wet/dry weight ratio, macroscopic appearance and histology.
Results: During EVLP there were no significant differences between groups in PaO2, PaCO2 or PVR at any investigated FiO_2 level (1.0, 0.5, 0.21).

EVLP data

	Heparin (n=6)	No Heparin (n=6)	p-value
Pao2 (FiO2- 1.0)	64.0±2.3	63.2±4.2	0.82
Pao2 (FiO2- 0.21)	12.9±1.0	12.4±0.9	0.82
PaCO2 (FiO2- 1.0)	4.3±0.2	4.6±0.3	0.49
PaCO2 (FiO2- 0.21)	4.1±0.2	4.6±0.3	0.31
PVR (FiO2- 1.0)	592±90	647±97	0.70
PVR (FiO2- 0.21)	761±117	804±138	0.21
Wet/Dry Ratio	5.8±0.2	6.1±0.3	0.70

Values expressed as mean ± SEM.

There were no significant differences between groups in wet/dry ratio, macroscopic apperance or histology.

Conclusion: The use of heparin is of no obvious benefit for the donor lungs in the uncontrolled NHBD situation. The exclusion of heparin will simplify lung donation from non heart beating donors.

RO-061 ENHANCING REFERRAL AND DONATION RATES: NORTH WEST EXPERIENCE

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Background: The North West region beleives that the Implementation of Early Notification Criteria for Organ Donation within its regional hospitals has resulted in a dramatically increased referral and donation rate during 2010.
Methods: Each Specialist Nurse - Organ Donation has challenged existing practice to promote and implement the concept of Required Referral within their hospital. Most of the Acute Hospitals in the Region have adopted Required Referral as a foundation for excellent practice. SN-OD's have delivered a tireless program of education and developed policies to support the concept within the critical care arenas. This has seen an encouraging increase in donation activity and referral rate within our regional hospital.
Results: Our team achieved a total of 1172 referrals during 2010. The basic triggers for referral include the plan to perform brain stem death tests or the decision to withdraw treatment based on futility. The North West celebrated a fantastic 121 successful organ donors during 2010. Our team also facilitated an additional 48 DCD's whereby consent was gained, teams mobilised but donation abandoned due to a prolonged time to asystole following withdrawal of treatment.
Conclusion: Our team has seen an increase in donation activity within the region due to the implementation of Required Referral. This concept ensures that families are offered the option of organ donation as a normal part of end of life care.

RO-062 PANCREAS ALLOGRAFT: IMPACT OF THE RETRIEVAL CENTRE ON THE UTILIZATION OF THE ORGAN

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Introduction: Pancreas allograft is precious resource, least utilised of all abdominal organs,technically challenging to recover. Successful retrieval and utilisation is dependent on intraoperative assessment and meticulous recovery of the organ by experienced surgeons. This study aims to evaluate the impact on transplantation rate of pancreases when procured by the same or different teams.
Methods: NHSBT database was interrogated from January 2004 to April 2010 to evaluate all pancreas retrieved by one team. Dataset included type of donor,whether the organ was retrieved for the retrieving or for another centre, whether discarded and the reasons.
Results: During this period the retrieving centre attended 407 pancreas donors. This comprised 348 (85.5%) DBD & 59 (14.5%) DCD donors. 323 (79.4%) pancreases were intended for use by the retrieving centre. 84 (20.6%) organs retrieved for other centres. 239 (73.9%) pancreas were transplanted by the same team. 51 (60.7%) were used by other centres. Overall discard rate was 28.7%, 49% (29/59) for DCD and 25.2% for DBD (88/348). Common discard reasons were fatty organ (6.3%, 26/407), no cause specified (5.6%, 23/407), long cold ischemia (5, 1.2%), organ damage (5, 1.2%). During the same period 221 pancreases were retrieved by other centres for the study Centre. 111 (50.3%) were transplanted. Main discard reasons were fatty organ (5.8%, 13/221), damage (4.5%, 10/110).
Conclusions: Pancreas utilisation is higher when retrieving and transplant centre are the same (73.9% vs 50.3%). Likely causes related to donor selection, confidence on the retrieving centre's organ assessment and procurement. This is interesting as National Organ Retrieval Service (NORS) took over the organ recovery responsibility in the UK in April 2010, increasing separation between retrieving and transplant centres. Revisiting this data in the NORS era will assess likely effect and may confirm the subjective pancreas assessment nature.

RO-063 LIVE DONATION IN AN ETHNICALLY DIVERSE INNER CITY COMMUNITY

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Renal transplantation provides the best quality of life and survival for patients with endstage renal failure and consequently the need for donors has incrementally increased. In the UK, the incidence of endstage renal failure is 5 to 10 times greater in the non caucasoid population. Our centre serves a west London community which is particularly ethnically diverse and has a relatively low rate of deceased donation.
As a consequence, we actively promote live donation. In this study, we describe our 6 year experience of live donation in such a community
1477 donors [mean age 48.6 years] came forward between January 2005 and December 2010. 743 [50.3%] were Caucasians [C], 412 [[27.9%] were South Asians [SA], 217 [14.7%] were Blacks [B] (Afro Caribbean or African), and 105 [7.1%] of other ethnicity [O].
316/1447 (21.3%) live donor transplants were subsequently performed during this 6 year period.
More females [f] came forward as potential donors than males [m], [826 (55.9%) f and 651 (44.1%) m donors, $P < 0.05$] which was demonstrated in all ethnicities.
There was a noticeable difference between related [r] and unrelated donors [u] in the Black [149r (68.6%), 68u (31.3%)] and Other [75r (71.4%), 30u (28.5%), $p<0.05$] groups whereas a similar number of r and u donors came forward in the Caucasian [393r (52.8%), 350u (47.1%)] and South Asian groups [224r (54.3%), 188u (45.6%)].
43% of the live donor transplants were pre emptive and 59.4% were from Caucasian donors.
18.4% of the donors were excluded because of blood group mismatch and or positive cross matches; 75 recipients successfully underwent antibody removal prior to transplantation.
20% of our potential donors go ahead with transplantation. More women come forward than men, and live related rather than unrelated live transplantation is ethnically determined.

RO-064 LESS LIVING DONOR NEPHRECTOMY: SURGICAL TECHNIQUE AND RESULTS

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Purpose: We present the initial six patients undergoing pure LaparoEndoscopic Single site Surgery (LESS) transumbilical live donnor nephrectomy, betwenn February and September 2010.
Materials and methods: LESS donor nephrectomy was performed through an umbilical incision. Different trocars were used: The SILS port (Covidien, Hamilton, Bermuda), le R-port (Olympus surgical, Orangeburg, NY) and standard trocars inserted through the same skin incision but through separate facial punctures. The surgical technique duplicates the standard laparoscopic technique. The kidney was pre entrapped in a retrieval bag and extracted transumbilicaly. Data were collected prospectively and questionnaires containing patient-reported oral pain medication duration and time to recovery.
Results: LESS donor nephrectomy was successful in all patients. Mean warm ischemia time was 6.6 ± 2.3 min, hospitalisation stay was 4.0 ± 0.6 days with a visual analog pain score at discharge at 1.9 ± 1.1. No intraoperative complication occured. Mean Time of oral pain medication was 9.8 ± 5.4 days and final scar length was 3.9 ± 0.4 cm. Each allograft was functional.
Conclusion: Although challenging, LESS transumbilical living donor nephrectomy appears feasible and safe. LESS has the potential to improve cosmetic results and decrease morbidity.

RO-065 OPTIMIZATION OF LONG-TERM GRAFT SURVIVAL AFTER LIVER TRANSPLANTATION: THE ROLE OF DONOR AGE

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Background: Nowadays, several solutions have been proposed for the minimization of either organ shortage and long waiting time: expansion of donor pool using aged donors represents a possible solution. However, it is not completely clear if use of "extreme" donors could cause inacceptable post-transplant adjunctive risks. The aim of this study is to evaluate the impact of donor age on long-term graft survival.
Materials and methods: From January 2001 to April 2009, 188 consecutive liver transplantation were performed at our Department. The entire cohort was stratified in 4 subgroups according to donor age: Group 1 (1st-2nd decade, n=34), Group 2 (3rd-4th, n=51), Group 3 (5th-6th, n=75) and Group 4 (7th-8th, n=28). Donor, recipient and transplantation characteristics were compared in the 4 groups.
Results: D: onor age, percentage of cerebrovascular deaths, BMI and DRI resulted higher in the last group. Male gender was prevalent in the 1st Group, while macrovescicular steatosis resulted higher in the 3rd Group. Recipient and immediate post-transplant features resulted homogeneous among the groups. At survival analysis, 5-year graft survival rates resulted progressively

worsened among the groups (82.4 *vs* 73.3 *vs* 64.7 *vs* 39.6%, respectively). Statistical significance was observed between the first 2 Groups and 4th one (*p*-value 0.003 and 0.006, respectively), while a boundary statistical significance was observed between 1st and 3rd Group.
Conclusions: In our experience, use of < 70 year-aged donors seems to be safe, while very aged (over 70) donors give poor long-term survivals, despite similar initial post-transplantation results. We could speculate that grafts procured by very aged donors could be easier targets of viral recurrence, late ischemia-reperfusion damage and chronic rejection. A better allocation system for these organs may be improved, preferring HCC recipients who exceed transplants criteria to HCV ones.

RO-066 IN THE CREATION OF DOCTORS' AWARENESS OF ORGAN DONATION THE ADEQUACY OF MEDICAL EDUCATION

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In this study, we aimed to determine the adequacy of the transplant education in Hacettepe University Faculty of Medicine.
The survey questions about organ donation answered by 100 first year medical students who hasn't received any education about organ transplantation and 100 last year medical students who are completing their medical education.
64% of first year medical students, 90% of last year medical students think their knowledge about organ transplantation is sufficient. However, the percentage of students who think brain death can turn back or have no idea in first year students 54%, in last year students 27%. 80% of last year students said they get 1-4 hours of theoretical transplant eduaction and 53% of these students do not intend to donate their own organs. 12% of first year and 10% of last year students stated that they had donated their organs. 20% of first and last year students do not intend to donate their relatives' organs who received diagnosis of brain death.
The 1-4 hours of theoretical education about brain death and organ transplantation given to Hacettepe University Faculty of Medicine students, is seen as inadequate. This education did not increase the rate of last year students' own and relatives' organ donation. 27% of last year students still think brain death can turn back.
To increase the number of transplants done in our country, it should be ensured the participation of doctors who are informative, persuasive, practitioner. Therefore, the duration and the quality of the education in medical school should be increased.

RO-067 THE SOCIO-ECONOMIC CHARACTERISTICS OF LIVE KIDNEY DONORS IN A SINGLE UK CENTRE

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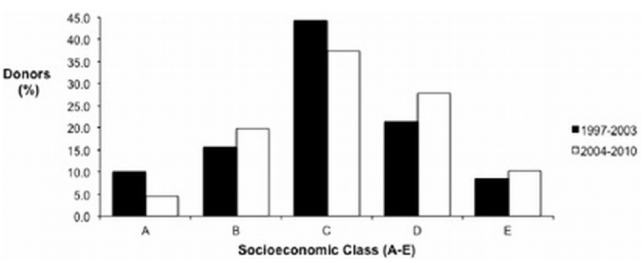
Background: Live donor nephrectomy (LDN) is a safe procedure with minimal impact upon donor quality of life [1]. Nonetheless, potential donors frequently cite loss of earnings and delayed return to work as disincentives. Financial recompense has been advocated to remove disincentives and improve rates of donation [2]. This study aimed to establish the socio-economic characteristics of our live donor population and to clarify changes occurring during the evolution of a live donor programme.
Methods: A retrospective study of our contemporaneous live donor database for the period January 1997 to March 2010 was performed. Donor occupation was classified according to the UK Office of National Statistics defined socio-economical classes (SEC). The SEC distribution was compared for earlier (1997 to 2003) and later years (2004 to 2010) of the programme.
Results: Thirty-nine (9%) donors were at or above the national retirement age



(60 yrs female, 65 yrs male). Seventy nine percent of donor occupations could be classified by the SEC scale (n=262) whilst 12% (n=32) were housewives and unclassified according to SEC. The SEC classifications showed 13, 38, 82, 53 and 20 donors in class A, B, C, D and E respectively. Figure 1 illustrates the SEC distribution remaining unchanged between 1997-2003 and 2004-2010 (Mann-Whitney U test, $p>0.05$).
Conclusion: Donor socio-economic demographics are unchanged when the early and later years of our live donor programme are compared. Knowledge of donor SEC demographics is important for live donor programmes, should a system of financial compensation be considered to motivate future donors.
References:
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2. Matas, A.J., *Design of a regulated system of compensation for living kidney donors.* Clin Transplant, 2008. 22(3): p. 378-84.

RO-068 THE FACTORS INCREASING THE RISK OF ACUTE KIDNEY INJURY IN DECEASED DONORS

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Background: As the organ donors shortage increases, the deceased patients with an acute kidney injury (AKI) diagnosed in an intensive care unit (ICU) are often considered as kidney donors. However, the risk factors for AKI development in kidney donors are only partly characterized. We analysed a broad spectrum of clinical and biochemical parameters, which might potentially increase the risk of AKI in our donor pool.
Material and methods: We collected data from all 61 deceased kidney donors, identified in one ICU between Jan 1999 and Dec 2006. They were stratified to the AKI or non-AKI group, according to RIFLE classification. We analyzed the management of deceased patients since the admission to ICU to the organ procurement.
Results: Out of 61 donors, 10 (16.4%) developed AKI. The creatinine concentration at the admission to ICU was similar in AKI and non-AKI group. Cerebral and multiorgan trauma were more frequent death causes in donors with AKI (80% vs. 35.3% in non-AKI group, p=0.014), whereas the prevalence of cardiovascular death was higher in non-AKI group (60.8% vs. 20%, p=0.034). Donors with AKI were characterized by twice as higher mean dopamine dose (10 *vs.* 5 μg/kg/min, $p<0.001$) and thrice as higher mean noradrenaline dose (0.65 *vs.* 0.2 μg/kg/min, p=0.06). Daily fluid supply and serum sodium concentration were similar at the time of drawing the suspicion of brain death, whereas the vasopressin dose was 10-fold lower in the last day before organ procurement (0.02 *vs.* 0.2 mg, $p<0.03$).
Conclusion: The intensive therapy with vasopressin immediately after drawing the suspicion of brain death may diminish the kidney injury and perhaps prevents AKI.

RO-069 WHAT PROPORTION OF POTENTIAL LIVE KIDNEY DONORS PROCEED TO DONATION? REVIEW OF 643 CASES WORKED UP BETWEEN 1996-2010

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Background: The number of live donor kidney transplants has increased dramatically in our unit from an average of 7 per year from 1996-2004 to 59 in 2010. The number of potential living donors entering workup has also increased year on year. This resulted in the rise of transplants despite a decrease in percentage of those who actually proceed to donation. We aim to identify the proportion of our potential donors that complete the work up and the reasons for not proceeding.
Methods: Prospectively collected data from all 643 potential live donors since 1996 has been analysed.
Results: 12% of all potential donors competed the workup satisfactorily and proceeded to donation. The main reasons for not proceeding were donor withdrawal (24%), inadequate GFR (19%), positive cross-match (10%), blood group incompatibility (10%), unfit recipient (6%), donor hypertension (5%), diabetes (4%) and obesity (1%). Over the 14 years, the leading causes for not proceeding was donor withdrawal and inadequate GFR. Donors presenting with hypertension, diabetes or obesity have been increasing over the last 5 years.
Conclusions: As the number of live donor kidney transplants increased over the last 6 years we simultaneously observed an increase in the numbers not

proceeding to donation. The most common reasons were donor withdrawal and inadequate GFR. There has also been an increase in the number of donors with hypertension, diabetes and obesity. Such donors may not be able to proceed but are treated earlier than they would normally have. Antibody incompatible transplantation and the pair exchange scheme will deal with some of the ABO and HLA incompatible cases. For now we have to workup more and more potential donors every year to keep the same level of activity.

RO-069A THE EFFECT OF EVOLVING CVA MANAGEMENT UPON TRANSPLANT DONATION IN THE UK

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Background: In 2010-11, 595 of 1010 (58.9%) UK cadaveric organ donors died of intracranial haemorrhage (CVA donors, NHSBT data) thus, evolving CVA management might affect organ donation.
Methods: The Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme (CMP) collects prospective data for consecutive admissions to adult critical care units in England, Wales and Northern Ireland. All admissions to critical care units participating in the ICNARC CMP, coded as *non-traumatic* subarachnoid haemorrhage, intracerebral haemorrhage, berry or other intracranial aneurysm or intracranial arterio-venous malformation (collectively termed CVA) were selected for analysis. Both a cohort of recent data (pooled data 2007-10) and trend data (annual cohorts 2000-2010) were identified.
Results: *Cohort analysis.* 8739 CVA admissions to 203 critical care units were identified between 2007-2010. Of these, 2725 (31.1%) died. Of those who died, 1122 (41.2%) were declared brain stem deaths and 1605 (58.9%) were circulatory deaths. These deaths yielded 610 and 175 donation episodes, respectively. Overall, 785 (8.9%) of patients admitted for critical care following CVA became organ donors.
Trended data: 26,012 CVA patients to 229 critical care units were identified between 2000-2010. Mean severity at presentation decreased, and more patients were treated on neurosciences units. Crude unadjusted critical care unit mortality decreased from 47.1% in 2000 (95% CI 44.4-50.0%) to 30.1% in 2010 (95% CI 28.6-31.6%). Brain stem death, as a proportion of all deaths, decreased from 48.6% (95% CI 44.7-52.6%) to 40.2% (95% CI 37.3-43.1%) over the same time period.
Conclusions: These data suggest critical care unit mortality may be decreasing in CVA patients, and more are now treated in neurosciences critical care units. The shift towards circulatory rather than brain death will decrease the number of available donors.
References: Devey, L. & Wigmore, S. J. Non-heart-beating organ donation. Br J Surg 96, 833-835 (2009).

RO-069B THE FIRST YEAR OF A NATIONAL ORGAN RETRIEVAL SERVICE IN THE UK

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Introduction: In April 2010, a National Organ Retrieval Service (NORS) was introduced in the UK as recommended by the UK Organ Donation Taskforce. We have reviewed the first 12 months of this national retrieval service.
Methods: The UK NORS comprises seven abdominal and six cardiothoracic organ retrieval teams, based in liver/pancreas/kidney and cardiothoracic transplant centres in the UK. Each team is on call 24 hours a day, seven days a week, and has a defined geographical area associated with it such that travel time to any of the donor hospitals in that area should not exceed 3 hours wherever possible. Each team is obliged to attend any donors identified in their area, unless they are already retrieving elsewhere. There is a defined rota for other teams to attend the donor hospital in these circumstances. Retrieval areas are not directly linked to areas defined for priority for organ allocation.
Results: In the first 12 months of the NORS, there were 1010 deceased organ donors in the UK representing a 5% increase over the previous year. 637 (63%) were donors after brain death (DBD) and 373 (37%) were donors after circulatory death (DCD). In addition, 299 non-proceeding donors were reported as attended by a retrieval team. All but 23 of the donors were attended by a NORS team. These exceptions were DCD kidney only donors attended by local kidney transplant teams. In total, donors were attended by the primary, designated team for that hospital in 79% of abdominal and 76% of cardiothoracic organ retrievals. Retrieval team travel times were within 3 hours for 94% of abdominal and 96% of cardiothoracic organ donors.
Conclusions: The UK has successfully introduced a national organ retrieval service to provide expeditious organ retrieval by dedicated, expert teams available 24 hours a day.

RO-069C NECMO IS BETTER THAN IMMEDIATE COOLING AFTER UNCONTROLLED CARDIO-CIRCULATORY DEATH

Benoit Barrou[1], Frederic Thibault[1], Karim Ferhi[1], Emmanuel Van Glabeke[1], Stéphane Bart[1], Nebjosa Zivanovitch[1], Armelle Nicolas Robin[3], Nadia Arzouk[2], Victor Gueutin[2], Saida Ourahma[3], Pascal Leprince[4], Gilbert Deray[3], Bruno Riou[3], Marc Olivier Bitker[1]. *[1]Urology, GH Pitié Salpetrière, APHP, Université Paris VI, Paris, France; [2]Nephrology, GH Pitié Salpetrière, APHP, Université Paris VI, Paris, France; [3]ICU, GH Pitié Salpetrière, APHP, Université Paris VI, Paris, France; [4]Cardiothoracic Surgery, GH Pitié Salpetrière, APHP, Université Paris VI, Paris, France*

Purpose: To compare normothermic abdominal reperfusion to immediate cooling in donors after cardio-circulatory death (DCD) on early renal transplant function recovery.
Methods: 45 kidney transplants were performed between May 2007 and Mars 2011, with the same immunosuppression regimen in a single institution. Two different ways of perfusing the kidneys were used, either by an initial normothermic Extracorporeal Oxygenation Membrane Support (nECMO) followed by a subsequent cooling phase (n=26), or by immediate cooling (IC, n=19). Grafts were all machine perfused (Lifeport®, ORS). Donor and recipient ages, cold and warm ischemia times were not statistically different. Statistical analysis was performed with the Fischer's and Wilcoxon's tests.
Results: Recovery of renal function occurred earlier in nECMO as assessed by 1) date of diuresis recovery (day 1.5±3 in nECMO vs. 5.4±6.7 in IC, $p<0,04$); 2) cases with no PO hemodialysis (35% in NECMO and 26% in IC, ns); 3) number of PO hemodialysis sessions (3.5±1.9 in nECMO vs. 5.6±1.8 in IC, p=0.009); 4) serum creatinine level at M1 (203 μmol/l ±98 in nECMO vs. 310 μmol/l ±155 in IC, p=0.009). Patients in nECMO were discharged earlier (21.4±8.7 days vs. 28.6±9.3 in IC group, p=0.01). With a mean follow-up of 19±13 months, patient and graft survivals were respectively 98% and 95,5%.
Conclusion: Management of DCDs with nECMO allows earlier renal function recovery and should be regarded as the method of choice.

Tissue injury / preservation I

RO-070 OXYGENATED IN SITU COLD PERFUSION OF DCD KIDNEYS IN PIGS

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Kidneys retrieved from Deceased Cardiac Death (DCD) donors are subjected to extended periods of warm ischemia (WI). To improve outcome after DCD donation we examined the effect of cold oxygenated in situ perfusion (ISP) in pigs.
Methods: Pigs were subjected to cardiac arrest followed by 20 min no-touch. In the ctrl group (n=7) a rapid laparotomy was performed and an abdominal systemic flush-out with 4 liters of UW solution through the aorta was performed. In the ISP group (n=8) flush-out was performed by pulsatile perfusion of oxygenated UW at 25 mmHg through the aorta using the ECOPS device (Organ Assist BV). After the abdominal flush-out, an isolated renal circulation was created. In both groups, aortic and renal flow as well as renal temp. was measured fro 90 minutes. Kindeys were retrieved and cold stored for 20 hrs in UW followed by transplantation. During the 14 day follow up period renal function was measured and biopsies were taken at time of sacrification.
Results: Donation: During the organ procurement procedure renal temp. during flush-out decreased to 25±3°C in the ctrl group and 23±3°C after 15 minutes. Flow-rate of UW in the aorta was higher in the ctrl group compared to the ISP group (221±12 ml/min vs. 147±24 ml/min), however renal artery flow did not differ due to large variation in the ctrl group. After 90 minutes, renal temperature in the ISP group (19±2°C) was significantly lower than the ctrl group (25±2°C).
Post transplant function: In the control group 2 animals suffered from PNF in contrast to none in the ISP group. At day 1and 2 after tx urine production was higher in the ISP group and a better GFR was observed. After 2 days no differences in renal function could be detected anymore.

RO-071 QUALITY ASSESSMENT OF HEART BEATING AND NON-HEART BEATING LIVER GRAFTS THROUGH microRNAs IN PRESERVATION SOLUTION

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Introduction: Biliary complications related to initial ischemic injury of the graft

are a severe clinical problem after liver transplantation (LTx), and are more common after non-heart beating (NHB) compared to heart beating (HB) donation. Outcome of transplantation could be improved if bile duct quality could be assessed prior to LTx. Recently, liver-derived microRNAs (miRNAs) have been identified as sensitive markers for liver injury in serum. Whether miRNAs are detectable in graft preservation solution is unknown. The aim of this study is to investigate if miRNAs are detectable in preservation solution at time of transplantation and can be used as a marker for injury in HB and NHB liver grafts.
Methods: Perfusate flush with University of Wisconsin (UW) solution of sixteen consecutive liver grafts were collected. Cell-free solutions were concentrated and analyzed for the presence of hepatocyte-abundant miRNAs (miR-122 and miR-148a) and cholangiocyte-abundant miRNAs (miR-30e and miR-296) by quantitative RT-PCR.
Results: Detection of hepatocyte and cholangiocyte-derived miRNAs in UW preservation solution proved to be technically feasible. Levels of hepatocyte and cholangiocyte-derived miRNAs were positively correlated ($R \geq 0.89$; $P < 0.001$). Additional analysis was performed determining the ratio between cholangiocyte-derived and hepatocyte-derived miRNAs from HB (n = 11) and NHB (n = 5) liver grafts. Significantly higher ratios were found in NHB versus HB liver grafts ($P < 0.05$).
Conclusion: Hepatocyte and cholangiocyte-derived miRNAs are detectable in liver graft preservation solution. The different ratio of cholangiocyte and hepatocyte-derived miRNAs between HB and NHB donors may reflect the more prominent bile duct injury known to be associated with NHB donation. The non-invasive detection of specific miRNAs in preservation solution may represent a novel method to assess graft quality early during LTx.

RO-072 PHARMACOLOGIC PRECONDITIONING PROTECTS LIVERS AND LUNGS AGAINST INFLAMMATORY REACTION OF THE SPLIT LIVER PROCEDURE

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Introduction: In split liver transplantation a high incidence of hepatic artery thrombosis and primary graft dysfunction can be observed. Beside surgical reasons inflammatory reactions are discussed. The present study analyzes the consequences of a in-situ split liver procedure and the influence of a multi-drug-donor preconditioning (MDDP).
Material and Methods: Sprague-Dawley rats were divided into 3 groups (n=8 each); In the control group (SLC) and the pretreatment group (SLM) we simulated a liver splitting with a 1-1,5cm cut in the left median liver lobe, while unsplitted livers served as Sham. MDDP was initiated 30min before starting the cold perfusion with HTK for organ harvesting by applying simvastatin, N-acetylcysteine, erythropoietin, pentoxyphylline, melatonin, glycine and DFO. The Sham and the SLC received 2.0ml NaCl 0.9% instead. Tissue samples of the liver and lung were taken immediately and after 8h cold storage in HTK.
Results: The leucocyte infiltration of the liver after 0 and 8h (SL: 2.2±0.4 CAE positive cells/HPF) were significantly higher in SLC compared to the Sham (0.86±0.2; $p<0.05$) and could be clearly reduce by MDDP (1.2±0.2; $p<0.05$). The TNF-alpha plasma and tissue levels were also significantly higher in SLC than in SLM (plasma: 350.4±91.3 versus 2.6±1.1 pg/ml; $p<0.05$ and tissue: 788.2±29.4 versus 570.6±47.5 pg/mg; $p<0.05$). Even in the lung, the leucocyte infiltration could be lowered by MDDP compared to SLC (3.0±0.4 versus 1.9±0.2 CAE positive cells/HPF, $p<0.05$).
Summary: In-situ liver splitting induced a marked release of proinflammatory cytokines. Our data showed a leucocyte migration in the liver and lung tissue, immediately after organ retrieval and after 8h preservation. MDDP could significantly decrease the intrahepatic and systemic inflammatory reactions.

RO-073 PRESERVATION SOLUTION AND METHOD AFFECT ORGAN TEMPERATURE DURING PROCUREMENT

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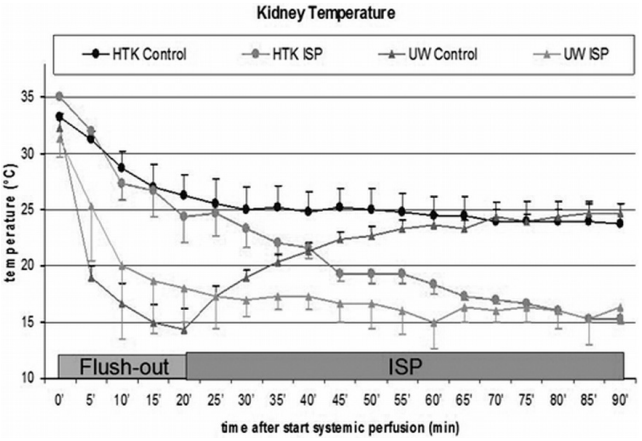
Rapid cooling during procurement by intravascular administration of preservation fluids combined with topical cooling is common practice to reduce metabolic rate (MR). The true reduction in MR depends on the efficacy of cooling. At 4°C MR is reduced with 90% while at 25°C a reduction of 50% is reached. Recent clinical assessment during procurement in our retrieval areas revealed renal temperatures at the end of procurement of 19.4±0.8 °C (Groningen) and 19.2±4.2°C (Paris) after flush-out with 4-6L UW.
To get more insight in the efficacy of cooling we compared in a pig model two commonly used preservation solutions UW and HTK. We also studied if cold continuous in situ perfusion (ISP) would result in lower temperatures. Four regimen were studied: Gravity flush with UW (Ctrl-UW) or HTK (Ctrl-HTK) and ISP with UW (ISP-UW) or HTK (ISP-HTK)
Exp: Methods: Cardiac arrest was induced by ventilator switch-off procedure. In the Ctrl groups a rapid laparotomy was performed followed by an abdominal systemic gravity-based flush-out with 5L UW or 9L HTK.
In the ISP groups flush-out was performed by pulsatile perfusion of oxygenated preservation solution at 25 mmHg. After the abdominal flush-out with 4 L UW or 8 L HTK, an isolated renal circulation was created. In all groups renal temperatures were measured.
Flush-out with UW resulted in lower temperatures compared to HTK. Despite topical cooling in the Ctrl groups renal temp. increased after flush-out. Compared to Ctrl in both ISP groups temperatures decreased further reaching a difference of 10°C.



It can be concluded that during clinical and experimental procurement renal temperatures are much higher than the desired 4 °C and depend on the type of solution used. ISP could be a valuable tool to decrease MR during procurement reducing WI and DGF.

RO-074 A PREOPERATIVE PROTEIN DEFICIENT DIET PROTECTS AGAINST RENAL AND HEPATIC ISCHEMIA AND REPERFUSION INJURY

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Background: Ischemia/reperfusion (I/R) injury is a serious complication after organ transplantation. Two weeks of 30% dietary restriction (DR) and three days of preoperative fasting protect against renal and hepatic I/R injury. We investigated whether the protective effect was induced by a reduction in calories, or a specific food component.
Materials and methods: C57BL/6 mice (n= 4-6/group) had ad libitum access to diets deficient in different food components for 14 or 3 days before induction of renal I/R injury. I/R injury was assessed by serum urea levels and signs of animal discomfort. Hepatic I/R injury was determined by serum ALAT and LDH levels and amount of hemorrhagic necrosis. Mice fed ad libitum control diets and pair-fed (PF) controls for the deficient diets were used as control.
Results: A 14 day protein-, methionine-, tryptophan- or leucine-deficient diet protected against renal I/R injury. PF controls revealed that mice on modified diets restricted their calorie intake by 30%. Since we previously showed that 30% dietary restriction for 14 days induces protection against I/R injury the effect of individual dietary components could not be separated from the effect of DR. Three days of DR does not induce protection against I/R injury. Therefore we showed that a deficiency in a specific food component induces protection. A protein-deficient diet protected against renal I/R injury. Whereas a 3 day protein- or leucine-deficient diet protected against hepatic I/R injury.
Conclusion: A preoperative protein-deficient diet protects against renal and hepatic I/R injury. These data show that proteins are responsible for the protection induced by DR.

RO-075 PRESERVATION OF NORMAL MORPHOLOGY OF HUMAN LIVERS AFTER 24 HOURS OF HYPOTHERMIC MACHINE PERFUSION. A FIRST-IN-MAN STUDY

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Background: Hypothermic Machine Perfusion (HMP) of kidneys preserves organ integrity better and longer than Simple Cold Storage (SCS). Interest in liver HMP is increasing but there are no data on the capacity of HMP to preserve the morphology of human livers for prolonged periods. We developed an HMP device for human livers with dual arterial/portal perfusion and separate pressure/flow controls.
Methods: After ethical and Belgian Liver Intestine Committee (BLIC) approval, 6 human livers considered potentially transplantable but discarded due to mild changes, recipient contra-indication and eventually failed ET-reallocation were machine-perfused during 24hrs at 4-6°C using preservation solution KPS-1™. Metabolic/biochemical/hemodynamics parameters and standard/electron microscopy were assessed.
Results: During HMP, pO2 decreased whereas pCO2 increased, suggestive of initial aerobic metabolism rapidly replaced by anaerobic metabolism as indicated by rising lactate and decreasing pH. AST in perfusate progressively increased: 538±484, 631±515, 927±657 and 945±573 IU/L at 30min, 1, 6 and 24hrs. Arterial and venous vascular resistances decreased from 1.29±0.67 and 0.25±0.30 (at the start) to 0.52±0.47 and 0.13±0.13 mmHg/min/ml after 24hrs HMP ($p=0.13$ and $p=1$, respectively). On detailed light/electron microscopic examination after 24hrs HMP, morphology/architecture was well-preserved. Some sinusoidal dilatation and enlargement of Disse space were seen. Hepatocytes, Kupffer and sinusoidal cells ultrastucture was well-maintained. Anoxic vacuoles were seen in some hepatocytes. Occasionally, hepatocytes contained slightly swollen mitochondria with less electron-dense matrix (reversible changes) or more rarely, flocculent densities (irreversible changes). Other cytoplasmic organelles appeared normal.
Conclusion: This study shows -for the first time- that HMP is capable to preserve the morphology and cellular integrity of human livers for prolonged periods (>24hrs). Randomized control trials of transplantation of machine-perfused livers are planned to determine the added value of HMP compared to SCS to preserve human livers.

RO-076 LIVER WASHOUT PRECONDITIONING: A USEFUL TOOL TO PROTECT THE GRAFT AGAINST REPERFUSION INJURY

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Antecedents: Hepatic ischemia reperfusion injury contributes to the initial poor function or primary non-function after transplantation. This is due to the cold preservation, rewarming and reperfusion, respectively. We evaluated the benefits of using a new rinse solution for flushing liver grafts before reperfusion.
Experimental: Sprague-Dawley rats (180-200 g; n= 6 for each group), were classified as follows: Group 1 (controls) = Livers preserved in UW solution (24 hours; 4 C) were flushed with Ringer lactate solution (at room temperature)and then subjected to 2 h-reperfusion at 37 C using an isolated perfused liver model; Group 2 (washout solution) = Same as 1 but the liver grafts were flushed (at room temperature) with the new rinse solution composed by CaCl2.2H2O (1.3 mM), KH2PO4 (5 mM), NaH2PO4 (20 mM), MgSO4.7H2O (5 mM), lactobionate (100 mM) and rafinose (30 mM) at pH=7.4; Group 3 = Same as 2 but with polyethyleneglycol-35 (PEG35) addition at 5g/L and Group 4 = Same as 3 but with PEG35 addition at 1g/L. Liver injury (AST/ALT) and function (Bile,%BSP, vascular resistance) were measured and correlated with activated adenosine monophosphate protein kinase (AMPK) and heme-oxygenase-1 (HO-1) and HSP70 activities, oxidative stress (MDA) and nitric oxide (NO).
Results: The use of this graft washout solution prevented liver injury (AST/ALT) and ameliorated hepatic function (bile production, vascular resistance) when compared to those washed with RLS, only. This was accompanied by decreases in GLDH levels (mitochondrial lesion) and oxidative stress. Graft washout benefits were associated with increases in NO (e-NOS activation); as well as the induction of cytoprotective factors such as AMPK and HO-1 and HSP70, respectively.
Conclusion: This new "washout" solution containing PEG35 protects the liver grafts against reperfusion injury.

RO-077 HYPOTERMIC MACHINE PERFUSION (HMP) VERSUS STATIC COLD STORAGE (CS) IN KIDNEY ALLOGRAFT PRESERVATION. PROSPECTIVE CASE-CONTROL TRIAL

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Background: The shortage of organ availability for transplant has led to an increased use of expanded criteria donors grafts to enlarge the donors pool. It has been suggested that HMP may improve early outcome after transplantation of kidneys donated after cardiac death, but no prospective case control trial have been reported in brain death donor. Aim of the present trial is to identify the most effective preserving method comparing in a randomized case-control trial hypothermic machine perfusion with the current standard of static cold storage preservation.
Methods: From October 2008 to February 2011, 59 pairs of kidney from consecutive 18 to 79 years old donors were included in the present trial. One kidney was randomly assigned to HMP and the contralateral kidney to CS. Among the 59 kidneys enrolled in HMP group, 11 have been excluded for technical/logistic issues or renal artery unavailability. Primary endpoint was delayed graft function (DGF), secondary endpoints were DGF lenght, primary non function (PNF), serum creatinine level and clearance, acute rejection, acute tubular necrosis, length of hospital stay and allograft and patient survival.
Results: No statistically significant difference was found between graft preserved by machine perfusion and cold storage in terms of DGF rate (37,8% vs 30%, respectively $p>0.05$). No significant differences were observed for the other secondary end points.
Conclusion: The effectiveness of preservation with HMP in brain death donors, both ideal and marginal, appear controversial; more data need to be collected in selected donors.

RO-078 GASEOUS HYDROGEN SULFIDE (H_2S) IS PROTECTIVE DURING CARDIAC ISCHEMIA/REPERFUSION

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H_2S can reversibly induce a hypometabolic state in mice, and has anti-apoptotic, anti-inflammatory and ROS scavenging properties. We investigated whether gaseous administration of H_2S is protective in cardiac IRI and whether a state of hypometabolism is required for a beneficial effect.
Male C57BL/6 mice were assigned to one of three different treatment regimens receiving 0 (control), 10 ppm, or 100 ppm H_2S starting 30 minutes pre-ischemia until 5 min pre-reperfusion. IRI was inflicted by temporary ligation of the left coronary artery for 30 minutes. Core body temperature was maintained at 37°C. CO_2-production during H_2S treatment was measured by respirometry. Cardiac damage and fibrosis were determined in haematoxylin-eosin (1 d) and Masson (7d) stained sections. To investigate granulocyte influx, sections were stained for Ly-6G.
CO_2-production of mice treated with 100 ppm H_2S rapidly declined to ~60% of basal levels. Treatment with 10 ppm had no effect on CO_2-production. IRI caused significant damage in controls compared to sham-operated animals after 1d and 7d ($p<0.01$). No effects of 10 ppm H_2S on relative infarct size was observed at 1d, while treatment with 100 ppm H_2S reduced infarct size by 62% ($p<0.05$). At 7d, both 10 ppm and 100 ppm H_2S showed a reduction in fibrosis compared to control animals (relative fibrotic area: sham 2.0%; control 17.2% ($p<0.001$ vs sham); 10 ppm 7.0%; 100 ppm 7.4% (both $p<0.01$ vs control)). The influx of granulocytes was reduced by 46% after treatment with 100 ppm H_2S ($p<0.05$) but was not affected by 10 ppm H_2S.
We conclude that gaseous administration of H_2S is a promising treatment for reducing cardiac IRI. Since IRI is a frequent and important cause of myocardial damage during cardiac transplantation, H_2S may be used in these settings to salvage myocardial function.

RO-079 IDENTIFICATION AND QUANTIFICATION OF CIRCULATING ENDOTHELIAL CELLS IN PORCINE MODELS

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Introduction: Endothelial cell damage is regarded as a crucial step in the pathogenesis of several vascular disorders. In humans, the amount of circulating endothelial cells (CECs) correlates to disease intensity and plasma markers as von Willebrand factor and E-selectin in ANCA-associated vasculitis, kid-

ney transplantation, diabetes, cardiovascular diseases, and cerebrovascular events. Since a large proportion of research in kidney transplantation and cardiovascular diseases is performed using pigs, identification and quantification of CEC potentially provides a vualuable tool as marker for disease intensity. This study is designed to identify and quantify porcine crossreactivity with anti-human antibodies.
Methods: Crossreactivity to porcine endothelium was tested in human umbilical vein endothelial cells (HUVEC) and its porcine equivalent (SUVEC) using Lectin-1, PAL-E, CD31, CD51, CD54, CD105, and CD144 with FACS analysis. CD146 (Mel-Cam) clones which are of particular interest due to its specificity for endothelium, were additionally tested using confocal microscopy of immunostained cell cultures (CM) to compare cellular binding sites. Activated HUVEC and SUVEC (Il-1 stimulated) were compared to non-activated cells for CD62E and CD106 expression.
Results: The CD105 clones MEM-229 and SN6 tested positive for porcine endothelium using FACS, but only MEM-229 provided sufficient staining for CM. The CD146 p1h12 clone tested positive on porcine endothelial cells. Lectin-1 also tested positive but induced significant changes in side scattering during FACS analysis of SUVECs. In contrast to HUVECs, CD106 (VCAM-1) tested positive in SUVECs despite the activation state of endothelial cells. The tested PAL-E, CD31, CD51, CD54, CD62E, and CD144 clones all tested negative using FACS.
Conclusion: CD146 p1h12 and CD105 MEM-229 showed crossreactivity with SUVECs and CM without displaying cellular alterations as with lectin-1. These findings show that CEC can be assessed on a quantitative basis in porcine models.

RO-080 THE EFFECT OF NORMOTHERMIC RECIRCULATION BEFORE COLD PRESERVATION ON POSTTRANSPLANT INJURY OF ISCHEMICALLY DAMAGED DONOR KIDNEYS

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Kidneys recovered from donation after cardiac death (DCD) are increasingly used to enlarge the deceased donor pool. Such renal grafts, especially those derived from uncontrolled DCD, have inevitably sustained profound warm ischemic injury, which compromises posttransplant function. Normothermic recirculation (NR) of the deceased donor's body before organ cooling could be an interesting approach to mitigate the detrimental effect of warm ischemia. To date, however, there is no evidence coming from preclinical studies to support the principle of NR in kidney transplantation. In this study, we subjected 48 Lewis rat kidneys to 15 or 30 min of warm ischemia, and subsequently 0, 1, or 2 h of NR. After 24 h cold storage kidneys were transplanted into a recipient animal and 24 h later we measured the percentage of cortical necrosis, and determined gene expression of heme oxigenase-1, heat shock protein-70, transforming growth factor-β, kidney injury molecule-1, interleukin-6, hypoxia inducible factor-1α, monocyte chemoattractant protein-1, and α-smooth muscle actin in kidney tissue. We found that NR had no significant influence on any of these markers. Therefore, we conclude that this preclinical study by no means supports the presumed beneficial effect of NR on kidneys that have been severely damaged by warm ischemia.

RO-081 STRATEGY FOR REDUCING THE DISCARD RATE FOR CADAVERIC KIDNEYS

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For 30 years the discard rate for cadaveric kidneys has ranged from 12%-18%. While discard criteria varies in terms of parameters, donor characteristics are imperfect indicators of subsequent graft function. The result is the discard of kidneys that may be usable and transplantation of allografts that perform poorly. Novel prognostic screening methodology that more accurately predicts posttransplant function, beyond kidney biopsies that do not correlate well with 1-year graft function, could help to reduce discard rates. We evaluated whether an acellular, near-normothermic perfusion technology could be used to prospectively evaluate function in human cadaveric kidneys procured for transplant but later discarded.
Methods/Materials: Ten human kidneys were obtained following discard. Reasons for discard included $>$20% GS, prolonged cold ischemia (CI) ranging from 25-50hours, adrenal pheochromocytoma, calculated CrCl and poor hypothermic perfusion characteristics. All kidneys were hypothermically stored prior to receipt. The kidneys were weighed, cannulated and transitioned to near-normothermic perfusion for 12-24 hours of evaluation. The evaluation consisted of oxidative metabolism, vascular dynamics and organ function.
Results: Resuscitated O_2-consumption ranged from 0.08-0.29cc/min/g, with the highest rates in the kidneys discarded due to prolonged CI. Once vascular dynamics normalized, stable MAP and flow rates were observed throughout the rest of the perfusion; although improvements were observed in some kidneys. In several cases, predominantly kidneys with prolonged CI, urine flow was restored suggesting that warm perfusion provided not only a means to evaluate discarded kidneys ex vivo but also a mechanism to restore function.
Conclusions: These results provide evidence that discarded kidneys can be evaluated prospectively for restored metabolism, vascular dynamics, regeneration, function and may provide a basis for lowering the discard rates based upon quantified data. The identification of biomarkers that can be evaluated while a kidney is actively metabolizing ex vivo could further enhance the prognostic testing.

RO-082 A NOVEL CELL CULTURE MODEL FOR STUDYING HEPATIC ISCHAEMIA REPERFUSION INJURY

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Introduction: Under standard tissue culture conditions (high glucose); a significant proportion of cellular ATP is generated from anaerobic glycolysis and not mitochondrial respiration. To reflect clinical liver preservation and transplantation, cell lines needs conditioning to utilize mitochondrial pathways for energy production. The objective of this study is to develop a liver line that can be switched to mitochondrial aerobic metabolism, making this an ideal model for studies of hepatic ischaemia-reperfusion injury.
Methods: Human liver stem cells and cancer cell lines (HepG2) were grown on standard culture media, reduced glucose levels or switched to mitochondrial substrate (glutamate) and examined for metabolic fluxes and energy production. Human liver stem cells (developed from fetal liver stem cells that express a range of markers for adult hepatocytes i.e. albumin, CK8, CK18 and P450 enzymes) were treated the same way. Mitochondria were isolated to measure mitochondrial state 3 & 4 respiration, respiratory control ratio (RCR) and ATP production. Live cell imaging was performed to assess mitochondrial membrane potential and mitochondrial morphology (mitotracker green).
Results: Human liver stem cells show a significant increase in mitochondria mass (Mitotracker green fluorescence, flocytometry) when incubated with the mitochondrial substrate glutamine and fourfold increase in mitochondrial RCR with parallel increase in ATP production ($p<0.005$). HepG2 liver cells were grown in the similar culture conditions (late passage) also showed similar change to mitochondrial metabolism. However early passage HepG2 cells remained anaerobically poised.
Conclusion: These data indicate that specific culture conditioning and mitochondrial substrate can drive cells to utilise mitochondrial oxidative phosphorylation for ATP generation. With its validation, this model could be more specific to study mechanisms related to hepatic ischemia reperfusion injury at the cellular and mitochondrial level.

RO-083 THE RELATIONSHIP BETWEEN THE PARAMETERS OF HYPOTHERMIC PULSATILE MACHINE PERFUSION (HPMP) OF KIDNEY GRAFTS FROM DONORS AFTER CARDIAC DEATH (DCD) AND POST-TRANSPLANT KIDNEY FUNCTION

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Introduction: DCD donors have increased rates of primary non-function and delayed graft function as compared to kidneys from Donors after Brain Death (DBD). Organs can be preserved using cold storage or HPMP. Recent evidence regarding the use of HPMP is controversial.
Methods: The records of machine-perfused (LifePort©) DCD kidney transplants performed at a single unit between 2002 and 2009 were reviewed. The times taken to achieve ideal flow ($\geq$80ml/min) and resistance ($\leq$0.25Ω) when placed on the machine were compared with serum creatinine (SCr) levels at one and three months post-transplantation. Comparison was also made with the number of days until graft function. Linear regression analysis was used to compare the data. Results were expressed as the coefficient of determination, R^2, to give a best-fit value from 0 to 1.
Results: 84 kidneys were machine-perfused before transplantation. Mean donor and recipient age were 39$\pm$14 years and 52$\pm$11.5 years respectively. Warm and cold ischaemia time were 10$\pm$24 minutes and 16$\pm$4.4 hours respectively. Re-warming time was 32$\pm$15.3 minutes. Kidney graft reperfusion was good in 87%, fair in 12% and patchy in 1%. SCr at one month and three

months were positively correlated with the time taken until normalisation of flow (R^2 = 0.4236 and 0.4812 respectively). SCr at one month and three months were positively correlated with the time until normalisation of resistance (R^2 = 0.5261 and 0.4714 respectively). The longer the period until normalisation of flow weakly correlated with a greater number of days until graft function (R^2 = 0.3563).
Conclusion: The time taken for the normalisation of perfusion parameters may provide a useful prognostic indicator of long-term DCD kidney transplant function and allow for early therapeutic intervention.

RO-084 ECULIZUMAB FOR SALVAGE IN POST-TRANSPLANT THROMBOTIC MICROANGIOPATHY

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Background: Eculizumab, a humanised monoclonal antibody targets complement protein C5, inhibiting cleavage into C5a and C5b, and therefore prevents formation of the Membrane Attack Complex (MAC). It has been used rarely in renal transplantation: there are two published case reports of its use in confirmed Antibody Mediated Rejection (AMR), but none in post-transplant Thrombotic Microangiopathy (TMA)
Methods: In a single centre's ABO blood group-incompatible renal transplant programme, 2 patients developed post-transplant TMA (with no previous history of atypical haemolytic uraemic syndrome). One patient had received alemtuzumab (Campath) induction, the other rituximab followed by three cycles of double filtration plasmapheresis (DFPP). Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil and steroids.
Both patients presented with deteriorating renal function. Percutaneous renal transplant biopsies demonstrated TMA, with no underlying cause identified. After a number of further inconclusive investigations, and treatment for probable causes (such as AMR and calcineurin inhibition), no improvement was seen. Both patients were therefore commenced on eculizumab: a single dose of 1200mg followed by 4 further 600mg doses at weekly intervals.
Results: In both patients, after administration of eculizumab, renal function and platelet count stabilised, allowing time for further investigations and treatment. One patient is 3.5 months post-transplant with a most recent creatinine of 378, the other is 4.5 months post-transplant with a most recent creatinine of 131.
Conclusion: This is the first report of the use of eculizumab in patients with post-transplant TMA of unknown cause. Eculizumab was used to protect the renal allograft, preventing further damage to the kidney and allowing time for accommodation to occur. We conclude that eculizumab can be used as salvage therapy in cases of TMA of unknown cause to protect the graft, preventing renal damage while diagnostic measures and appropriate treatments are performed.

Ethics, legal and psychosocial aspects of transplantation

RO-085 ETHICAL DILEMMAS IN RELIGION-BASED ORGAN DONATION

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Background: Although the majority of world religions are in favor of organ transplantation, few of them are actively promoting it. Such is the case of the Jesus Christians, who represent a group of people among whom the majority of them have performed unrelated living donation of a kidney out of religious reasons. The paper will inquire into the ethical and religious dimensions of their donations, as our main focus is on the ethical attitude of altruist donation.
Materials/Methods: We perform a literature review on the Jesus Christians, focusing mainly on the ethical and religious aspects of altruistic live donation. In addition, the impact of their acts is analyzed in both traditional and non-traditional media.
Results: Although the altruist dimension of live donation is highly praised, many transplant professionals have difficulties and ethical dilemmas in assessing the role of religious motivations for religious groups. Moreover, the problematic issues of solicited donations, lack of anonymity, and search for publicity are analyzed as factors impeding on donation.
Conclusions: It is evident that this group, as a case study, is more important for the ethical and religious issues than for the medical issues related to organ donation and transplantation. However, it suggests the potential that, in certain cultural contexts, ethics and religion may have in promoting the idea of altruist donation.

RO-086 A MODEL FOR ORGAN DONATION IN SWITZERLAND, THE LATIN ORGAN DONATION PROGRAMME (LODP); AN ONGOING SUCCESSFUL REGIONAL INITIATIVE

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Background: The 1st Swiss federal Transplant Law was finally enforced in July 2007 with the obligation to promote quality and efficiency in transplant procedures. The LODP was created to develop organ and tissue donation in the Latin area of Switzerland covering seventeen hospitals (29% of the population).
Methods: Each of the partner hospitals designated at least one Local Donor Coordinator (LDC), member of the Intensive Care team, trained in the organ donation (OD) process. The principal tasks of the LDC's are the introduction of OD procedures, organisation of educational sessions for hospital staff and execution of the Donor Action programme. The LODP has been operational since July 2009, when training of the LDC's was completed, the web-site and hotline activated and the attendance of Transplant Procurement Coordinators (TPC) during the OD process organised.
Results: National and regional guidelines are accessible on the LODP website. The Hospital Attitude Survey obtained a 57% return rate. Many of the staff requested training and sessions are now running in the partner hospitals. The Medical Record Revue revealed an increase in the conversion rate from 3.5% to 4.5%. During the 5 years before creation of LODP the average annual number of utilised donors was 31, an increase of 70%, has since been observed.
Conclusion: This clear progression in utilised donors in the past two years can be attributed to the fact that partner hospitals benefit from the various support given (hotline, website and from TPC's). Despite the increase in OD within the LODP the Swiss donation rates remain low, on average 11.9 donors per million population. This successful model should be applied throughout Switzerland, but the crucial point is to obtain financial support.

RO-087 EUROPEAN LIVING DONOR PSYCHOSOCIAL FOLLOW-UP (ELIPSY PROJECT)

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Background: The number of living donor (LD) transplantations has increased in the European countries in the last years. Nevertheless the impact of donation in the psychosocial sphere, quality of life (QOL) and well-being of the donors has not been sufficiently studied until now so we are unable to identify

the risk factors that could predict the impact of the donation process in living donors.
ELIPSY is a project co-funded by EAHC which aim is to contribute guaranteeing high quality of living organ donation programs by creating an assessment model for the LD's psychosocial well-being and QOL, including the impact of the recipient's outcome on the donor and the donor's perception of the process.
Methods/Materials: Two main studies are going on; a Prospective one to compare the LD psychosocial well-being, QOL and the impact of the recipient's outcome on the LD before and after donation during 15 months. In the Retrospective study the same data are collected for a period of 15 months from donors who donated one, three and five years ago.
Results: At this moment we have achieved the following tasks:
A) Design and creation of the tools:
Survey about current psychosocial assessment practices, which has been made in 10 countries and 65 centres, among partner's centres and other European hospitals, to get data about the follow-up methodology and recipient's evaluation.
Questionnaire for the preoperative psychosocial assessment
Questionnaire for the postoperative psychosocial follow-up
Survey of recipient follow-up to correlate the recipient's outcome, one for kidney living donor programs and the other for Liver
B) Development and standardization on the methodology to be used for the LD psychosocial follow-up.
Conclusion: The harmonisation of LD psychosocial follow-up among Europe will guarantee a high quality model for living donation programs.

RO-088 ETHNIC BACKGROUND GOVERNING ATTITUDES TOWARDS INFLUENZA AND SWINE FLU VACCINATION AMONGST RENAL TRANSPLANT PATIENTS

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Introduction: Annual prophylaxis against influenza and swine flu (H1N1) is recommended in immunocompromised patients, including post-renal transplant. We aimed to assess the effect of ethnic origin on uptake of these vaccines amongst a renal transplant population.
Methods: Patients who had a renal transplant over a 30 month period (January 2007 - July 2009) were included in a telephone based survey to determine vaccination status for influenza and H1N1 influenza for the 2009-10 flu season. Demographics including patient age, ethnicity and sex, and graft age were assessed.
Results: 334 patients were eligible for the study, of which 201 were contactable and agreeable to inclusion. Mean age at transplant was 49.3 years (range 16.8-78.8). 114 (56.7%) patients were male. Mean time since transplant was 19.3 months (range 6-36). 154 (76.6%) patients were White, 32 (15.9%) were Asian, 13 (6.5%) were Black and 2 (1%) were classified as other ethnic group. There was no difference between the mean age of patients who had the influenza vaccination and those that did not (49.8 and 46.6 years respectively; p=NS); and this finding was replicated for the H1N1 vaccination (50.2 and 47 years respectively; p=NS.)There were no differences in uptake of influenza vaccination amongst White, Asian or Black patients (128 (83.1%), 29 (90.6%) 9 (69.2%) respectively.) 121 (78.6%) White patients received the H1N1 vaccination, which was significantly greater than the uptake seen amongst Asian and Black patients (16 (50%; $p<0.005$) and 6 (46.1%; $p<0.05$) respectively).
Discussion: Ethnicity appears a critical factor for uptake of H1N1 vaccination. Cultural barriers may exist resulting in this phenomenon. These groups should be specifically targeted to ensure adequate education as to the importance of vaccination to ensure adequate uptake of the H1N1 vaccine.

RO-089 PSYCHOSOCIAL CHARACTERISTICS PREDICTIVE OF POST-OPERATIVE MENTAL HEALTH IN LIVING-RELATED LIVER OR KIDNEY DONORS: A SYSTEMATIC LITERATURE REVIEW

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Background: It was demonstrated that psychosocial outcome following living donation is predominantly favorable. However, little is known about which factors at time of screening of the donor predicts poor mental health in living liver and kidney donors after donation. A systematic literature review was initiated to identify the available empirical research on these markers for post-donation vulnerability. The long-term objective is producing evidence-based guidance that may support clinicians in donor screening, monitoring and counseling.
Methods: Eligible studies incorporate assessment of mental illness parameters both pre- and post-donation, according to a pre-defined assessment tool, in a population of living liver or kidney donors. No restrictions were used regarding language and date of publication. Scientific reports were searched for through PubMed, PsychInfo, and Embase. Two independent reviewers evaluated major outcomes, socio-demographic donor characteristics, and properties of design and measurement tools.
Results: Of 227 abstracts screened, 54% merely focused on either recipient well-being or physiological safety of the donor. Seven studies fully met the inclusion criteria. The mean sample size of donors enrolled was 44, with two of seven studies being non-European. Main concepts of interest were mood (n=6), quality of life (n=3) and DSM-IV disorders (n=2). Overall, results indicated no signs that quality of life, mood or the psychosocial status was impaired after donation. Two studies sought for factors predictive of worse psychological outcome, and found that higher levels of anger and lower levels of self-esteem in the donor prior to transplantation related to less favorable outcomes.
Conclusions: The published evidence so far does suggest that living donation does not affect mental health. However, the low sample sizes might have influenced the low incidence of psychosocial problems found, and their subsequent lack of predictive capacity.

RO-090 ROLE OF TRANSPLANT COORDINATORS FOR INTEGRAL DONOR PROTECTION IN LIVING KIDNEY TRANSPLANT

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Introduction: In spite of a high deceased donor rate, the change in donor profile (43% of donors are >60 years old), have enforced to offer Living Kidney Donation (LKD) to young recipients. LKD represents more than 35% of our current total activity. In order to guaranty donor quality of life and improve protection, emotional, social and economical donor's situation need to be evaluated.
Methods: A prospective cohort study of all LKD from January 2006 to December 2010 was realized applying a personal donor's interview with Transplant Coordinators to aknowledge biological risk factors, emotional, social and demographic characteristics before donation.
Results: 214 LKD (64,7% females) were evaluated. Medium age was 49,05 years old (24-75 years) with 55% >50 years. Our hospital is a National Reference Centre for LKD with 58% living in the Catalan region. 95% were related donors: siblings 36.3%, followed by parents specially the mother 20.6%. With respect to emotionally related the most common was the wife 18.6% and husband 10.8%. Donor's marital status was 70.5% and 16.6% singles. The vast majority were actively working (62%), however, specially in the last 2 years, 15% have recently lost their jobs. 45% needed to ask for sick leave to avoid difficulties at work. Economically, 12% have a mortgage with some economical difficulties especially when LKD were between couples and considering that 44.1% of donors have some kids economically dependent from them.
Discussion: An independent role based in the Transplant Coordinator as the donor's advocate, favours an active donor protection to avoid biological, social or economical risks to achieve the highest standards of care. The issue of the recognition of the value of living donation to achieve a protected situation require a more wide participation of all-responsible at a national level.

RO-091 EUROPEAN DONATION DAY: TOWARDS A COMMON EUROPEAN AWARENESS-RAISING COMPAIGN

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Background: Promotion of transplantation medicine and increasing public awareness of the donation of human body parts for treatment is a challenging task. It is also one of the priorities of the European Commission Action Plan for Health (2009-2015). Although the promotion and communication with the general public about the subject is a multilevel and ongoing activity, there was a need to establish one day dedicated specifically to organ and tissue donation and transplantation in order to attract more attention to the issue, establish greater trust, disseminate credible information and sensitize the public. Every second Saturday in October a unified European Donation Day celebration thought out European countries is seen a primary awareness raising event when the public will be addressed about organ donation issues in a credible, professional, trustworthy, and highly ethical manner.
Methods/Material: The booklet *EDD: Toolkit for future organisers* has been developed during the EU-funded project *"Developing Guidelines for the Organization of a European Donation Day"(2009-2011).* Second goal of the project was to evaluate awareness-raising potential of EDD.
A EDD evaluation survey conducted in 2008 by Slovenia Transplant was the basic for more elaborated and comparative statistical survey conducted in 2010, when Slovenia, Austria, Croatia, Czech Republic and Slovakia were to

measure the awareness-raising potential of the EDD celebration among the general public. Web interviewing (CAWI) was performed in two waves. In each country a sample of 700 respondents was used.
Results: The results showed that the celebration not only sensitized the public, but also informed it significantly about organ donation.
Conclusion: The EDD celebration is seen to become a primary awareness-raising "voice" and event regarding organ and tissue donation and transplantation in Europe. The *EDD: Toolkit for future organisers* offers substantial support for the event.

RO-092 VALIDATION STUDY OF THE MTSOSD-59 IN THE ITALIAN CONTEXT

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Background: Chronic immunosuppression is the main stay of the success of transplantation. Several methods have been developed to analyze the effect of chronic administration of antirejection therapy on recipient's experience.
Aim: The aim of the study was to validate the MTSOSD-59 Scale in a national context (Italy).
Materials and Methods: The study was carried out in three phases: 1) Cultural and language translation, 2) Validation and 3) Symptoms and distress evaluation. *Back-forward translation* method was adopted for the translation. For the validation process, three strategies were carried out: 1) Test-retest reliability analysed using the Pearson's coefficient. 2) Internal consistency measured by the Cronbach's alpha coefficient. For the statistical analysis SPSS v15.00 used. The MTSOSD-59 was distributed to 45 stable liver transplant recipients (22% female and 78% male) with a mean age of 56,49±9,84 years; time from transplant was 42,2±31 months. Forty-five patients answered the questionnaire.
Results: The test-retest was undertaken on 20 patients, 15 days after the initial test. The time request for compilation the test was 12,7±4,3 minutes. The correlation (Person's coefficient) of single items ranged from 0,64 e 0,88. Internal consistency of the MTSOSD-59 Scale, measured by α-Cronbach test, was 0,899. The most frequent symptoms are fatigue and abdominal tenderness, while the most stressful symptoms are anxiety, erection problems and muscle cramps.
Conclusions: The MTSOSD-59 has a excellent internal consistency. Reliability test-retest is significant, in fact stable values have been obtained from test-retest.

RO-093 THE PHYSICIAN SAID: "YOU HAVE HAD A TRANSPLANT, YOU SHOULD BE HAPPIER!"; AN ANTHROPOLOGICAL APPROACH TO PATIENTS' DISAPPOINTMENT AFTER A RENAL TRANSPLANTATION

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Despite the absence of any complication, some patients express disappointment after a renal transplantation. This reaction impacts on their quality of life and/or their observance causing the doctor's incomprehension.
The study's purpose was to find the relevant element in the patients' experiences to analyse this phenomenon.
Methods: From 2005 to 2010, parallel to a work of participant observation, qualitative interviews were conducted with 62 patients with chronic renal failure. The interviews were subjected to content analysis and thematically compared.
Results: Among patients treated with renal transplantation (40 patients), 8 expressed their disappointment. Their experience highlighted a common representation: the confusion between hemodialysis and a disease.
Hemodialysis is a heavy treatment with significant side effects but other points could be identified to understand this representation:
Chronic renal failure can be asymptomatic and is not associated to strong social representations. If its diagnosis doesn't expose the patients to the experience of "biographical disruption", the treatment, as for it, creates profound changes in patients' lives.
The features of serious illness, which are usually related to the awareness of a dysfunctional body and to the perspective of mortality, become those of hemodialysis.
Due to this representation, patients expect that renal transplantation treats them of hemodialysis and not of chronic renal failure. They even expect that it "cures" them but realizing that renal transplantation is not a return to health, they express their disappointment.
Conclusions: This representation should be identified during educative diagnosis with patients on hemodialysis because it could be an indicator of a bad experience of renal transplantation. This study also shows that we should focus on the announcement of chronic renal failure which, most often, is turned into the announcement of hemodialysis.

RO-094 DISPARITIES IN INTERNET EDUCATION ABOUT LIVING KIDNEY DONATION FOR HISPANICS

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Background: Hispanics need disproportionately more kidney transplants (KT), yet compared to non-Hispanic whites, Hispanics receive disproportionately fewer KT (53.4% versus 14.7%) and living donor kidney transplants (LDKT) (66.3% versus 14.7%). Lack of knowledge, cultural beliefs, and negative attitudes about living kidney donation (LKD) contribute to these disparities. The Internet is an optimal venue to educate underserved, low-literate populations. We evaluated Internet sites for culturally competent information on LKD tailored to Hispanics.
Methods: Hispanic websites and on-line resources were identified through the Google search engine, using search terms: Hispanic, Latino, "trasplante de riñón por donante vivo" and "donación en vivo de riñón" [living kidney donation], and "donante vivo de riñón" [living kidney donor], and through transplant professional organizations. Websites were eligible for analysis if they addressed LKD. Websites were evaluated for: number of links required to access information on LKD, links required to access all information on LKD, and pages containing information on LKD; readability, measured by the Spanish Lexile® Measure; and content regarding surgery and short-term risks, recovery, long-term risks, psychosocial risks, and cultural competency.
Results: Eleven online resources (6 websites and 5 on-line pamphlets or videos) met inclusion criteria. Websites contained 2.5 pages on LKD, required 1.8 links to access any LKD information, and 3.3 links to access all LKD information. Average readability was at the 11th grade level. Few sites addressed any information regarding surgery and short-term risks (n=4), long-term risks (n=5), recovery (n=6), psychosocial risks (n=8), cultural beliefs (n=7), or used culturally sensitive colors/images (n=3). All sites were in Spanish.
Conclusions: Few Internet sites provide comprehensive or tailored information to Hispanics about LKD. More comprehensive and culturally competent websites are needed to increase Hispanics' understanding of treatment options, which may help reduce disparities in LKD.

RO-095 SYSTEM FACTORS AS CORRELATES OF MEDICATION ADHERENCE IN TRANSPLANT AND HIV POPULATIONS: A SYSTEMATIC REVIEW

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Purpose: Medication adherence (MA) is influenced not only by characteristics of the individual patient, but also by factors at the healthcare system level, i.e., micro- (e.g. healthcare worker, social support), meso- (e.g. factors related to the healthcare organization or setting in which care is received) and macro-level factors (e.g. regulations on reimbursement for medication). To date most research has focused on factors at the patient level which offer limited explanation of the broad variability in MA. The aim of this study is to identify and summarize quantitative studies addressing factors at the micro-, meso-, and macro-level of the healthcare system that are associated with MA in individuals who have received an organ transplant (Tx) or who have HIV, two populations necessitating strict adherence to prevent poor outcomes.
Methods: Searches were conducted in PubMed, EMBASE and Cinahl databases. Quantitative studies, published in English between January 1999 and December 2009, were included. To be eligible, studies had to investigate MA as an outcome, have described the MA measurement used, and have reported on the relationship between micro-, meso-, and/or macro-level healthcare system characteristics and MA in adults with a Tx or HIV.
Results: The electronic searches returned 5,341 citations. Seven articles in the Tx literature and 55 in the HIV literature met all inclusion criteria. The micro-level factor most consistently related to adherence was trust in the healthcare provider. At the meso-level, it was drug access/dispensing. Cost-related characteristics (macro-level) were significantly associated ($p<.05$) with adherence 50% of the times they were studied.
Conclusions: While the findings of studies examining the relationship between the system level factors and MA are inconsistent, this systematic review provides preliminary evidence to suggest that some of the system level factors are important contributors to MA.

RO-096 LACK OF MOTIVATION AMONG THE ICU DOCTORS FOR DONATION PROGRAMME

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Backgrounds: The ICU doctors play an important role in the donation activities as they are responsible for several tasks in the donation process. The estimations from Slovenia show that in the last ten years only 1/3 of the potencial for the donation was realised. In hospitals the ICU doctors are too busy, regularly. Their perception of the activities related to donation is unrealistic and it is understood as additional burden in their daily routine practice. There is a need for better knowledge about the donation and brain death diagnostics among the ICU professionals. Successful release of psychological burden for higher motivation and establishing greater trust regarding donation activities should be considered. The lack of communication skills concerning bad news, difficult situations and the lack of interests for donation are also very important issues to overcome.
Method: A validated questionnaire by Delphi method was send to 100 intensive care unit doctors. The main purpose of the survey was to realize *what kind of* emotions the ICU doctors feel when they perform brain death diagnostics and donation activities. Secondly we evaluated how well the doctors trust the donation activities and brain death procedures.
Results: Among 100 respondents 93, 4% respondents felt anxiety, 94, 30 emptiness and exhaustion, 48, 30 sadness and 25% fear of professional failure.
85% of respondents trusted much and very much and 15% somewhat procedures in transplantation medicine and feared possible irregularities, unethical treatments or abuses in this area.
To the question do you trust instrumental and clinical procedures for BD diagnostics 58% of respondents answered with completely and 42% with almost.
Conclusion: The results should be considered when making action plan in the field of donation activities in order to increase donor rate and realise the potential of the donation.

RO-097 HIGHER REFUSAL RATES BY RELATIVES OF POTENTIAL UNCONTROLLED ORGAN DONORS VERSUS UNCONTROLLED ORGAN DONORS: A SINGLE CENTER STUDY

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Background: A main cause of the gap between potential organ donors and effectuated organ donors is the refusal of relatives for organ donation after death. In our University Hospital in The Netherlands we have expanded our donorpool by the use of donation after cardiac death (DCD) donors; Maastricht category 2 (uncontrolled) and 3 (controlled). To assess the difference in refusal rate of the relatives between the uncontrolled organ donor, and the controlled organ donor (DCD category 3, and donation after brain death donor) we performed this study.
Methods: Included into the study were 533 potential organ donors between 2003 and 2011 in a 715 bed University Hospital. The refusal rate of the relatives for donation in the different groups of donors was assessed retrospectively.
Results: Of the 533 consecutive potential donors, there were 103 uncontrolled and 420 controlled donors. The uncontrolled donor was younger (52 vs.55 years, p 0.036) and more often male (69% vs. 52%, p 0.002). There were no differences between registration in the Donor Register (DR) in the two groups. 52% of the uncontrolled and 43% of the controlled potential donors were not registered in the DR. The refusal rate of the relatives was higher in the controlled donor group (71% vs. 47%, p 0.0001).
Conclusion: Less than 50% of the potential donors are registered in the Donor Register. Therefore the relatives play an important role in the decision for organ donation. The refusal rate in controlled donors was higher than in uncontrolled donors. Future evaluation in larger groups is necessary to account for this difference. The outcome can be used to decrease the refusal rate.

RO-098 "EUROCET": THE EUROPEAN NETWORK OF THE COMPETENT AUTHORITIES FOR TISSUES AND CELLS

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Background: From the original European (EU) funded project, Eurocet evolved itself into: the EU Registry of the Competent Authorities (CAs) for tissues and cells, the registry of tissue establishments (TEs) coming from all CAs and the registry of data on tissues, hematopoietic (HPC) and reproductive cells (ART) donation and transplantation activities provided by all national CAs.
Methods/Materials: Eurocet is the official information website for all EU and extra-EU citizens, patients, professional operators and institutions, accessible via internet. With the application of Directive 23/2004 every Member State (MS) should establish a network linking the national TE registers (art. 10.3 23/2004). TEs have to be provided from EU CAs, designed by MS, in charged of the implementation of quality and safety standards related to donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (art. 4-6 23/2004). Eurocet collects data coming only from official EU CAs.
Results: For donor and transplant coordinators' convenience, we present annual data on donation, transplantation, processing and import-export activities of tissues per country; the overall number of tissue donations, presented into different categories (cadaveric and living donation) and into different origins (cornea, skin, cardiac tissues, musculoskeletal and placenta); the updated number of procured tissues, presented into different categories (cadaveric and living donation) and into different origins (cornea, skin, cardiac tissues, musculoskeletal and placenta); tissue banking activities, divided into different phases (distribution, processing and storage); import-export activities in EU and extra-EU countries and the number of patients and tissues transplanted.
Conclusion: Thanks to mutual and regular cooperation with EU CAs, Eurocet was in charged to represent themselves in a common Registry. Nowadays, EU MS can rely on a complete database in order to respond to tissues and cells Directives.

RO-099 PIERDUB: KEEP IMPROVING TRAINING OF UNIVERSITY STUDENTS ABOUT DONATION AND TRANSPLANTATION

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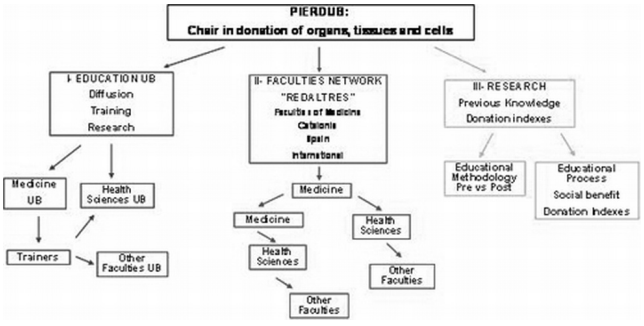
Background: Donation and transplantation fields are still considered as new subjects in the historical Medical Schools from all around the world. Inside those institutions there is no specific training for it.
Methods/Materials: The main goals of the project are:
– Knowledge diffusion about donation to clarify doubts and stimulate positive attitudes toward donation
– Training university students in the donation and transplantation process
– Research about the previous donation knowledge and the impact in donation indexes
Three implementation phases:
1. Training the UB (Univesity of Barcelona) Health Sciences School students: Train the trainers by giving theoretical and practical educational courses to medical students (MS) about donation process. One day of educative campaigns to inform about donation and stimulate positive attitudes. Repeat the same educative and promotional campaigns of one day duration in other Health Sciences Schools.
2. Training the Health Sciences School students in others faculties in Catalonia, Spain and International: Create a faculty's network to apply the same educative model for MS to develop potential future trainers.
3. Research: Evaluation of the methodology, before and after training. Evaluation of the educational process: Social benefits and impact of the educational activities in local donation indexes.
Results: PIERDUB started in 2005, since then 201 MS have been trained in the 45h course, 401 university students have attended the annual Donation day and 14 promotional campaigns have been carried out in UB's faculties. During 2011, the trained MS will organize campaigns in 10 faculties from 4 Universities, collecting their knowledge and attitudes towards donation using the survey from which we already have 962 answered.



Conclusions: Taking into account the great relevance of the professional and society acceptance and knowledge of the donation concepts, PIERDUB has been created to supply this need in the universities.

Immunobiology / basic science I

RO-100 HYPOXIA INDUCES MATURATION OF DENDRITIC CELLS TRIGGERING THE SPECIFIC PROLIFERATION OF B-LYMPHOCYTE SUBSETS. TARGETING ABC TRANSPORTERS INTERFERES HYPOXIA DC MATURATION

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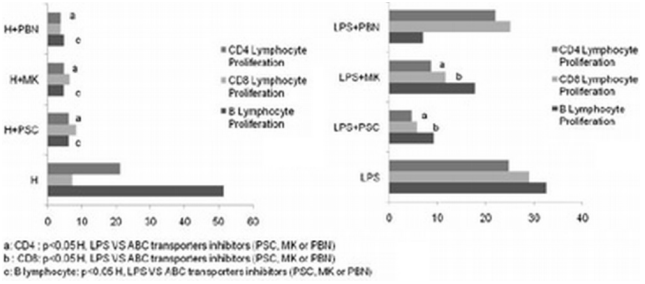
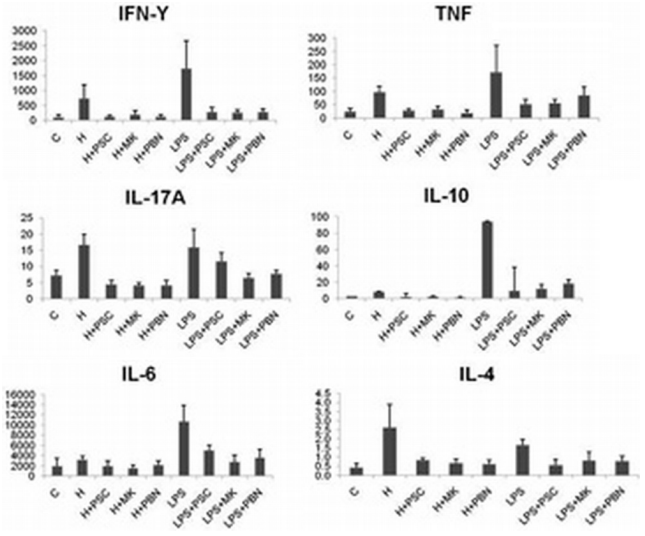
Dendritic cells (DCs) are the most potent antigen-presenting cells and fine-tune the immune response. We have investigated hypoxia's effects on DCs maturation and its effects on DC functions. We also studied the specific functional role of ABC transporters as a potential therapeutic target in alloimmunity modulation.
Peripheral blood monocytes were transformed into DCs by IL-4/GM-CSF. Maturation phenotype of iDCs after hypoxia or LPS stimulation with or without ABC transporter inhibitors was evaluated by means of specific mature dendritic cell markers by flow cytometry. The functional capacity of DCs depending on their maturation status to elicit T-cell alloresponse was studied on mixed lymphocyte reaction. Different lymphocyte subsets profile (CD4, CD8 and B lymphocytes) and the specific cytokines release were analyzed.
Our results show that mDCs generation occurs under hypoxic or LPS conditions, with different DCs maturation markers over-regulation (CD40, CD80, CD83, CD86, HLADR, CD54). Furthermore, hypoxia DCs induced more B-lymphocyte proliferation in contrast to myeloid DCs that induced more CD8 T-lymphocyte proliferation, triggering differently the release of inflammatory cytokines (mainly Th17 and IL 4 for hypoxia-DCs and IFN, TNF, IL10, and IL6 for LPS-DCs).



On the other hand, ABC transporters (MDR1 and MRP1) interfered in DC maturation modifying mDCs phenotype. Both DCs subsets co-cultured with lymphocytes under ABC transporter inhibitors induced significantly less alloimmune T-cell proliferation than stimulated DCs without inhibitors, at the same time decreasing TH2 or TH1 cytokines release depending on the stimuli.



Our study provides more information on hypoxia DCs maturation pathways. On the other hand, ABC transporter molecules appears to be a potential target in immunosuppressive therapies interfering DCs maturation thus abrogating innate immune response when it is activated after ischemia or antigenic stimulus.

RO-101 NITRIC OXIDE POST-PERFUSION LEVELS DIFFER IN DCD AND DBD DONOR TRANSPLANTS

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Background: DCD kidneys graft survival is similar to that of DBD donors. They have a higher incidence and duration of DGF that does not have the same impact to survival as in DBD kidneys. Nitric oxide is a free radical that plays a role in ischemic reperfusion injury. Following reperfusion, IFN-γ is upregulated, and induces iNOS synthesis and NO production.
Aim: To see if the pattern of change of NO level post reperfusion differs between DBD and DCD kidneys and could explain their different behaviour.
Methods: Blood was collected pre and post perfusion (2h) from 32 DCD and 42 DBD kidney recipients. NO was measured with a calorimetric method as NO3. The ratio of the post to the pre-perfusion values (reperfusion ratio-RRt) was used and compared between the two groups and correlated to risk factors for DGF.
Results: The median preperfusion value of NO was not correlated with the kidney disease, sex or the recipient age.
The median RRt was 0: 82 (mean 0.86) in DBD kidneys whereas it was 0.89 (mean 1.13) in DCD kidneys (Mann Whitney p=0.05).
In DCD kidneys the RRt correlated with Donor age so that patients with donors over 55 had RRt 0.85 that was lower that the RRt 1.02 in patients with donors over 55 (p=0.07). In addition, in DCD kidneys the NO RRt in recipients with CIT over 12h was 1.17 that was significantly higher than the RRt 0.88 measured in recipients with CIT less than 12h (p=0.04). In DBD kidneys the post/pre Reperfusion Ratio was not correlated with either donor age, sex or CIT.
Conclusion: The RRt of NO is significantly higher in DCD compared to DBD kidney transplants, perhaps because DCD recipients' NO post reperfusion is significantly affected by long CIT unlike in DBD recipients.

RO-102 INCREASED PROPORTION OF CIRCULATING BASOPHILS IN LUNG TRANSPLANT PATIENTS WITH OBLITERATIVE BRONCHIOLITIS

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Introduction: Obliterative Bronchiolitis (OB) is the single most important factor in longterm survival following lung transplantation. The pathogenesis of OB is complex, with both immune and non-immune contributing factors. To date there is no evidence for a role of basophils in disease progression, yet this cell type has the capacity to mediate immune responses in the lung.
Methods: Whole blood was collected from 25 lung allograft recipients. Flow cytometry was performed using CD123 and HLA-DR to identify basophils, and CD63 as an activation marker in accordance with the Basophil Activation Test (BAT).
Results: Using Pearsons correlation coefficient, the total percentage of circulating basophils identified via CD123+ HLA-DR- cell surface expression increased (p=0.009). Interestingly, there was no systemic activation observed through mean cell surface expression of CD63 (p=0.335) in patients with OB (determined via BOS grading using FEV1 criteria).
Conclusion: Our findings demonstrate that there is a convergence of the circulating granulocyte population towards basophils in response to a deterioration in lung allograft function (determined via deterioration in FEV1 and BOS grade). This novel finding requires further work to define the activation status of pulmonary basophils in the transplanted lung.

RO-103 THE SOURCE OF SOLUBLE CD30 DURING THE ALLOIMMUNE RESPONSE

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Background: Soluble CD30 (sCD30) has been reported to be a useful marker for predicting outcome in kidney, islet and lung transplantation. However, mechanisms by which sCD30 contributes to poor allograft survival are poorly understood. We investigated the source of sCD30 during the alloimmune response.
Methods: Enriched $CD3^+$ lymphocytes of 16 dialysis patients and 16 matched controls were stimulated with HLA-DR mismatched lymphocytes in mixed lymphocyte culture (MLC). Expression of CD30 on T cells was determined by flow cytometry and release of sCD30 by ELISA. In additional experiments, purified

$CD3^+$ and naive and memory $CD4^+$ and $CD8^+$ T cells were used as responder cells to determine the exact source of sCD30.
Results: Although dialysis patients had higher levels of serum sCD30 than controls, both groups exhibited a similar proliferative response in MLC. Compared to autologous stimulation, allogeneic stimulation of patient cells for 96 hours resulted in a 4.5- and 7.5-fold higher increase of CD30 expression on $CD4^+$ and $CD8^+$ T cells, respectively (p=0.002 and 0.004), whereas in controls a 3.3-fold increase of CD30 expression was observed on $CD4^+$ T cells only (p=0.033). In both groups, the majority (>70%) of $CD30^+$ cells were found in the central memory compartment with the $CD27^+CD45RO^+$ phenotype. Evaluation of membrane-bound and released sCD30 using purified T cell subsets indicated that $CD4^+$ and $CD8^+$ memory T cells are the main source of sCD30 during the allogeneic immune response.
Conclusion: Allostimulation of lymphocytes of dialysis patients results in up-regulation of the T cell activation marker CD30 on CD4- and CD8-positive memory T cells and in increased release of sCD30 from these cells. Our results are in line with clinical findings showing an association of high serum sCD30 levels with increased alloreactivity and poor graft outcome.

RO-104 AN HIF-1α-INDEPENDENT NEOANGIOGENIC PATHWAY REGULATED BY THE UNFOLDED PROTEIN RESPONSE DURING RENAL ISCHEMIA

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Background: Acute and chronic ischemic injuries permanently stress renal allograft that challenge cell viability. Adaptive responses to ischemia are mostly mediated by the activation of the transcriptional factor HIF-1α. Other adaptive pathways promoting neoangiogenesis are being investigated.
Ischemia promotes glucose deprivation (GD), ATP deprivation, hypoxia that triggers Endoplasmic Reticulum (ER) Stress followed by the adaptive response termed Unfolded Protein Response (UPR).
The aim of this study was to test whether the UPR would promote neoangiogenesis independently of HIF-1α pathway during ischemic stress.
Methods/Materials: qPCR, immunoblots and ELISA were performed on human kidney tubular cell lines (HK2) exposed to GD and/or hypoxia to evaluate the expression of the UPR markers BiP, CHOP and ATF4 and the expression of neoangiogenic inducers Vascular Endothelial Growth Factor (VEGF) basic Fibroblast Growth Factor (bFGF), Angiopoietin 1, Angiogenin and Platelet Derived Growth Factor. ARN interference directed against the three transducers of the UPR, *ATF6, PERK* and *IRE1* was performed to test which UPR axis is involved in mediating VEGF and bFGF expression.
Results: GD and hypoxia significantly increased the expression of VEGF, bFGF both at the mRNA and protein levels. GD does not alter HIF-1α protein or mRNA levels suggesting that this pathway is not involved, whereas HIF-1α is upregulated during hypoxia.
GD, not hypoxia, increases the expression level of the UPR markers BiP, CHOP, ATF4, and the spliced XBP1 mRNA, suggesting that GD, not hypoxia, promotes ER stress and triggers the UPR.
RNA interference directed against *PERK* and *IRE-1α* decreased VEGF and bFGF expression whereas RNA interference against *ATF6* decreases only bFGF mRNA level.
Conclusion: This work demonstrates that ischemia increases the expression of neoangiogenesis inducers VEGF and bFGF independently of the HIF-1α pathway in human kidney tubular cells and that the UPR could play a role in neoangiogenesis during kidney ischemia.

RO-105 ALTERED CYTOKINES PATTERN IN PATIENTS WITH ISCHEMIC TYPE BILIARY LESIONS FOLLOWING LIVER TRANSPLANTATION

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Introduction: Cytokines are potent mediators of a number of cell functions and are essential in coordinating inflammatory responses.
Aim: To investigate cytokines levels in association with activation of $CD4^+$ T cells and inflammation.
Methods: A total of 136 LT recipients were enrolled in the study (93 patients without biliary complications and 43 patients with ITBL). Cytokines were assessed by flow cytometry with the "BD Cytometric Bead Array (CBA) Human Th1/Th2/Th17 Cytokine Kit". Student's t-test or Mann-Whitney-U-test, when appropriate, was used for comparing continuous variables.
Results: There were 36.8% females and 63.2% males with a mean age at LT of 47.1±11.6 years. A significantly increased serum level of IFN-γ (1.4±0.6 vs 1±0.8pg/mL, p=0.007), TNF-α (1.1±0.4 vs 0.8±0.6pg/mL p=0.02), IL-10 (1.8±0.1 vs 1.3±0.1pg/mL, p=0.001), IL-6 (6.6±1.5 vs 4.1±1.5pg/mL, p=0.0001), IL-4 (1.3±0.6 vs 1±0.8pg/mL, p=0.03), IL-2 (1.7±0.8 vs 1.2±0.9pg/mL, p=0.01) were detected in the subgroup with ITBL compared to controls. IL-17 serum concentration and IL-4/IFN-γ ratio did not differ between the 2 groups. IL-17 serum levels showed a positive correlation with serum levels of IFN-γ (r =0.43, p=0.007) and IL-2 (r =0.40, p=0.01) in patients with ITBL. There was a significantly higher ratio IL-4/IL-2 (p=0.04), IL-10/IFN-γ (p=0.01) and IL-10/IL-2 (p=0.006) in the ITBL group compared to controls. 37.2% of the patients with ITBL had advanced fibrosis (F3-F4) compared to 20.4% in the control group. In the ITBL subgroup, patients with F3-F4 had significantly higher IL-6 levels compared to patients with F0-F2 (p=0.02).
Conclusions: Inflammatory cytokines and Th2-cell mediated immunity seem to play a central role in the pathogenesis of ITBL. Protocol liver biopsies for severe fibrosis in ITBL patients should be performed in patients with increased IL-6 serum levels.

RO-106 TACROLIMUS AT CLINICALLY RELEVANT CONCENTRATIONS INDUCES A MYOFIBROBLAST-LIKE PHENOTYPE IN HUMAN KIDNEY FIBROBLASTS BY LIGAND-FREE ACTIVATION OF TGF-β RECEPTOR

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Introduction: TGF-β is considered a strong inducer of renal interstitial fibrosis, which is a dominant factor in long-term outcome of kidney transplant recipients. Here we demonstrate the TGF-β-like effects of tacrolimus on kidney fibroblasts in vitro and the modulatory effect of NAD(P)H-oxidase 4 on this process.
Methods: The human renal fibroblast cell line TK-173 was treated with varying doses of tacrolimus (FK-506, Prograf®) for three days. mRNA expression levels for NAD(P)H-oxidase 4, transgelin (a myofibroblast marker), TGF-β1, tropomyosin 1, and the collagen chain alpha-1(V) were determined by real-time qPCR. NOX4 protein expression and intracellular peroxide concentration were also determined.
Results: Tacrolimus-treated renal fibroblasts showed increased expression of NOX4, transgelin, tropomyosin 1, TGF-β1, and collagen mRNA. The effect started at low nanomolar levels, and reached saturation at 100-300 nM of tacrolimus. NOX4 up-regulation lead to a 20% (max.) increase in intracellular hydrogen peroxide levels. TGF-β1 treatment duplicated the effects of tacrolimus. Specific inhibition of the TGF-β pathway repressed the effects of both tacrolimus and TGF-β1. Neutralization of extracellular TGF-β by specific antibodies almost completely abolished the reaction to TGF-β1, but left the response to tacrolimus unchanged. Si-RNA mediated knock-down of NOX4 had little effect on the tacrolimus-induced effects, except that COL5A1 expression was decreased in tacrolimus- treated cells.
Conclusion: Tacrolimus at clinically relevant concentrations had TGF-β-like effects on cultured human renal fibroblasts. The binding of tacrolimus to FK-506 binding protein 12 (FKBP12) leads to increased TGF-β receptor activity, even in the complete absence of ligand. This effect was sufficient to induce a myofibroblast-like phenotype and might thereby contribute to the induction of interstitial fibrosis in immunosuppressed kidney transplant patients. NOX4 activity may partially modulate the fibrogenic effect.

RO-107 TERLIPRESSIN IMPROVES LIVER REGENERATION IN A SMALL-FOR-SIZE LIVER REMNANT MOUSE MODEL

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Background: Small-for-size liver grafts are associated with pre- and intrahepatic portal hypertension that in turn may impair postoperative hepatocellular regeneration. Surgical attempts to reduce perioperative portal pressure such as ligation of the splenic artery are associated with additional morbidity. The aim of this study was to assess the effect of pharmacological reduction of portal pressure by terlipressin a vasopressin agonist on liver regeneration.
Methods/Materials: Male C57/Bl6 mice were subjected to extended (80%) liver resection. Outcome was compared between a group with intravenous administration of terlipressin (0.05 μg/g mouse) versus PBS (5 μl/g mouse). Injections were given intraoperatively and 8 hours post resection. Liver regener-

ation was assessed by immunohistochemistry (BrdU and Ki-67) after 48 hours. Portal pressures were measured invasively before and after liver resection during 30 minutes.
Results: Invasive pressure measurements showed an elevation of portal pressure after extended liver resection (8.4±1.2 before versus 10.9±1.6 cmH2O after resection; p=0.003). Treatment with terlipressin was associated with a significant reduction of portal pressure post extended resection (10.9±1.6 versus 8.8±0.4 cmH2O; p=0.02). Liver regeneration post 80% hepatectomy is significantly increased with terlipressin compared to controls (24±6 versus 17±5 BrdU positive cells per high power field (HPF), p=0.02; 61±15 versus 43±11 Ki-67 positive cells per HPF, p=0.02). Mortality (0% in both groups) or extent of liver cell damage assessed by AST and ALT were not different between the two treatment groups.
Conclusion: Portal pressure is elevated post partial hepatectomy. Intra- and postoperative administration of terlipressin lead to improved liver regeneration in a small-for-size remnant liver model. This effect might be explained by protection of the liver from increased postoperative portal pressure.

RO-108 HIGH PRODUCTION OF INF-GAMMA DURING THE ALLOIMMUNE RESPONSE IS ASSOCIATED WITH HIGH RELEASE OF SOLUBLE CD30

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Background: Patients on hemodialysis display alterations in the immune response commonly associated with a state of chronic inflammation. Clinical evidence suggests that patients with high levels of soluble CD30 (sCD30) are at an increased risk of graft loss and we show in a separate abstract that sCD30 is released by memory T cells. Herein we investigated whether INF-γ is involved in CD30 release.
Methods: The allogeneic response of dialysis patients (N=15) and matched healthy controls (N=15) was evaluated in mixed lymphocyte culture (MLC). Gene expression analysis was performed by Real-Time PCR, and release of CD30 and 32 different cytokines were quantitated by ELISA and Luminex, respectively.
Results: Neither in blood nor after allogeneic stimulation in MLC were significant differences observed in gene expression or cytokine patterns of patients and controls. However, after allogeneic stimulation transcripts of the regulatory genes TGF-β and IL-10, and genes related to CD30 release and activation, such as ADAM10, ADAM17 and CD30L were upregulated, whereas FOXP3 transcripts were downregulated. When patients were separated according to low or high production of IFN-γ in MLC, high producers of IFN-γ exhibited not only a higher release of sIL-2Rα, IL-17, GM-CSF, MIP-1α and MIP-1β but also a higher release of sCD30 (in all cases $p<0.05$ as compared to low producers), as well as an augmented expression of certain genes, such as IL-10 and CD30L (both $P<0.001$).
Conclusion: Our findings indicate that patients with a high IFN-γ response to alloantigens also exhibit a higher release of sCD30. These results are in line with clinical findings that indicate an association of high serum sCD30 content and a high INF-γ T cell response with poor kidney allograft prognosis.

RO-109 INTERLAB CROSSVALIDATION OF IFN-γ ELISPOT ASSAY FOR MEASURING ALLOREACTIVE MEMORY/EFFECTOR T-CELL RESPONSES IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Assessment of donor-specific alloreactive memory/effector T-cell responses may be monitored by using an IFN-γ ELispot assay. Here, we report the cross-validation data of the IFN-γ Elispot assay performed within 5 European laboratories.
Methods: For this purpose, comparisons of lectures of the same IFN-γ plate using the same Elispot reader (Autoimmun diagnostika, Germany) has been done within all 5 labs using the same settings (size, colour and gradient intensity). Also, an intra and interlab analyses using the same IFN-γ ELispot SOP, evaluating peptide (CMV) and allogeneic stimuli (in both healthy volunteers and renal transplant patients) assessing both fresh and frozen samples has been performed among 3 labs. The assessment of the intra and interlab assay variability was evaluated using the coefficient of variation (CV).
Results: IFN-γ plate analysis of both allogeneic and CMV-peptide stimuli showed a high concordance between the 5 Elispot readers. Intralab analyses between 1-month frozen and fresh samples showed a difference of CV between 20 to 30% in all different stimuli (either peptide or allogeneic), being particularly sensible the allogeneic stimuli and especially those that had been shipped (28%). When evaluating the interlab analysis for both the allogeneic and peptide stimuli, a CV between 10 to 15% for the allogeneic stimuli while between 38 and 40% for the peptide stimuli. Moreover, the INF-γ ELispot assay was also evaluated among kidney transplanted patients. Here, a similarly low CV between labs was observed both at the pre-transplant and at the post-transplant clinical setting.
Conclusions: The assessment of highly alloreactive memory/effector T cells circulating in peripheral blood using an INF-γ ELispot assay can be accurately achieved using the same SOP, Elispot reader and experienced technicians in order to be used as an immune-monitoring tool in kidney transplant patients.

RO-110 DONOR SPECIFIC ANTIBODIES AND THEIR IMPACT ON GRAFT FUNCTION, REJECTION EPISODES- A SINGLE CENTRE EXPERIENCE

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Background: The clinical significance of the presence of donor specific antibodies (DSAb) prior to renal transplantation remains unclear. This study aimed to assess the effect of donor specific antibodies detected by Luminex test and its early predictability of graft function and biopsy proven acute rejection (BPAR) in renal transplantation in our centre.
Materials and Methods: This study was carried out on a retrospectively collected data of all consecutive renal transplant recipients between 2007-2009 with 1 year follow-up. During the data collection the investigator was blinded for results; graft function was assessed by estimated GFR (eGFR) and rejection episodes. All recipients were on standard tacrolimus/rapamycin, MMF and prednisolone immunosuppression.
Results: All recipients (n= 141; cadaveric= = 53, live donor = 88) were grouped according to the donor specific antibody results. The DSAb positivity noted in 33 and was negative in 101.The DSAb versus DSAb negative group did not show any difference in e GFR (49±14.98 versus 52±14.98) at 1 year (P =0.81) after transplantation. DSAb positive group had higher rejection rate (P =0.0067) compare with DSAb negative group.
Conclusion: From our study we conclude that DSAb does not affect early and intermediate graft function and DSAb positivity is an independent risk factor for biopsy proven acute rejection.

RO-111 ENDOTHELIAL AND THROMBOCYTE ACTIVATION ARE NOT MEDIATORS IN EARLY ISCHEMIA-REPERFUSION INJURY IN HUMAN KIDNEY TRANSPLANTATION

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Background: The endothelium is very sensitive to hypoxia, and is a strong initiator of thrombocyte activation once damaged. Thrombocytes are specialized cells of the innate immune defense and modulators of the inflammatory response in addition to their evident role in hemostasis and thrombosis. We hypothesized that the inflammatory cascade of I/R injury is initiated by endothelial damage and consequent thrombocyte activation. This hypothesis was studied in clinical kidney transplantation using our unique method of arteriovenous measurements over the reperfused kidney.
Methods: Paired arterial and renal venous blood samples were collected at consecutive time-points during early reperfusion. Samples were analyzed on markers of endothelial activation; i.e. angiopoietin (ang)-1, ang-2, von Willebrand factor (vWF) and vWF propeptide. To assess consecutive thrombocyte activation, b-thromboglobulin, glycoprotein Ib, regulated on activation normal T-cell expressed and secreted (RANTES) and platelet derived growth factor were measured.
Results: Arteriovenous samples showed that shortly after reperfusion, ang-2 was released by both living and cadaveric donor kidneys. Other markers of endothelial damage did not show a response to reperfusion. There was no full blown thrombocyte activation after reperfusion of the kidney. To test for more subtle changes in thrombocyte activation state, the excitability of thrombocytes was measured. This sensitive assay indicated that thrombocytes in renal venous blood are less excitable than before having passed the kidney, i.e. in the arterial sample.
Conclusion: The results of this study unequivocally show that there is mild endothelial damage that does not induce thrombocyte activation in early reperfusion injury in both living and cadaveric donor kidney transplantation. Moreover,

thrombocyte activation is even repressed when thrombocytes pass the reperfused kidney, indicating that endothelial cells in the kidney may have released thrombocyte inhibitors.

RO-112 DNAM-1 – A NEW PLAYER IN RENAL ALLOGRAFT REJECTION

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Despite effective treatment protocols to prevent rejection many renal allografts are lost due to the toxicity of immunosuppressants. Thus, more specific and less toxic immunosuppression is needed. DNAM-1 (CD226) on T cells has been shown to play an important role for allogeneic graft-versus-host responses. DNAM-1 has two ligands: the adhesion molecules CD155 and CD112. The role of DNAM-1 during renal allograft rejection is unknown.
Primary cultures of murine renal tubular epithelial cells (rTECs) were prestimulated with IFN-β and IFN-γ to induce high surface expression of MHC. Surface expression of CD155 and CD112 was tested by FACS. Responder T cells were restimulated in vitro with allogeneic fully MHC-mismatched splenocytes. From these restimulation cocultures we measured proliferation (thymidine incorporation), cytokine production (ELISA) and cytotoxicity against IFN-stimulated rTECs from WT or $CD155^{-/-}$ mice (^{51}Cr-release-assay). To test for a role of this pathway in vivo, we performed fully MHC-mismatched skin and kidney grafts.
CD155 and CD112 were both highly expressed on rTECs and could be further increased by IFN-stimulation. However, when CD155 was missing on targets in an allospecific chromium-release-assay, no difference in cytotoxicity was measured compared to WT targets. Also, allospecific T cell proliferation and IFN-γ secretion were not altered, when stimulator cells lacked CD155. In contrast, with the use of a blocking antibody against DNAM-1, allospecific T cell proliferation could be reduced. When testing for the role of this pathway for allograft rejection in vivo, no difference between skin graft survival of WT and $CD155^{-/-}$was observed. Experiments blocking DNAM1 or CD112 in vivo are planned.
Thus, DNAM-1 is an important costimulatory receptor for alloreactive T cells. However, the important ligand might be CD112 rather than CD155. Thus, blocking DNAM-1 or CD112 might be a therapeutically interesting option to prevent renal allograft rejection.

Monday, 5 September 2011

Kidney III

RO-113 INCIDENCE AND RISK FACTORS FOR DE-NOVO CANCERS IN ITALIAN KIDNEY TRANSPLANT (KT) RECIPIENTS

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An augmented cancer risk among KT recipients has been well documented in several countries. In Italy on average 1500 KTs are carried yearly but few large scale studies were conducted. To quantify the risk of de-novo cancers and to identify major risk factors for cancer occurrence we carried out a multicenter investigation in 15 KT Italian centers.A retrospective-cohort study was implemented on 7143pts (64% men, median age 49yrs) who underwent KT in 1997-2007 followed up thru Dec-2009. Person-years (PY) at risk of cancer were computed from 30-days post-KT to date of cancer, death, return to dialysis or end of study. Number of observed cancers was compared with expected one from National Cancer Registries through sex-, age-, area of residence-standardized IR (SIR and 95% confidence intervals, CI). Incidence rate ratios (IRR) were computed through Poisson multivariate regression analysis to identify risk factors. On 39280-PY at-risk of cancer 391 cancer diagnoses were observed in 378pts, mostly solid tumors (65%), followed by Kaposi's sarcoma (KS, 72 cases) and non-Hodgkin lymphoma (NHL, 39 cases). Overall incidence rate was 10.2 cases/10.000 PY and the excess risk was 1.7 (95% CI: 1.6-1.9). Elevated SIRs were noted for KS (136), NHL (4.5) and kidney cancers (5.0). No excess risk was found for the most commonly diagnosed cancers in the general population (e.g. lung, prostate, colon-rectum and breast). KT recipients treated with mTOR showed a 30% significantly reduced risk for all combined cancer (IRR=0.70, 95% CI: 0.51-0.97). Risk reduction was particularly evident for NHL (SIR=0.28) and kidney cancers (IRR=0.48). Among the principal risk factors it is worth mentioning that people born in southern Italy were at reduced risk for kidney cancer and NHL, whereas their risk of KS was higher than those born in northern Italy.

RO-114 BIOMARKERS OF KIDNEY REJECTION IN ORGAN TRANSPLANTATION

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Slowly deteriorating kidney allografts pose a clinical challenge to the transplant physician as the therapeutic options in this situation are limited. The gold standard procedure is to perform a biopsy of the graft but the information obtained will inform little as to the risk of the recipients to lose their graft. Identifying biomarkers for either imminent graft loss or for a process that is fundamentally immunologically driven, and in theory treatable, would allow an individually tailored approach to the management of these recipients.
Gene expression was analysed on an immune-specific array platform, namely RISET 2.0. Expression was screened on RNA samples from a *training set* that included 9 patients with a recent biopsy where immunologically driven chronic rejection could be identified. Recipient groups with different immunosuppressive regimes and stable function were used as controls. Highly predictive findings were repeated on an independent *test set* that included a set patients with clinical features of chronic allograft nephropathy from the USA.
Using SAM for feature selection, at an FDR of 8% and a minimum fold change of 2; nine genes were significantly upregulated and 16 downregulated in CR recipients. We used Elastic Net and cross-validation to build a multivariate predictive model, which provided an area under the ROC curve of 0.992 in the training set. Gene set enrichment analysis for biological processes reveals a picture of active tissue remodelling and a small set of miRNA targets. When external validation was attempted in the test set an AUC of 0.68 was obtained. Methods and pitfalls for external validation will be discussed. The clinical usefulness of these biomarkers and their added value to current gold standart diagnostic tools are being assessed.

RO-115 HYPERTENSIVE KIDNEY DONORS PERFORM WELL AT SHORT TERM POST-DONATION FOLLOW-UP

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Background: Due to donor organ shortage, living kidney donor selection has become more liberal with acceptation of hypertensive donors. This raises a new set of issues. Little is known whether hypertensive donors are at increased risk for impaired residual renal function post-donation. Furthermore, the course of blood pressure following kidney donation in preexistent hypertensive donors is also poorly documented.
Methods/Materials: We compared short term outcome of hypertensive donors to sex, age and BMI matched control donors. Hypertension was defined as pre-donation antihypertensive drug use. All donors had GFR (^{125}I-iothalamate) and ERPF (^{131}I-hippuran) measured 4 months prior and 2 months post-donation. Renal reserve capacity (GFR_{RC} and $ERPF_{RC}$) was measured by use of dopamine and was calculated as [stimulated renal function – basal renal function]. A subset of donors had serum creatinine and spot-urine protein excretion measured one year post-donation.
Results: Results are shown in the table. Pre-donation mean arterial pressure (MAP) was significantly higher in hypertensive donors compared to control

donors. There were no differences in basal renal function or reserve capacity. Post-donation, hypertensive donors had similar MAP and renal function compared to controls. The previously described increase in blood pressure could not be detected in hypertensive donors, while in control donors MAP increased ($p<0.05$).
One year follow-up was available for 25 hypertensive donors and 25 controls. There was no difference in serum creatinine or urinary protein excretion: 108±23 *vs.* 114±22 μmol/L and 0.1[0] *vs.* 0.1[0] g/L.

		Non-hypertensive donor	Hypertensive donors	p
Pre-donation	N (% female)	68 (46)	46 (46)	ns
	Age (years)	57±8	57±8	ns
	BMI (kg/m^2	28±3	28±3	ns
	MAP (mmHg)	94±9	101±11	<0.01
	GFR (ml/min)	113±18	118±20	ns
	ERPF (ml/min)	412±74	419±88	ns
	GFRrc (ml/min)	9±10	10±10	ns
	ERPFrc (ml/min)	96±50	95±70	ns
Early post-donation	MAP (mmHg)	96±10	99±9	ns
	GFR (ml/min)	70±13	73±13	ns
	ERPF (ml/min)	264±46	266±50	ns
	GFRrc (ml/min)	2±4	1±4	ns
	ERPFrc (ml/min)	40±21	38±33	ns

ns: not significant.

Conclusion: In summary, hypertensive living kidney donors perform similarly to control donors early and one year post-donation. Despite these reassuring findings we like to emphasize that these donors were strictly selected and well regulated with strict blood pressure management. More long term data are necessary to ensure long term donor safety.

RO-116 TRANSPLANT NEPHRECTOMY IN ALLOGRAFT FAILURE: A SINGLE CENTER REVIEW

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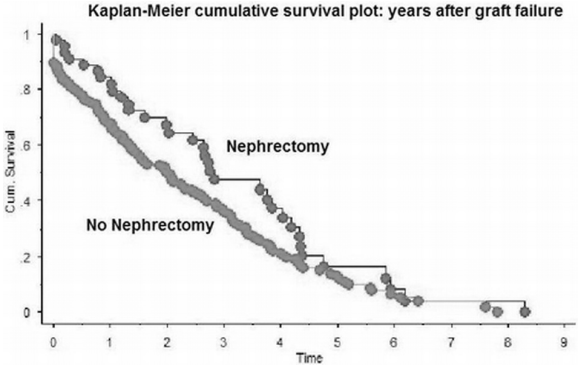
Background: Registry studies show a survival benefit for allograft nephrectomy in patients with kidney allograft failure. These studies are limited by varying practices and unclear indications for nephrectomy among heterogeneous populations.
Methods: We performed a single center retrospective review of kidney transplant recipients from 2000-2010 with allograft failure. Allograft nephrectomy was performed when patients had clinical indications such as hyperacute rejection, infection, graft thrombosis, fever, or pain. Characteristics and Kaplan-Meier estimated survival of patients that underwent nephrectomy following graft failure were compared to patients that did not have nephrectomy using student's t-tests and the logrank test. Survival was measured from the time of graft failure to death or end of follow up. Multivariate analysis was performed using a stepwise proportional hazard analysis.
Results: 2309 consecutive kidney only transplant recipients from 2000-2010 with 291 (12.6%) instances of graft failure were reviewed. Of these 291 patients, 66 patients had early graft failure, defined as return to dialysis within the first 100 days; these recipients were excluded from further analysis. Of the 225 patients with graft failure after 100 days, 45 underwent allograft nephrectomy (20%). Mean follow-up after graft failure was 5.6 years. Seventy-one patients (31.5%) died during the follow-up period. Patients that underwent allograft nephrectomy were younger and more likely to have a deceased donor graft or a previous transplant compared to patients that did not require nephrectomy. Though not statistically significant, patients that underwent nephrectomy had improved 1 and 5 year survival.

Univariate analysis

	Nephrectomy (%)	No Nephrectomy (%)	p value
N	45	180	
Age at transplant	36	41	0.6830
Age at graft failure	37.79	45.62	0.0108
Deceased donor	32 (71.1)	93 (52.2)	0.0265
HLA mismatch	3.190	3.278	0.7886
Number of transplants	1.38	1.183	0.0274
Retransplanted after graft failure	9 (20)	34 (19)	0.5992
Mean days to graft failure	831	1565	<0.0001
1 year patient survival	100	99	0.4797
5 year patient survival	84	84	0.7907

35% of patients who underwent nephrectomy required transfusion. Patients that had nephrectomy developed graft failure sooner on average (2.3 vs 4.3 years). One and five-year survival was 100% and 84% for those with nephrectomy vs. 99% and 84% without nephrectomy.
Conclusion: In our single center retrospective review, allograft nephrectomy was associated with improved survival. While these results validate the larger



registry studies, data from our single center study may provide insight into this survival benefit.

RO-117 INCIDENCE, SITE AND RISK FACTOR OF POST-TRANSPLANT MALIGNANCIES – ANALYSIS OF 771 RENAL TRANSPLANT RECIPIRNTS FOR 40 YRS IN JAPANESE SINGLE CENTER

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Backgrounds: A number of studies have observed increased cancer incidence rates among renal transplant recipients. However, the interval from transplant and the site of malignancies quite vary by era and region.
Methods: We retrospectively reviewed the records of 771 renal transplant recipients who received renal allograft in Kyoto Prefectural University of Medicine between 1970 and 2010. 172 were done in conventional era (1970.4-1982.3), and 599 were done in calcineurin inhibiter (CNI) era (1982.4-). Overall incidence, site and risk factor of malignancies were analyzed.
Results: A total of 63 kidney recipients out of 771 developed 66 malignancies with mean interval of 133±89 (7-340) months after transplant. The tumors included 13 skin cancers, 12 gastro-intestinal tract cancers, 9 liver cancers, 6 breast cancers, 6 renal cell carcinomas, 5 leukemia, 5 lymphoma and 10 others. Cumulative incidence of malignancies in CNI era at 5, 10 and 20 years were 2.5%, 5.1% and 9.5%, while those in conventional era were 1.2%, 2.9% and 12.2%. Site of malignancies occurring within three years following transplantation were breast, uterus, liver, leukemia, ATL, KS and PTLD.
Univariate analysis showed age at the time of transplantation (≥50 yo, OR=7.0, $p<0.01$), diabetic nephropathy (OR=6.6, $p<0.01$), ABO-incompatible transplant (OR=5.7, $p<0.01$) and use of mycophenolate mofetil (OR=4.5, $p<0.01$) were significant risk factors to develop malignancies within 5 years. Among them, age at the time of transplantation (OR=4.6, p=0.031) and diabetic nephropathy (OR=4.3, $p<0.038$) were found to be independent risk factors by multivariate analysis.
Discussions: Our results demonstrated that recent potent immunosuppressive regimen shortened the interval between transplantation and increased viral-related malignancies. In the long-term follow-up, it is crucial to pay special attention to the groups that have risk factors to develop malignancies.

RO-118 METABOLIC STRESS PROMOTES TUBULAR INFLAMMATION BY TRIGGERING THE UNFOLDED PROTEIN RESPONSE

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Background: Tissular ischemia subjected by the renal graft generates an inflammatory response contributing to the development of an alloimmune response. Renal tubular epithelium plays a major role in the inflammatory reaction and renal fibrosis. Ischemia provokes, in addition to the hypoxia, a metabolic stress characterized by nutrients starvation, amino acids and glucose, but its role in the activation of inflammation is unknown. Nutrients starvation induces an endoplasmic reticulum (ER) stress and activates the adaptive response UPR (Unfolded Protein Response).
The aim of this study is to demonstrate that the UPR response induced by a metabolic stress can be responsible for a tubular inflammatory response mediated by the NF-κB pathway.

Materials/Methods: In an in vitro model of primary cultures of human renal tubular cells, we studied the role of the UPR response in the inflammation in condition of glucose starvation. In vivo, we evaluated the expression of ER stress markers.
Results: In vitro, we demonstrated that nutrients starvation generates an ER stress and activates PERK and IRE1α pathways of the UPR response. This metabolic stress activates NF-κB pathway and induces proinflammatory cytokines and chemokines transcription (IL-6, IL-8, TNF-α, RANTES and MCP-1). PERK/eIF2α pathway inhibition by RNA interference inhibits RANTES expression when metabolic stress occurs and the activation of this pathway by salubrinal increases the inflammatory response. IRE1 pathway inhibition by RNA interference also inhibits RANTES expression but this of IL-8 and TNF-α too when metabolic stress occurs.
From preimplantation biopsies of renal grafts, we highlighted an expression significantly more important of the ER stress marker BiP/GRP78 and of p65/RelA in renal tubules, in comparison with control biopsies.
Conclusion: In conclusion, this work establishes for the first time a link between a metabolic stress induced by ischemia, activation of the UPR response and production of a tubular inflammatory response.

RO-119 EVALUATION OF THE IMPACT OF EARLY PROTOCOL BIOPSY ON RENAL FUNCTION AT MONTH 12 IN *DE NOVO* MARGINAL KIDNEY TRANSPLANT: PRELIMINARY RESULT AT 12 WEEKS

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Due to the current organ shortage, there is an increasing use of organs from Expanded Criteria Donors (ECD). The use of these organs is associated with inferior results when compared with Standard Criteria Donors kidneys. Early protocol biopsies might improve the management of these patients and hence the results. We present here the preliminary results of a prospective study.
The objective of this analysis was to evaluate the impact of the fibrosis score on the pre-implantation graft biopsy, using centralized automatic quantification, on the renal function at W12.
Sixty-six recipients of ECD kidneys were randomized (65% men, mean age 62.8±7.2 years) to have a biopsy or not to 10 days. Based on histological results, immunosuppressive therapy was adapted.
The donor characteristics were as follows: mean age 66.3±8.2 years and cerebrovascular death (82%).
The fibrosis score on the pre-implantation graft biopsy was grade 1 [<25%] in 76% of patients, grade 2 [25%-50%] for 24% with a mean fibrosis score of 19.3%. (±8.6).
At W12, the median eGFR (MDRD formula) was 40.4 ml/mn/1.73m^2 with a range [4.1; 97.2]. According to the fibrosis score, the median eGFR was 42.5 ml/mn/1.73m^2 with a range [4.1; 83.23] in grade 1 and 38.3 ml/min/1.73m^2 [12.4; 97.2] in grade 2. The graft function was delayed or slows in 56% and 74% of the patients with a grade 1 and 2, respectively. 45% of patients presented at least one serious adverse event and none of them was related with the pre-implantation graft biopsy.
In spite of the use of marginal kidneys, the incidence of grade 2 fibrosis was low as was its impact on W12 renal function.

RO-120 FACTORS AFFECTING OUTCOMES OF PATIENTS WITH POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)

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Objective: PTLD is associated with high mortality, morbidity. Here, we report a single unit experience of PTLD on kidney transplanted recipients (KTRs) analysing factors affecting graft function, graft and patient survival.
Methods: Data of KTRs developing PTLD over the last 14 years at our unit were retrospectively analysed. Demographics, time to presentation of biopsy proven PTLD, extent of immunosuppression (IS) reduction, biopsy proven acute rejections (AR), associated malignancies, use of Rituximab (Rx), patient and graft survivals and graft function after diagnosis were analysed.
Results: We identified 44 patients who developed PTLD. The median age of recipients at transplantation and at diagnosis was 37.16 [4-66] and 44.8 [12.8-70.2]. The median time to presentation was 120.1 [8-308] months. 9% developed other malignancies. Majority (88.6%) were deceased donor transplants. 30% had GI origin, 30% was diffuse and 21.6% confined to lymph nodes. 84% was B-cell origin. 16% experienced AR. IS was reduced for treatment in 87.5%. The use of Rx but not the reduction of IS resulted in significant survival benefit (Log Rank p=0.006). Patient survival was not influenced by age, gender or AR. Response to treatment was 71.4%. Survival of patients with disseminated disease was inferior to localized ones. 1-, 2- and 5- year patient survival after diagnosis was 59%, 48%, 39%. 1-, 2- and 5-year graft survival of patients surviving minimum 6 months after diagnosis was 82%, 68%, 47%. Median eGFR at diagnosis, and 6, 12, 24 months after, was 31.9 [6-80], 34.5 [0-124], 27.0 [0-124], 13.8 [0-92]. Rx or IS reduction had no effect on graft function.
Conclusions: We demonstrated that the presentation of PTLD is late, patient survival was not influenced by age, gender, AR, reduction of IS, but positively by the use of Rx in concordance with the literature.

RO-121 USE OF ELDERLY LIVING KIDNEY DONORS – 20 YEARS EXPERIENCE ON THE BALKANS

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Introduction: Despite the efforts for deceased donor transplants, living renal transplantation (LRT) is still predominant in the Balkan countries. Trying to solve the organ shortage we started to accept expanded criteria living donors including elderly (ED), marginal, unrelated and ABO incompatible donors. The authors presented their 20 years experience with ED transplants.
Methods: 230 LRT are performed in our Unit in the last 20 years. 90 of them were with the donors older than 65 years (mean age 68±4, range 65-86). The mean age of the recipients was 45±6 years (range 18 – 66). The quadruple sequential protocol was used in all cases with ATG or Daclizumab induction and Cyclosporine, MMF and Prednisolon as a maintenance therapy. The Kaplan Meier 5 years graft survival, rejection episodes, delayed graft function (DGF) and renal function were analysed. The results were compared with the group of 110 younger donors (mean age 53.4 years, range 25 – 62) and their recipients (mean age 32.2, range 16-42), performed in the same time (YD).
Results: The 3 and 5 years cumulative graft survival rate in the ED was 81% and 72% compared with 85% and 81% in the YD ($p > 0.9$). The rejection episodes were also comparable within two groups of the patients (19 and 17%, respectively). DGF revealed in 15% of the ED and only in 8% in YD. The serum creatinine on the end of 60 months of follow up was 146.04 in ED compared with 123.38 in YD ($p < 0.01$).
Conclusion: The elderly living donors remain a valuable source of kidneys especialy in the regions where deceased donor transplantation is not yet established. After 20 years experience the authors confirm the beneficial effect of LRT on organ shortage in the region.

RO-121A RENOVASCULAR RESISTANCE OF MACHINE PERFUSED DCD KIDNEYS IS ASSOCIATED WITH PRIMARY NON-FUNCTION

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Background: Donation after cardiac death (DCD) has shown to be a valuable extension of the donor pool despite a higher percentage of primary non-function (PNF) and delayed graft function (DGF). Limiting the incidence of primary non-function is of crucial importance because transplantation of nonviable kidneys results in unnecessary risk of surgery and immunosuppression, and sensitizes the recipient for future transplants. Moreover, viable donor kidneys should be prevented from being discarded. Renovascular resistance is said to predict graft outcome, however literature is not unambiguous. Therefore, we studied the association between renovascular resistance during machine perfusion and short-term and long-term graft and patient survival.
Methods: All transplanted and contralateral DCD kidneys preserved by machine perfusion in our center between 1993 and 2007 were analyzed (n=440). We used multivariable analyses to determine if renovascular resistance was independently associated with outcome measures.
Results: 439 recipients were transplanted with Maastricht category 1 to 4 DCD kidneys. We showed that renovascular resistance at the start (T_0) and after 1, 2, and 4 hours of machine perfusion was significantly and independently associated with PNF (T_0: OR 2.040, 95% CI 1.362 to 3.056; p=0.001) and DGF (T_0: OR 2.345, 95% CI 1.110 to 4.955; p=0.025). Long-term renal function,

graft survival and patient survival, were not significantly associated with renovascular resistance, however graft survival of kidneys with a renovascular resistance of >2,5 mmHg/ml/min/100g had a PNF rate of > 58% and a 5-year graft survival of less than 40%, which is unacceptable.
Conclusion: Renovascular resistance in DCD kidneys at the start of machine perfusion is an independent risk factor for PNF and must therefore be considered in viability assessment.

Kidney IV

RO-122 GENETIC ASSOCIATION OF FOXP3 GENE POLYMORPHISMS WITH ALLOGRAFT REJECTION IN RENAL TRANSPLANT PATIENTS

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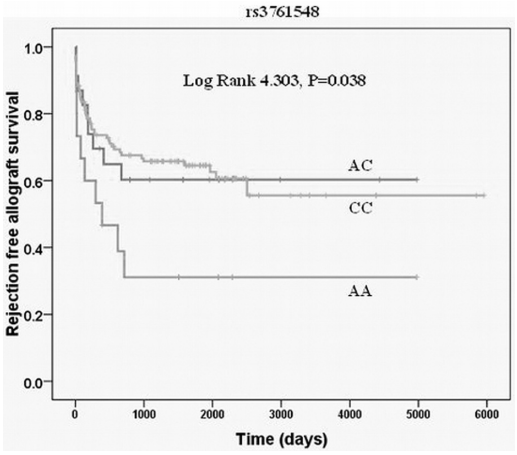
Background: FOXP3 gene is known to be important for regulatory T cell development and function, and is associated with the rejection of human kidney transplants. The present study was therefore conducted to determine the impact of FOXP3 polymorphisms on allograft rejection in renal transplant recipients.
Methods: A total of 166 adult patients were categorized into either a Rejection group (65 patients) or a No rejection group (101 patients). All transplant patients were on triple immunosuppressive therapy consisting of calcineurin inhibitors, mycophenolate mofetil and prednisolone. Rs3761547, rs3761548 and rs2232365 variant alleles in the FOXP3 gene were genotyped using a TaqMan probe technique, and their relationships with rejection were investigated.
Results: The allele frequencies of rs3761547-G, rs3761548-C and rs2232365-G were 13.8%, 84.1%, and 24.6%, respectively. There was no significant difference in the genotype frequencies of rs3761547 and rs2232365 variants between patients with and without rejection history (P>0.05). The rs3761548 AA genotype carriers were associated with about a four-fold greater risk for allograft rejection compared with patients with the CC genotype (two years post-transplant: odds ratio 4.40, 95% confidence interval 1.41-13.7, p=0.011; three years post-transplant: odds ratio 4.10, 95% confidence interval 1.32-12.74, p=0.015; five years post-transplant: odds ratio 3.95, 95% confidence interval 1.27-12.29, p=0.018).

Genotype frequencies in the groups of patients with and without rejection history

Location	Genotype	Rejection (%)	No rejection (%)	OR (95% CI)	P value
1 year post-transplant					
rs3761547	AA	38 (80.9)	83 (69.7)	1	
	AG	9 (19.1)	36 (30.3)	1.83 (0.80–4.18)	0.147
rs3761548	CC	33 (70.2)	95 (79.8)	1	
	AC	7 (14.9)	16 (13.4)	1.26(0.48–3.33)	0.642
	AA	7 (14.9)	8 (6.7)	2.52(0.85–7.48)	0.096 0.096
rs2232365	AA	24 (51.1)	61 (51.3)	1	
	AG	23 (48.9)	58 (48.7)	0.99 (0.51–1.95)	0.982
2 years post-transplant					
rs3761547	AA	47 (79.7)	74 (69.2)	1	
	AG	12 (20.3)	33 (30.8)	1.75 (0.82–3.72)	0.145
rs3761548	CC	40(67.8)	88(82.2)	1	
	AC	9(15.3)	14(13.1)	1.41 (0.57–3.54)	0.459 0.459
	AA	10(16.9)	5(4.7)	4.40 (1.41–13.7)	0.011
rs2232365	AA	28 (47.5)	57 (53.3)	1	
	AG	31 (52.5)	50 (46.7)	0.79(0.42–1.50)	0.473
3 years post-transplant					
rs3761547	AA	49 (80.3)	72 (68.6)	1	
	AG	12 (19.7)	33 (31.4)	1.87(0.88–3.98)	0.1
rs3761548	CC	42 (68.9)	86 (81.9)	1	
	AC	9 (14.8)	14 (13.3)	1.32 (0.53–3.29)	0.556
	AA	10 (16.4)	5 (4.8)	4.10 (1.32–12.74)	0.015
rs2232365	AA	30 (49.2)	55 (52.4)	1	
	AG	31 (50.8)	50 (47.6)	0.88(0.47–1.65)	0.691
5 years post-transplant					
rs3761547	AA	49 (79)	72 (69.2)	1	
	AG	13 (21)	32 (30.8)	1.68 (0.80–3.51)	0.169
rs3761548	CC	43 (69.4)	85 (81.7)	1	
	AC	9 (14.5)	14 (13.5)	1.27 (0.51–3.17)	0.607
	AA	10 (16.1)	5 (4.8)	3.95 (1.27–12.29)	0.018
rs2232365	AA	30 (48.4)	55 (52.9)	1	
	AG	32 (51.6)	49 (47.1)	0.84 (0.45–1.57)	0.575

Kaplan-Meier analysis revealed a significantly lower mean time for the first rejection in rs3761548 AA compared with CC genotype patients (Log rank=4.303, p=0.038).
The FOXP3 haplotype had no significant effect on allograft rejection.



Conclusion: Our results firstly suggest that patients with the FOXP3 rs3761548 AA genotype were at higher risk for rejection compared with CC genotype patients. These results may also have implications for improving the outcome of kidney transplantation and the efficacy of immunosuppressive regimen treatments.

RO-123 IMPACT OF RENAL TRANSPLANTECTOMY ON SECOND KIDNEY TRANSPLANT SURVIVAL

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Background: To determine impact of non functional graft nephrectomy on second renal transplantation survival.
Methods: We performed a retrospective study spreading from April 1989 to December 2009. We compared number of graft acute rejection episodes and grafts survival including patients who undergone a first renal transplantation with (group I) or without (group II) graft nephrectomy before second transplantation. Lymphocytotoxic antibodies (LCA) level, HLA matching was analyzed in both group.
Results: 84 patients received a second renal graft. 42 undergone graft nephrectomy and 42 conserved their non functional renal graft. There were no differences about LCA level, number of HLA compatibility or mismatch. Median follow up after second transplantation was 3,9 years (0-15). Acute rejections in Group I were 9.5% (n = 4) and in Group II 14, 3% (n=6). The difference was not statistically significant (p=0.2). Five (11%) grafts failed in Group I and eight (19%) in Group II. One, three and five years' actuarial graft survival in Group I was 100%, 97% and 93,2% while in Group II, it was 94.4%, 84.9% and 80.8%, respectively (p=0.008) (Figure 1). Five-year actuarial patient survival in the two groups was 100% and 90.3%, respectively (p=0.04). Multivariate analysis showed only PRA level had a statistically significant influence on patient and graft survival, irrespective of whether the patient had nephrectomy or not (p=0.04).

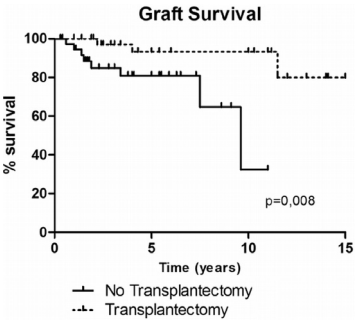

Figure 1

Conclusion: Nephrectomy of a failed allograft seems to significantly influence the survival of a subsequent graft. To let a previous graft on patients with potentially long time of dialysis could decreased second graft survival #.

RO-124 QT INTERVAL VARIABILITY ONE YEAR AFTER KIDNEY TRANSPLANTATION IS ASSOCIATED WITH LEFT VENTRICULAR MASS AND FUTURE CARDIOVASCULAR EVENTS

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Introduction: Cardiovascular events (CVE) represent the leading cause of death in kidney transplant recipients. Increased QT interval variability (QTV) is a risk factor for arrhythmia and CVE. This study investigated the associations of QTV with left ventricular mass (LVM) one year after transplantation and future CVE beyond one year post-transplant.
Methods: A total of 68 incident non-diabetic kidney transplant recipients were included in the study. All patients underwent echocardiography and 5-minute 12-lead electrocardiogram. Beat-to-beat algorithm was used to calculate SDNN-QT (standard deviation of normal-to-normal QT interval) and rMSSD-QT (root-mean-square of the successive QT interval difference) QTV indices. To quantify QTV relative to heart rate fluctuations, QTRR index was calculated. Cardiac CVE (myocardial infarction or sudden death) were followed beyond one year post-transplant.
Results: Left ventricular hypertrophy (LVH) was present in 44 patients (65%). Patients with LVH had significantly higher values of SDNN-QT, rMSSD-QT, and QTRR indices as compared with patients without LVH (4.9±3.2 ms, 6.5±4.1 ms, and 0.15±0.09 vs. 3.0±1.7 ms, 4.4±2.6 ms, and 0.06±0.04, respectively; $P<0.05$). A direct correlation was found between LVM and SDNN-QT (R=0.47; $P<0.001$), rMSSD-QT (R=0.27; P=0.034), and QTRR (R=0.55; $P<0.001$) indices. After a median follow-up of 5.3 years, 18 patients (26.5%) had cardiac CVE. Comparisons between event and non-event patients revealed greater LVM and higher values of SDNN-QT, rMSSD-QT and QTRR indices in patients with cardiac CVE (256±49 g, 5.4±3.5 ms, 7.0±3.2 ms, and 0.17±0.11 vs. 214±54 g, 3.8±2.5 ms, 5.3±2.6 ms, and 0.10±0.09, respectively; $P<0.05$). In logistic regression analysis, increased QTRR index and presence of LVH were independently associated with future cardiac CVE.
Conclusion: In kidney transplant recipients, increased QTV at 1 year post-transplant was associated with greater LVM and an increased risk for future CVE.

RO-125 ARE THERE DIFFERENCES IN ADHERENCE TO IMMUNOSUPPRESSIVE DRUGS BETWEEN LIVING-RELATED AND DECEASED DONOR TRANSPLANT RECIPIENTS?

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Background: Evidence exists that adherence to immunosuppressive drugs is lower in recipients of living donor kidney grafts than those with deceased donors. This study's aim was to explore such differences and to examine possible explanatory factors.
Methods: Adherence levels to immunosuppressive drugs were compared between patients with living-related, living-unrelated and deceased donor grafts using data from two similar cross-sectional studies conducted at two transplant centers in Switzerland. Medication adherence was assessed by self-report, with or without additional electronic monitoring. The assessed variables included among others age, beliefs regarding immunosuppressive drugs, depression, pre-emptive transplantation, and the number of transplants received. Data from the studies were analysed by using proportional odds modeling.
Results: Unadjusted non-adherence odds were 2 to 3 times higher in living-related than deceased donor transplantation (odds ratios: 2.09-3.05; $p<0.05$). After adjustment for confounders, the strength of the relationship declined (odds ratios: 1.01 to 1.94; $p<0.05$). Differences in adherence between recipients of living-related and deceased donors were associated most strongly with the younger age of living-related subjects and their frequent belief that immunosuppressive drugs are less important for living donations.
Conclusion: Recipients of living-related donor kidneys show substantially lower adherence to immunosuppressive drugs than deceased donor recipients. Adherence may benefit in recipients of living-related donor kidneys by addressing false health beliefs of relative protection that promotes a sense of invulnerability.

RO-126 INFLUENCE OF DONOR RELATED FACTORS ON OUTCOMES WITH TACROLIMUS-BASED IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANTATION – THE OSAKA STUDY (OPTIMIZING IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANTATION WITH Advagraf®

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Background: Extended criteria donors and living donation rates are increasing. The OSAKA study, one of the largest ever randomised controlled trials in kidney transplantation, allows analysis of the effect of donor factors on kidney transplant outcomes.
Methods: Subjects (n=1251) were randomised to 24 weeks' treatment with tacrolimus immediate release (BID) 0.2mg/kg/day (Arm 1; n=309), prolonged release (QD) 0.2mg/kg/day (Arm 2; n=302), tacrolimus QD 0.3mg/kg/day (Arm 3; n=304) all with MMF and corticosteroids, or tacrolimus QD 0.2mg/kg/day with MMF, basiliximab and corticosteroids given only perioperatively (Arm 4; n=283). Efficacy failure was defined as the incidence and time to first incidence of either graft loss, biopsy confirmed acute rejection (BCAR) or graft dysfunction (eGFR <40mL/min/1.73m^2) at 24 weeks.
Results: The mean age of donors was ~51.5 years: ~50% were extended criteria donors and ~12% were living donors. Efficacy failure increased markedly with donor age (21.6% in donors <30 years; 63.1% in donors 60–70 years) and recipient age (34.1% in recipients <30 years; 57.2% in recipients 60–70 years) (Figure 1). Living organ donation was associated with a better outcome for renal function (GFR was higher with living donors, especially early post-transplant), particularly in the steroid avoidance arm (Figure 2). HLA mismatch

Figure 1: Line graph showing mean GFR plotted against donor age group for all four treatment regimens and also showing the effect in living donor recipients

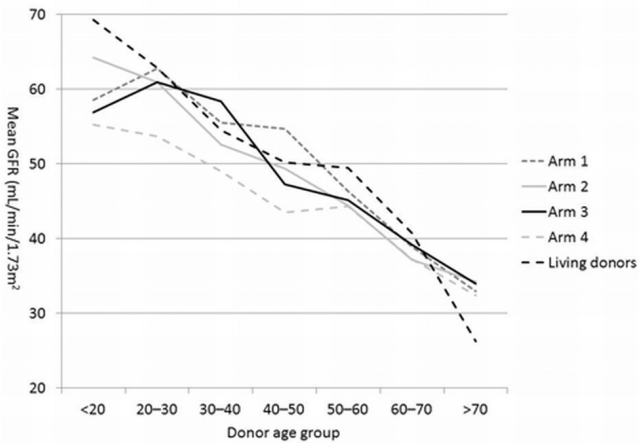
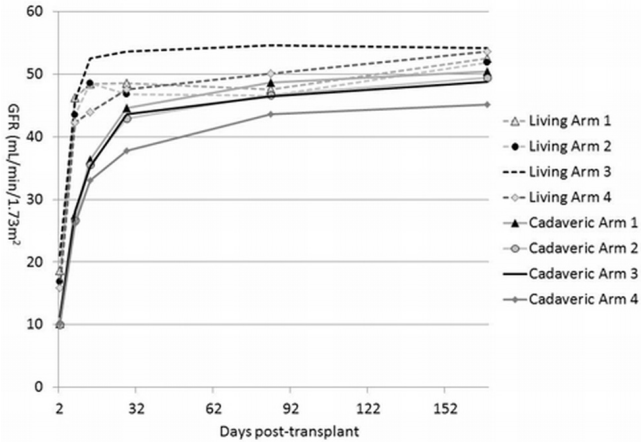


Figure 2: Line graph showing GFR following living and cadaveric renal transplantation in each of the four treatment regimens



increased the incidence of BCAR seen with tacrolimus QD 0.2mg/kg/day (2.7% with 0–1 and 10.1% with 4–6 mismatches) and tacrolimus BID (7.9% and 17.1%, respectively). Efficacy failure was slightly lower with male than female donors (failure rates of 41.4% and 49.4%, respectively).
Conclusion: The over-riding factor influencing kidney function after transplantation is donor age. Recipient age, HLA matching and living donation also contribute more than tacrolimus dose or formulation.

RO-127 CD20+ CELL INFILTRATION AND THE OUTCOME OF ACUTE CELLULAR RENAL ALLOGRAFT REJECTION: CORRELATION OF DENSITY WITH TIME-COURSE

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Background: The relationship between CD20+ B cell infiltration and the outcome of acute rejection at different time-periods (stages) is unknown.
Methods: The time course for 55 renal transplant patients diagnosed with acute cellular rejection was categorized into three stages; (a) very early rejection (<2 weeks n=17); (b) early rejection (2 weeks to 6 months, n=16) and (c) late rejection (> 6 months, n=22). The immunophenotypic markers of CD4, CD8, CD20, CD68 and HLA-DR were characterized by immunohistochemical staining. The density of each marker was quantified and correlated with renal allograft outcome. Comparison was made among the three groups during different periods of acute rejection.
Results: The density of CD20+ B cells in the very early rejection group was lower than early and late acute rejection groups. the density of CD4, CD8, and CD68 and HLA-DR did not differ among the three groups.

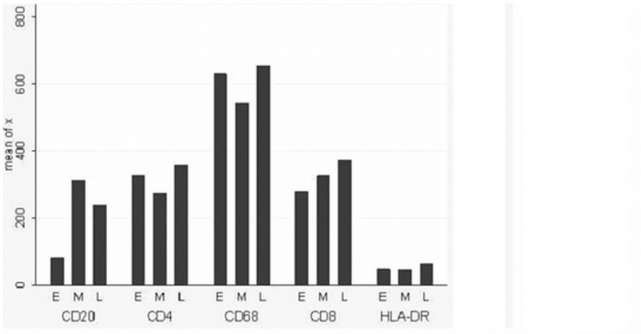

Figure 1 The different monocytes density among three period acute rejection.E: very early group, M: early group, L :late group. density of CD20: E lower than M and L group P <0.001, The density of CD4, CD8,CD68 and the HLA-DR expression on the tubular of allograft have no difference.

The ratio of (CD4+ & CD8+) to CD20+ in the very early rejection group was higher than the early and late acute rejection groups. The survival of the high density CD20+ group did not differ from the low density of CD20+ during the early and late acute rejection periods. However, the survival of the high density CD20+ group was worse than low density of CD20+. In all acute rejection groups. The CD4, CD8, CD68 and HLA-DR did not differ between high density CD20+ group and low density CD20+ groups.

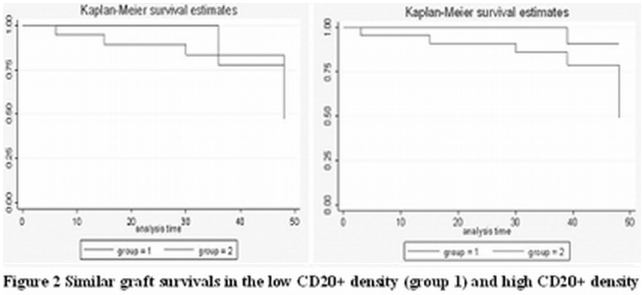

Figure 2 Similar graft survivals in the low CD20+ density (group 1) and high CD20+ density (group 2) of recipients with acute rejection over two weeks.
Figure 3 The graft survival in high CD20+ density (group 2) compared with the low CD20+ density group (group 1) is significantly (P=0.0356) for all recipients with acute rejection.

Conclusion: Very early acute cellular rejection occurs in absence of dense CD20+ cell infiltration. Aggregation of CD20+ cells occurred mostly after two weeks in the acute rejection. The time course of acute rejection rather than density of CD20+ in the allograft has influence on the outcome of the allograft survival.

RO-128 SERUM ANGIOTENSIN CONVERTING ENZYME (ACE)-2 ACTIVITY AS A MARKER OF GRAFT FUNCTION IN KIDNEY TRANSPLANT (KT) PATIENTS

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Angiotensin-converting enzyme (ACE)-2 is the only known active homologue of ACE, and its function is to degrade Angiotensin II to Angiotensin 1-7, a vasodilator peptide. The role of ACE2 in kidney transplant (KT) function is unknown. We previously showed that serum ACE2 activity is increased in male mice and human. The aim of this study is to investigate whether ACE2 activity in serum and urine is altered in KT patients as compared with controls. We also studied the relation between serum/urine ACE2 activity, kidney function and cardiovascular risk markers in KT patients.
Serum/urine ACE2 activity was assessed using a fluorescent assay in 113 KT patients (age 55±13yr, GFR-MDRD 44.8±11.3 mL/min). CKD-Stage 3 patients (n=27, age 57±10 yr, GFR-MDRD 41.4±8.6) age, gender and MDRD-matched served as controls.
Serum ACE2 activity was decreased in KT as compared to CKD patients (mean/SE 98±6.42 vs 138.7±17.9 RFU/uL/h, $p < 0.05$). In concordance, urine ACE2 activity was also decreased in KT as compared to CKD patients (lnACE2 activity in urine: 1.28±0.10 vs 4.16±0.34 RFU/uL/h, $p < 0.05$). In the univariate analysis, serum ACE2 activity was significantly increased in KT patients with ischemic heart disease (IHD) as compared with KT without IHD (105.9±8.69 vs 97.1±7.05 RFU/uL/h, $p < 0.05$). Renin angiotensin system blockade did not influence serum ACE2 activity. In multiple regression analysis, age, serum creatinine, and serum gamma glutamyl transferase, were independent predictors of serum ACE2 activity (r^2=0.35, p<0.01). Additionally, blood glucose and body mass index were independent predictors of urine ACE2 activity (r^2=0.15, p<0.001).

Multiple linear regression analysis of independent predictors of serum ACE2 activity in KT patients		
Risk factor	Standardized coefficient (Beta)	p-value
Serum creatinine (mg/dL)	0.241	0.002
Gamma glutamyl transferase (UI/L)	0.501	<0.001
Age (years)	0.202	0.009
Multiple linear regression analysis of independent predictors of urine lnACE2 activity in KT patients		
Blood glucose (mg/dl)	0.244	0.018
Body mass index	-0.305	0.003

In conclusion, serum ACE2 activity directly correlates with age, graft and liver function parameters. Measurement of the enzymatic activity of ACE2 in serum may become an easy tool to detect graft dysfunction in KT patients.

RO-129 TRANSPLANTATION WITH KIDNEYS AFFECTED BY SMALL TUMOURS

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Introduction: Renal transplantation confers both survival and quality of life benefit for end stage renal failure patients. Despite recent concerted efforts at national level to increase the organ donation in the UK, there remains a gap between the number of patients on waiting lists and kidneys available. One potential new source to address the universal shortage of the organs is the use of kidneys removed for small tumours (T1a <4cm) for transplantation. Nephron sparing surgery (NSS) has comparable outcomes to the radical nephrectomy (RN) for small tumours, yet large proportions of patients still undergo RN. There is a huge potential to increase the organ donor pool by utilising such restored organs after addressing the ethical issues. We aimed to look at the current evidence for use of such organs.
Methods: Pubmed, medline, EMBASE and CINHAL were linked searched for "renal tumour/tumor," "kidney tumour/tumor," "allograft tumour/tumor," "nephron sparing surgery," "partial nephrectomy," and "transplant" to indentify potentially relevant articles. Articles concerning the use of kidneys after resection of renal tumour for transplant and partial nephrectomy of allograft for renal tumours were selected. References of the selected article were also searched to identify further articles of interest.
Results: Current evidence could be described into two categories (see Tables 1 and 2).
Conclusions: The rate of recurrence is very low even after long follow up periods. The key has been to remove the tumour completely before the transplantation. Instances where residual tumour has been left behind, the recurrence

Table 1. Use of kidneys after resection of RCC

Group	Patients	Follow up (months)	Recurrence
Penn I.	14	Upto 210	Nil
Buell et al.	14	Upto 200	Nil
Nicol et al.	31	Upto 108	1
Mannami et al.	8	–	Nil
Case reports	6	More than 120	Nil

Table 2. Partial nephrectomy for tumours diagnosed after transplantation

Group	Patients	Follow up (months)	Recurrence
Case reports	35	Up to 120	1

has been almost certain with disastrous consequences. Thus if utilised carefully these restored kidneys could prove to be an important new source for transplantation.

RO-130 ARTERIAL STIFFNESS AND ANKLE BRACHIAL INDEX MONITORING AMONG KIDNEY TRANSPLATED PATIENTS

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Atherosclerosis development is accelerated in end stage renal failure patients. The measurement of the arterial stiffness widely used non invasive method for assesing the stiffness of the arterial wall, pulse wave velocity, and the endothel dysfunction. Changing of these parameters can forebode cardiovascular disease development. Ankle brachial pressure index (ABI) is widely used to predict the severity of peripheral arterial disease (PAD) can be linked to a higher risk of heart attack or stroke. Stiffness parameters were measured with TensiomedTM Arteriograph. 50 cadaver kidney transplanted patients with stable and good kidney function ($<$140 μmol/l) were followed up in a cross sectional single center study. We analysed the correlation between the stiffness parameters and ABI during a short (the first 3 weeks after transplantation) and long (3 years) term. We investigated te correlation between the main labor parameters, immunosuppressive therapy, age of the patients, time since transplantation and the stiffness parameters and ABI. In our cross sectional study, there was significant correlation between the stiffness parameters and ABI. (right ATP, PWV: R= - 0,36 p=0,01 n=50; right ADP, PWV: R= - 0,42 p=0,002 n=50). In our 3 years longitudinal study we found significant elevation in PWV ($p<0.001$). In our short term longitudinal study there was no significant change in the stiffness parameters, but a moderate decreasing tendency was found. We found significant correlation between PWV, ABI and cretainine, age of the patients, and negative correlation with GFR ($p<0.001$). ArteriographTM and ABI monitoring are non-invasive, objective and convenient method for the early diagnosis and follow-up of atherosclerosis, arterial calcification and stiffness. Prevention of cardiovascular event is to perform transplantation in as early age as it possible in case of end stage renal failure patients.

RO-131 ANEMIA AFTER KIDNEY TRANSPLANTATION AND ITS RISK FACTORS

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Background and aims: Post-transplantation anemia (PTA) is a common complication after kidney transplantation. Although bone marrow suppression was not a Known side effect of cyclosporine (CsA), it may cause anemia among kidney transplant patients. We conducted a large study to examine the prevalence of PTA and its relation to CsA blood level.
Materials and Methods: In a retrospective study on 5536 kidney transplant patients, correlation of PTA and CsA was evaluated between 2007 and 2010. All tests were done in a single laboratory. We considered anemia as hemoglobin concentration of 13 g/dl or less in men and 12 g/dl or less in women and severe anemia was defined as $\leq$ 10 g/dl in both gender. Univariate and multivariate analyses were performed to determine the correlation of PTA with other risk factors such as renal allograft function, CsA blood levels and other biochemical parameters.
Result: A total of 5536 patients were recruited from different Transplant Centers of Tehran, Iran. The mean age of recipients was 38$\pm$15 years; 62.7% male and 37.3% female. The prevalence PTA in this survey was 49% (n=2731) of cases, 37% mild to moderate anemia and 12% severe anemia. It was more prevalent (70%) in 3 months following transplantation. In multivariate regression analysis, a significant relationship was seen between serum hemoglobin and CsA trough level (p=0.000). There were also significant correlations between hemoglobin concentration with older age of donors (p=0.009), female gender of recipients (p=0.000), impaired renal function (p=0.000) and lipid profile (p=0.00).
Conclusion: In the present study, we concluded that prevalence of PTA is quite high. CsA level correlated with anemia and it must be mentioned drug doses could be diminished as possible.

Liver III

RO-132 THE IMPORTANCE OF TOTAL WARM ISCHEMIA TIME (WIT) FOR THE OUTCOME OF LIVER TRANSPLANTATION (LTx) FROM DONORS AFTER CARDIAC DEATH (DCD) – SINGLE CENTER EXPERIENCE

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Background: DCD are valuable source of organs for LTx. However, LTx using DCD livers is associated with inferior graft survival and higher rate of biliary complications. This single center, retrospective study analyzed the outcome of LTx from DCD with respect to patient and graft survival as well as biliary complications rate. Additional search was made for the risk factors for the outcome.
Material/methods: Between October 2001 and December 2010 fourty-eight livers out of 378 (12.7%) were transplanted from DCD. The review of prospectively collected donor, recipient and transplant data was performed.
Results: Overall patient survival at 1-, 3 and 5-year was 81%, 71% and 59%, respectively. Overall graft survival at the same time points was 64%, 55% and 44%. Primary non function rate occurred in 3 patients (6%) and initial poor function (IPF) in two (4%). The most common complications were biliary complications (43%), followed by bleeding complications (40%). 20 patients required one or more reoperations (42%). Retransplantation rate was 27.1% with biliary non-anastomotic strictures as a leading cause of retransplantation. Multivariate analysis revealed that reoperation (p=0.00), recipient age (p=0.02) and total WIT (p=0.00) were independent risk factors for patient survival. For the graft survival sepsis (p=0.00) and donor BMI (p=0.00) were risk factors after multivariate analysis. No risk factors could be found for biliary complications in this study.
Conclusions: Although excellent patient survival can be obtained after LTx from DCD, it is influenced by recipient age, prolonged total WIT and the need for reoperation. At the same time the main risk factor for graft survival is sepsis and donor BMI. The biliary complications rate is high and it remains the main cause of retransplantation after LTx from DCD.

RO-133 LIVING DONOR RELATED LIVER TRANSPLANTATION – A PREFERABLE TREATMENT OPTION IN PATIENTS WITH PERIHILAR CHOLANGIOCARCINOMA

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Introduction: Liver transplantation (LT) can be performed in carefully selected patients with unresectable perihilar cholangiocarcinoma (PHCC). Due to the donor organ shortage, liver transplantation in patients with PHCC is possibly associated with an excessive waiting time prior the performance of LT. Living donor related liver transplantation (LDLT) can decrease the waiting time and may therefore be a feasible option for patients with PHCC. We report about the experience with LDLT in PHCC patients in a german single center.
Methods: Since 2004, eight patients with PHCC underwent LT at our department. In five cases (62,5%) LDLT was performed compared to group of three patients whereby two patients (25%) underwent fullsize-LT and one patient (12,5%) received a domino graft. Follow-up ranges from two weeks to 67 months.
Results: Three of the five LDLT patients (60%) are still alive and in good clinical condition. There is no evidence for tumor recurrence in these patients. Two of the five LDLT died due to tumor recurrence approximately 25 months post-LDLT. The patients of the other group all died (100% mortality) whereby one patient died 20 months after fullsize-LT due to tumor recurrence, one patient died one month after fullsize-LT due to a bleeding complication and the patient receiving the domino graft died six months after LT due to multi-organ failure.
Discussion: We believe that LDLT is an excellent treatment option for patients with PHCC. The waiting is shortened and therefore the risk of continuing tumor growth and the risk of extrahepatic tumor spread is decreased. However, patients should be carefully selected before the performance of LDLT.

RO-134 LIVING DONOR LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: THE IMPACT OF NEO-ADJUVANT TREATMENTS ON THE LONG TERM RESULTS

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Introduction: Living Donor Liver Transplantation (LDLT) may represent a valid therapeutic option allowing several advantages for patients affected by Hepatocellular Carcinoma (HCC) and waiting for Liver Transplantation (LT).
Methods: Among 1145 patients underwent LT at our Institute, 70 recipients have received LDLT. From January 2000 to December 2008, 179 patients underwent LT due to HCC, 30 out of them (16.7%) received LDLT, and 154 (86.0%) received DDLT. Trans-arterial chemoembolization, Radiofrequency Ablation, Percutaneous Alcholization, or Liver Resection were applied as downstaging procedure while the waiting list.
Results: The overall 3- and 5- years survival rate was 77.3% and 68.7% versus 82.8% and 76.7% respectively for LDLT and DDLT recipient with not significant differences at the log rank test. Moreover, 3- and 5- years of recurrence free survival rate was 95.5% (LDLT) versus 90.5% and 89.4% (DDLT) and resulted not significantly different.
Conclusion: An aggressive downstaging policy seems to improve the long-term results also in LDLT, thus LRT may be considered not only useful to prevent tumor progression awaiting for transplantation, but also as neoadjuvant therapy for HCC. A literature detailed meta-analysis could definitely clarify if LDLT is or not an independent risk factor for HCC recurrence.

RO-135 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN HIV CO-INFECTED PATIENTS: A SINGLE CENTRE EXPERIENCE

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Background: HIV positive patients are likely to have hepatitis B and/or C virus co-infection because of exposure to common risk factors. In HIV-positive patients longer survival observed since the introduction of highly active antiretroviral therapy (HAART) may permit the progression of the liver disease and increase mortality due to complications including liver failure and hepatocellular carcinoma (HCC). The aim of our study was to assess the outcome of liver transplantation (LT) in HIV patients.
Methods/Materials: From October 2004 to January 2011 fifteen HIV positive patients underwent LT at our Centre. These patients were retrospectively analyzed as regards to general and viro-immunological pre –LT features and pathological data as number, maximum and total diameter of the nodules, microvascular invasion, satellites, Edmondson grade and percentage of necrosis.
Results: Fourteen patients were male and one female. Median MELD score was 21,67 points (range 11-32). All the patients but one had an undetectable HIV viral load pre-LT. Median pre-LT CD4 T-cell count was 284,4/mmc (range 129-956). All patients were pre-operatively inside Milan Criteria. For HCC down-staging during the waiting list both loco-regional techniques such as trans-arterial chemoembolization and/or radiofrequency ablation and liver resection were performed. Primary immunosuppression consisted in calcineurin inhibitors (CNI) eventually switched to Rapamycin in case of CNI toxicity or in patients with an important tumour burden before LT. In one patient HCC recurrence occurred with hepatic and pulmonary localization. Five patients out of twelve died. Median follow up was 30,2 months (range 1,3-68,9).
Conclusion: According to our experience LT in HIV positive patients with HCC is feasible and HCC recurrence does not particularly affect these patients compared to HIV negative patients. However further studies in large clinical settings are needed to establish the safety and effectiveness of this treatment.

RO-136 THE IMPACT OF TRANSARTERIAL CHEMOEMBOLISATION AS BRIDGING THERAPY FOR HCC BEFORE LIVER TRANSPLANTATION IN THE ERA OF MELD ALLOCATION

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Background: Transarterial chemoembolisation (TACE) is the most common bridging therapy to prevent tumour progress of HCC. The aim of our study was to evaluate the impact of TACE in the era of MELD allocation.
Methods: In a retrospective single center study we included all patients with a TACE therapy for HCC, which received a liver transplantation between January 2007 and December 2009. Beside demographic data, we analysed the course and complications during TACE bridging and after transplantation as well as the correlation of imaging and histopathology.
Results: During this period we transplanted 31 men and 8 women with HCC, which received a TACE bridging. The mean age was 58,6 ($\pm$10,4) years. In the initial radiologic evaluation 28 of 39 patients were within Milan criteria. The mean waiting time before transplantation was 9,5 months. During this period patients received a mean number of 4,2 ($\pm$2,1) TACE sessions. 35 patients (89,7%) demonstrated a stable disease concerning radiologic follow-up. Complications associated with TACE therapy occured in 9% of our patients. Only one patient had to stop TACE bridging due to sepsis.
In 7 patients the histological examination showed a complete tumour necrosis without viable tumour. In 6 patients tumour size and spread within the liver was underestimated. Five patients developed a recurrent HCC within 18 months after liver transplantation. Six of our patients died after transplantation due to sepsis, multiorgan or graft failure.
Conclusion: The results of our study show that TACE is an effective bridging therapy with low morbidity for a high percentage of patients with HCC. MELD allocation and still increasing waiting times require a close-meshed TACE-algorithm to prevent drop-outs on the waiting list. A still unresolved problem is the radiologic underestimation of the tumour stage.

RO-137 ROLE OF α-FETOPROTEIN AS PREDICTOR OF RECURRENCE IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is the treatment of choice for patients with hepatocellular carcinoma (HCC). Milan criteria (MC) is based exclusively on morphological aspects, while some expanded criteria also use biological features as selective criteria. However, biological features such as tumor grading and microvascular invasion require a tumor biopsy for their detection. The aim of the study was to evaluate both pre-LT biological and morphological parameters in order to evaluate their tumor recurrence prediction.
Methods: A cohort of 153 consecutive adult patients who underwent LT for HCC on cirrhosis from January 1999 to March 2009 was retrospectively analyzed. The minimal follow-up was 2 years.
Results: HCC recurrence was observed in 12 patients (7.8%). At univariate analysis, serum alpha-fetoprotein (AFP), total tumor volume (TTV) and radiological MC-out status resulted significant.
At multivariate logistic regression analysis, serum AFP was the unique independent negative risk factor for the development of HCC recurrence (OR 2.0,95% CI 1.5-4.0, *p*-value 0.03), while TTV and MC failed in this role. A cut-off value of 210 ng/mL was obtained using ROC analysis.
Patients who exceeded this value showed a 5-year survival rate of 23.3% respect to a 76.2% of patients who presented an AFP $<$ 210 ng/mL (log-rank test: $<$ 0.0001).
Conclusions: AFP resulted the strongest predictor of HCC recurrence, more than tumor number and dimensions did. Exclusive use of AFP as selective criterion seems not to be recommended, due to the presence of recurred tumors with pre-LT low AFP values; however, at the same time, we think the combination of morphological features and AFP is necessary, in this way avoiding to transplant patients with small but biologically aggressive tumors. Further larger studies aimed to evaluate the combination of morphological and biological criteria are needed.

RO-138 RECURRENCE-FREE LONG-TERM SURVIVAL AFTER LIVING DONOR LIVER TRANSPLANTATION FOR HCC IS INDEPENDENT FROM CLINICAL TUMOR MACROMORPHOLOGY

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Background: The Milan criteria are based on cadaveric and not on living related liver transplantation (LRLT). The aim of this trial was to analyze predictive variables for recurrence-free long-term survival in patients undergoing LRLT versus deceased donor liver transplantation (DDLT).

Patients: 91 patients with HCC were included in this trial. Twelve patients underwent LDLT, while 78 patients received a deceased donor liver transplant. DDLT was based on Milan criteria. Significant biological tumor progression (major vessel infiltration, extrahepatic tumor spread) resulted in patient drop out from the transplant list. The impact of clinical and biological (AFP-level, grading, vascular invasion, 18F-FDG-uptake on PET, response to neoadjuvant bridging) parameters was analyzed by uni- and multivariate analysis.
Results: Mean follow-up posttransplantation was 65,2 months. Based on clinical staging, 50% of patients in the LRLT-group but only 35% of patients in the DDLT population demonstrated HCC beyond the Milan burden at transplantation. Mean size of the major tumor nodule was significantly higher in the LRLT-group (5,7 cm) than in the DDLT-subpopulation (3,9 cm; P = 0,03), while total tumor diameter tended to be higher in the LRLT-group (7,6cm versus 6,1cm). Besides, mean waiting time for transplantation was significantly lower in the LRLT-group (4 months) compared to the DDLT-group (12 months; P = 0,01)
Five-year recurrence-free survival post-LT was 71% after DDLT and 82,5% after LDLT, respectively.
None of macromorphologic parameters, but only AFP level and 18F-FDG-uptake on PET had an impacton long-term outcome in the LDLT-group.
Conclusion: Macromorphologic parameters do not impact outcome after LRLT in patients with HCC. Based on pretransplant biological tumor features, such as AFP level and glucose metabolism on PET, in combination with a significantly reduced waiting time for transplantation, LRLT leads to excellent long-term results in patients with advanced HCC.

RO-139 APPLICABILITY OF CRITERIA FOR EARLY ALLOGRAFT DYSFUNCTION IN LIVER TRANSPLANTATION ACCORDING TO DONOR TYPE

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A definition for early allograft dysfunction (EAD) after liver transplantation was validated in deceased donors (Olthoff 2010).
Aim: Evaluate the prevalence of and criteria for EAD among recipients of livers from donation after brain death (DBD), donation after cardiac death (DCD), and living donation (LD) donors.
Methods: Transplants performed between 8/04 and 12/10 were analyzed. EAD was defined by AST/ALT >2000 IU/L in week 1, total bilirubin ≥10 mg/dL on POD7, and/or INR ≥1.6 on POD7.
Results: There were 432 recipients: 364 DBD, 30 DCD, and 38 LD; 70% were men and 51% HCV positive. Median donor age was 53 years (25-75% interquartile range 36-66) and recipient age 54 (47-61). A total of 118 recipients (27%) developed EAD: 90 DBD (25%), 17 DCD (57%), and 11 LD (29%) (*P*=0.001). A greater proportion of DCD *vs* DBD met EAD criteria based on transaminases and bilirubin (*P*=0.003 and <0.001, respectively) (TABLE). Bilirubin was, furthermore, the criteria by which the majority of LD met EAD criteria, and a higher proportion of LD *vs* DBD met EAD criteria based on bilirubin (*P*=0.002). However, only 2 LD recipients met EAD criteria based on transaminases, while none met EAD criteria based on INR.
Six-month graft loss occurred in 32 DBD (9%), 8 DCD (27%), and 2 LD (6%) (*P*=0.031 and 0.044 for DCD *vs* DBD and LD, respectively). Six-month patient death occurred in 27 DBD (8%), 5 DCD (17%), and 2 LD (6%). Eight recipients (2%) developed PNF (7 DBD, 1 DCD), all of whom met EAD criteria.

Recipients meeting criteria for EAD according to donor type

Group	AST/ALT >2000 in week 1*	Bilirubin ≥10 on POD7*	INR ≥1.6 on POD 7*
DBD (N=364)	52 (14%)	29 (8%)	27 (8%)
DCD (N=30)	10 (36%)	9 (33%)	0
LD (N=38)	2 (5%)	9 (24%)	0

*Criteria may overlap among patients within the same group.

Comment: The utility of the recently validated definition for EAD is still being investigated. Though it may be useful when evaluating deceased donors, it appears to overestimate the true prevalence of graft dysfunction among LD grafts.

RO-140 DEVELOPMENT AND VALIDATION OF AN INSTRUMENT EVALUATING THE IMPACT OF ANTI HBV IMMUNOGLOBULIN THERAPY (HBIg) ON QUALITY OF LIFE (HRQOL) IN LIVER TRANSPLANTATED (LT) PATIENTS

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Background: The impact of HBV long-term prophylaxis after LT on HRQOL and treatment satisfaction are pivotal aspects in ensuring adherence, but hard to explore due to the lack of specific instruments. Aim of this study was to develop and validate a specific instrument measuring the impact of HBIg on HRQOL and patient satisfaction in HBV-related liver disease LT-recipients.
Methods: The Immunoglobulin Therapy after Liver transplantation-Questionnaire (ITaLi-Q), 41 items covering 5 domains related to HBIg side-effects, positive/negative feelings, impact on daily activities flexibility, support for therapy management and satisfaction.
Results: 172 patients completed the questionnaire (72% males, 38% >60 years, 26% primary school, 59% treated with i.m. and 41% with i.v. HBIg). The scale score was obtained by adding each item points (range 0-100). The correlation between item and scale (convergent validity) >0.4 was good. Multitrait-multi-item analysis showed that ITaLi-Q has very good psychometric characteristics with item-scale correlation >0.4 for all the items but 1, high scaling success rate (>90% for all the scales, but 1), excellent internal consistency (Cronbach's alpha >0.80 for all the scales), and reproducibility (test-retest >0.70 for all the scales, but 2). ITALI-Q was able to discriminate patient subgroups according to clinical and socio-demographic characteristics. Patients treated with i.m. as compared with i.v. HBIg, reported significantly higher HRQOL on flexibility (81.5±21.4 vs. 73.1±24.2, p=0.01) and negative-feelings (90.1±17.3 vs.85.4±20.7; p=0.04), and lower HRQOL on side-effects (81.8±22.8 vs. 95.6±7.4; p<0.001). No differences emerged between modalities of administration as for satisfaction, positive feelings, impact and therapy support for therapy.
Conclusion: ITaLi-Q showed adequate psychometric characteristics. The HBIg route of administration can have a different impact on specific quality of life domains, without influence on patient satisfaction.

RO-141 PRELIMINARY STUDIES WITH A NEW BIOARTIFICIAL LIVER

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Fulminate hepatic failure (FHF) is associated with jaundice, coagulopathy and encephalopathy, and a significant mortality. Many patients can be salvaged by liver transplantation, but the supply of donor livers is limited. There is a need for an artificial hepatic-support device, either as a definitive treatment in FHF or as a bridge to liver transplantation. We present preliminary results with a new Bioartificial Liver (BAL).
Fulminant hepatic failure was induced in Large White X Landrace pigs (n=26) by total devascularization of the liver and the creation of a portacaval shunt. Catheters were inserted into the splenic vein and the external jugular vein for attachment to the BAL. The BAL consisted of two circuits, a primary plasmapherasis circuit, and a secondary circuit with the BAL which is populated by cultured human hepatocyte cell lines in alginate capsules. Typically 2-6×10^{10} cells were used. Pig liver weights varied from 900 to 1200g, and were proportional to body weight in range 20-30kg.
There were three groups of animals: Group 1 = control; Group 2 = BAL without cells; Group 3 = BAL with cells. In some animals in Group 3, there was a delay in the rise in the ICP, and an initial rise and stabilization of the ICP in others. The animals in Group 3 also had an improvement in the acidosis. There was evidence of conjugation of bilirubin in the animals on the BAL with cells. There was no evidence of improvement in coagulation.
In conclusion, the preliminary results with a new bioartificial liver showed improvements in some of the parameters of acute liver failure in pigs.

Liver IV

RO-142 LIVER HANGING MANEUVER WITH EXTRA-GLISSONIAN APPROACH IN RIGHT LOBE DONOR HEPATECTOMY: IS IT SAFE?

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Living Donor Liver transplantation is the mainstream of liver transplantation in many developing countries like Turkey. However living donor hepatectomy is still controversial due to its morbidity and mortality. Refinement of the surgical technique may improve the safety of this procedure.
Aim: We present a modification of right living donor hepatectomy by liver hanging maneuver with extra-glissonian approach (LH-EG).
Material and Methods: Patients whom underwent living donor right lobe donor hepatectomy between January 2008 and December 2010 in Ankara University Medical Faculty were included into the study retrospectively. We have been performing right lobe donor hepatectomy with LH-EG approach since January 2008. Surgical technique includes liver hanging with a vascular tape with extra-glissonian approach following dissection of right portal vein and right hepatic artery. This maneuver allows safe parenchyma dissection leaving all vital structures below vascular tape including biliary structures. Besides demographics, blood transfusion, operative time and complications were recorded.
Results: 48 patients (12 female, 36 male) were included into the study. The mean age was 31 years (18-56). Mean operative time was 255 minutes (230-320). The mean of blood transfusion was found 0.5 units (0-2 units). There was no operative and postoperative mortality. One patient had pneumothorax due to central venous catheter insertion. One patient had surgical site infection. There was no bilioma.
Conclusion: LH-EG approach in right lobe donor hepatectomy is a safe technique which may improve operative times.

RO-143 COMPARATIVE ANALYSIS BETWEEN THE USE OF COMPLETE LIVER GRAFT AND A PARTIAL ONE IN PEDIATRIC PATIENTS

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Background: Liver transplantation is an effective treatment for child with end stage liver disease. The scarcity of organs specially affects this group of patients. The use of partial liver grafts (SPLIT or living donor) has increased the availability of organs for these patients and are considered as a good alternative to complete liver grafts from brain-dead donors.
Methods/Material: Between January 2003 and December 2009, 45 liver transplantation were done in patients younger than 13 years. A complete graft was used in 20 cases (group A) and a partial one in 25 cases (group B) (14 SPLIT and 11 living-donors). A comparative analysis was done between the 2 groups.
Results: Both groups had similar characteristics with respect to demographic, technical and basal data. After a median follow-up of 44+29 months (range: 2-92), we observed 8 deaths (18%): 4 patients with relapse of the main disease, 3 with septic shock and 1 with an herpetic hepatitis over the graft. Actuarial patient survival rate at 1, 3 and 5 years were 91%, 85% and 82% in group A respectively; whereas they were 88%, 81% and 77% in group B. No statistical differences were found. 60% of all the cases (27 patients) had post-transplantation complications: 11% primary graft dysfunction, 31% vascular complications, 26% biliary complications, 42% acute rejection, 68% infectious complications and 9% had a lymphoproliferative disorder. No statistical differences with respect to complications were found between both groups, except for the rate of infections, which was significantly higher in group B (64%) in comparison to group A (36%) (p=0.03).
Conclusion: The use of partial liver grafts in pediatric patients is a good alternative to the use of complete grafts, with a higher rate of infectious complications.

RO-144 OUTCOMES AND DIAGNOSTIC CHALLENGES POSED BY INCIDENTAL CHOLANGIOCARCINOMA AFTER LIVER TRANSPLANTATION

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Introduction: Liver transplantation in the presence of cholangiocarcinoma (CCA) generally carries a poor prognosis. However, the outcome of patients found to have incidental CCA on explanted liver histology is less clear. We have evaluated the outcomes of incidental CCA in our liver transplant population.
Methods: A retrospective search was made of the transplantation and histopathology databases for patients fulfilling our definition for incidental CCA. All records, including archived histopathological slides were retrieved and analysed.
Results: Of 1288 patients undergoing liver transplantation over the twenty year period 1988-2008, nine were found to have incidental CCA (0.70%). Seven of the nine patients underwent liver transplantation for primary sclerosing cholangitis. Three additional patients who were transplanted for presumed hepatocellular carcinoma which subsequently turned out to be CCA were identified, but excluded from survival analysis.
The majority of tumours were early stage (T2 or below), but five (55.6%) had positive biliary transection margins. Median follow up was 51 months. Five patients (55.6%) developed recurrence of CCA after a median interval of 25.8 months, giving a disease-free survival of 100% at 1 year, and 66.7% at 3 years. There was no demonstrable difference between patients who experienced recurrence and those who have not in median follow-up, age, sex, CA 19-9, MELD score, tumour stage, tumour grade or tumour margin status. Three patients have died of recurrence, with a median interval from transplantation of 25 months. The overall 3 year survival was 66.7%.
Discussion: Incidental CCA's highlight the challenge of diagnosing this elusive disease. Although they tend to be early stage tumours, in keeping with the aggressive nature of the disease, the recurrence rate is high, and prognosis relatively poor. Prospective liver transplant recipients, especially those with PSC, should be investigated rigorously to exclude CCA.

RO-145 AB0-(IN)COMPATIBLE CADAVERIC DONOR LIVER TRANSPLANTATIONS – DOES REALLY CHANGE AN OUTCOMES?

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LTx using AB0-incompatible grafts is rarely performed because the reported outcome is significantly poorer than with compatible grafts. Adult AB0-incompatible LTx is associated with a high risk of graft failure due to antibody-mediated humoral rejection. Only shortage of donors in cases of acute liver failure causes considerable risk of death may force to use this type of graft for LTx.
714 LTx was performed in our Department until 15.12.08. Acute liver failure were indications in 193 cases. A retrospective study was carried out, including all cases of AB0-incompatible LTx performed in between 10.01 and 11.08. There were 5 men and 7 women in the mean age 35 ± 13. All 12 pts were qualified with UNOS 1 status in course of ALF. Detailed urgent indications for LTx were: Wilsons disease 3pts, Budd-Chiari syndrome 3pts, cryptogenic 3pts, fulminant HBV 1pts, ALD 1pts, postoperative liver insufficiency 1pts. In 6 cases albumin dialyses were performed before LTx. In 10 cases AB0-compatible (AB0-C) and in 2 cases AB0-incompatible (AB0-In) LTx were performed. In the post operation time, all transplantees received standardised strong 4 drug immunosuppressive treatment: Bazyliksimab, FK-506, mycophenolate mofetil and steroids.
Early complications after LTx were as follows: acute renal failure treated successfully with dialysotherapy 3pts, postoperative bleeding 4pts, PNF 1pts, neurological problems 4pts, biliary fistula 1pts, AR treated with high doses of steroids 2pts. 6 (50%) deaths was observed in early postoperative period (5x AB0-C and 1x AB0-In). 6 recipients survived (4x AB0-C, 1x AB0-In, 1x after reLTx). Actuarial survival rate after LTx was 50% at 1 year, median 13 months (1 to 20), 3 years after reLTx.
AB0-(in)compatible LTx is an acceptable option to cure liver failure in emergency. Intensive perioperative supervision and appropriate immunosuppressive treatment are essential to improve the effect of AB0-(in)compatible LTx.

RO-146 THE PRESENCE OF INCREASED PERIPHERAL Th17 LYMPHOCYTES AND SERUM LEVELS OF IL-17 DURING ACUTE REJECTION IN LIVER TRANSPLANT PATIENTS

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Background: Th17 cells are known to have potent proinflammatory functions in human inflammatory and autoimmune diseases. Therefore, it is tempting to speculate that Th17 cells and their effector cytokines are significant in the inflammatory response after organ transplantation. We assessed the circulating IL-17 producing $CD4^+$ cells (Th17 cells) and serum levels of IL-17 in patients with benign end-stage liver disease after liver transplantation and research on the relationship between Th17 cells in the peripheral blood (PB) and acute rejection.
Methods: A prospective analysis was performed on 52 consecutive patients who underwent liver transplantation from 2006 to 2010. PB was obtained from

liver transplant patients at different time points longitudinally: pre-transplant, post-transplant within one year and at the diagnosis of acute rejection. The circulating IL-17-producing $CD4^+$ cells in PB were measured by flow cytometry; serum levels of IL-17 were measured using an enzyme-linked-immunosorbent-assay. Blood samples were collected at the diagnosis of acute rejection and liver biopsy was performed at the same time. These patients were divided into 2 groups: group 1 was composed of 15 patients with acute rejection, and group 2 was composed of 37 patients without acute rejection.
Results: Compared with the nonrejection group, there is a significant increase of the levels of circulating IL-17-producing $CD4^+$ cells in the rejection group during acute rejection ($2.79\pm0.86\%$ vs. $1.83\pm0.74\%$, $P<0.01$). Serum levels of IL-17 was increased significantly in the rejection group versus the nonrejection group (97.26 ± 51.49 vs. 27.62 ± 22.37, $P<0.01$). Furthmore, the frequency of IL-17-producing $CD4^+$ cells in PB was positively correlated with Rejection Activity Index ($r = 0.76$, $P<0.01$).
Conclusions: These findings suggest a role for Th17 cells in human liver allograft rejection.

RO-147 INFLUENCE OF REJECTIONS EPISODES ON QUALITY OF LIFE FOLLOWING LIVER TRANSPLANTATION

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Background: Liver transplantation (LTx) is a well established procedure for end stage liver diseases. Since long term survival rates are satisfactory, nowadays quality of life (QOL) gains increasing interest depending on rejection episodes and individualized immunosuppressive drug selection (IDS).
Method: The influence of rejections on general QOL (gQOL) and gastrointestinal dysfunction (GID) were analysed during predefined post operative time periods. N=648 postoperative courses of liver transplant recipients were analysed during a time period between 25 days and 22 years after LTx. The impact of rejection episodes as well as GID and gQOL were accessed through standardised EYPASCH's QOL questionnaire form. Referring to histological findings patients were subdivided into two groups: A) without any rejections (n=459) and B) with biopsy proven rejection (n=192). For the time being histological findings of all included patients were considered.
Results: 1. Only n= 192 of 648 cases turned out with biopsy proven rejections. 2. If rejection happened in a period of 90 days prior to inquiry (n = 31) gQOL decreased while GID increased (not significant). 3. Interestingly a period of -90 to -30 days prior to inquiry showed significant decrease of gQOL (p=0,039) and almost significant increase of GID (p=0,075) for group B. 4. Beyond this period inqueries of group B (n = 176) didn't result in a significant influence on gQOL or GID compared to group A query results.
Conclusion: Eventhough 648 queries with 192 rejection episodes were performed overall heterogenecy of the query results seems to be too extensive for a proper statistically significant proof.
Nevertheless, past rejections influence gQOL and GID. Our findings did not show any "rejection predictive" value of EYPASCH's QOL questionnaire form in clinical use.

RO-148 RELEVANCE OF PROCALCITONIN IN THE EARLY POSTOPERATIVE PERIOD AFTER LIVER TRANSPLANTATION

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Background: Bacterial infections are a serious clinical issue after solid organ transplantation. The diagnosis can be complicated due to the immunsuppressive state of the recipient. Nowadays, the spectrum of diagnostic tools is broadened with the determination of Procalcitonin (PCT).
In this study, we correlated PCT levels with the clinical course of liver graft recipients in the early postoperative period.
Methods: We analysed 226 patients after liver transplantation in their clinical course up to the 14th postoperative day (POD).
We correlated PCT levels in relation to early postoperative complications, infections and graft dysfunctions.
Results: We found increased PCT levels in patients suffering from infections as well as from graft dysfunctions.
A graft dysfunction showed significantly increased PCT levels on POD three to five and seven. The PCT peak was on POD two (15,6 ng/ml in patients with graft dysfunction; 8,5 ng/ml in patients with normal graft function).
Furthermore, we verified that increased PCT levels after liver transplantation are associated with a worsened outcome.
Conclusion: Increased PCT levels are not necessarily associated with infectious complications. Instead, a PCT increase should be seen in the clinical context, since this could be a predictor of a graft dysfunction.

RO-149 THE IMPACT OF LIVER RETRANSPLANTATION ON SURVIVAL AFTER THE USE OF PARTIAL LIVER GRAFTS IN PATIENTS YOUNGER THAN 13 YEARS

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Background: Liver retransplantation rate, in pediatric patients, varies from 8% to 29% according to the different published articles. Its main indications are the primary dysfunction and the arterial thrombosis of the graft. When early retransplantation is done, patient survival at 5 years is over 80%, while it is less than 50% when the retransplantation is late, mainly because the long evolution of the liver dysfunction is accompanied by other organ dysfunction.
Methods/Materials: Between January 2003 and December 2009, 45 liver transplantations were done in patients younger than 13 years old. A complete graft was used in 20 cases (group A) and a partial one in 25 cases (group B) (14 SPLIT and 11 living-donors). A comparative analysis was done between the 2 groups.
Results: Both groups had similar characteristics with respect to demographic, technical and basal data. After a median follow-up of 45+29 months (range: 2-92 months), no overall and actuarial survival differences between both groups were observed. Retransplantation was done in 15.5% of the cases (7 patients): 3 of whom received a complete graft and 4 a partial one. In group A, patient actuarial survival rates at 1, 3 and 5 years after the retransplantation were 100% at all times; and in group B they were 75%, 50% and 50% respectively (p=0.07).
Conclusion: Although no statistical differences were found between both groups, liver retransplantation seems to diminish the long term survival rates in pediatric patients after the use of a first partial liver graft. It would be necessary to analyze a larger sample to confirm this association.

RO-150 EARLY USE OF PROLIFERATION SIGNAL INHIBITORS IS AN INDIPENDENT RISK FACTOR OF INCISIONAL HERNIA DEVELOPEMENT AFTER LIVER TRANSPLANTATION

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Introduction: Incisional hernia (IH) is a common complication after liver transplantation (LT) with an incidence reported between 1.7 and 34.3%. Immunosuppressive therapy is implicated in IH development but not as an independent risk factor in multivariate analysis. The purpose of the present retrospective study is to evaluate the risk factors of IH development after LT, focusing on the role of immunosuppressive therapy.
Materials and Methods: We retrospectively analysed 373 patients underwent LT in our Institute. Patients were divided in two groups on the basis of the postoperative course: IH group (121 pts, 32.4%) or no IH group (252 pts, 67.6%) considering a mean follow-up of 40.4 months. We recorded and analyzed in the statistical analysis the immunosuppressive therapy administered during the first month after LT.
Results: We observed 121 (32.4%) IH after a mean time of 18.4 ± 17.3 months (range 1.01-107 months). Patient survival resulted significantly better in IH group. At univariate analysis the parameters that resulted related to the development of IH were male gender (p=0.029), BMI$>$29 (p=0.005), era of LT after 2004 (p=0.023), MELD score $\geq$22, HBV infection (p=0.017). The highest incidence of IH was found in patients treated with PSI in monotheraphy (54.5%, p=0.004). Multivariate analysis revealed male gender (p=0.026, OR=2.15 - 95% CI 1.1-4.2), pre transplant MELD score $\geq$22 (p=0.04, OR=2.3 - 95% CI 1.3-4.0) and use of PSI (p=0.001, OR=2.5 - 95% CI 1.5-4.2) as independent risk for IH after LT.
Conclusion: Immunosuppressive therapy with PSI is an important independent risk factor for IH development after LT and if not strictly necessary, we should avoid the use of PSI during the first month after LT to reduce the incidence of IH.

RO-151 **CONVERSION TO SUBCUTANEOUS ANTI-HEPATITIS B IMMUNOGLOBULINS (Zutectra™) IN MAINTENANCE LIVER TRANSPLANT PATIENTS: PRELIMINARY RESULTS OF A MULTICENTER, PROSPECTIVE, SINGLE-ARM STUDY**

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We carried out a multicenter, prospective trial to assess the efficacy, feasibility, and safety of subcutaneous anti-hepatitis B immunoglobulins (HBIG) (Zutectra™) in maintenance liver transplant (LT) recipients. Inclusion criteria were: adult (≥18 years), maintenance (≥3 months) consenting LT recipients transplanted for HBsAg-related liver disease and on long-term, intravenous or intramuscular immunoprophylaxis; HBsAg and HBV-DNA negativity in two determinations within 3 months prior to study enrolment; and anti-HBs titre between 200 mIU/mL and 350 mIU/mL prior to the first dose administration. Patients were converted to Zutectra™ within 4 weeks of the last HBIG administration. Zutectra was administered weekly at 500 IU if body weight <75Kg, and 1,000 IU if body weight ≥75Kg. Concurrent antinucleos(t)ide medication was left unchanged. The study period was 24 weeks with an optional extension of 24 weeks for adherent patients with stable anti-HBs titres. Patients were followed-up for efficacy (anti-HBs titre ≥100 mUI/mL and/or HBV-DNA breakthrough) safety, and feasibility, defined as percent of patients achieving self-administration, time to first self-administration, and time to complete self-administration.

From June 2009 until June 2010 a total of 72 LT patients were screened in 7 centers. Sixty-six complied with the eligibility criteria and were enrolled. Eight patients (12.1%) were dropped out within 24 weeks due to adverse events in 4 cases (6.1%), lost to follow-up in 2 cases (3%), and nonadherence to study procedures in 2 cases (3%). All patients who completed the initial 24-week phase proceeded to the extension period. The full set of efficacy, safety, and feasibility data for the first 24 weeks will be discussed.

Conversion to Zutectra™ appears feasible starting 3 months after transplantation. Longer follow-up are needed to derive data on long-term safety, tolerability, and treatment adherence.

Heart: challenges in heart transplantation

RO-152 **DONATION AFTER CARDIAC DEATH: CAN HEARTS BE SUCCESSFULLY REANIMATED?**

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Background: The success of organ donation after cardiac death (DCD) has yet to extend into cardiac transplantation. Rescuing hearts from donors after cardiac death would allow significant expansion of the donor pool. This study used an *ex vivo* circuit to reperfuse porcine hearts in a simulated DCD model with the aim of restoring myocardial activity, testing various combinations of both established and novel perfusion solutions.

Materials/Methods: Eleven cross-Yorkshire Landrace pigs (mean weight 29.4±5.7 kg) were euthanased humanely by Schedule-1 (intravenous administration of phenobarbitone). The non-beating hearts were procured after being subjected to 10 minutes of warm ischaemia. All hearts (n=11) underwent initial antegrade flush with 250mls of AQIX® RS-I solution (a novel non-phosphate pH buffered preservation solution) at ambient room temperature. Hearts 3 to 11 were flushed with a further 250mls of either cold AQIX® RS-I (n6) or cold University of Wisconsin (UW) solution (n3). Static cold storage was in either AQIX® RS-I (n6) or UW solution (n5). Reperfusion was performed on a Langendorff modification of Model 30 Functional Circulation circuit, using a mixture of heparinised, leukocyte-depleted blood and AQIX® RS-I solution. Drugs (adrenaline, calcium gluconate, dopamine) and DC cardioversion were used to initiate left ventricular activity, which was measured by ultrasonic probes on the left ventricular outflow.

Results:

n	Flush / preservation	Drugs	Cardioversion	Activity/pressure
1, 2	250mls RS-I[1] / RS-I[2]	None	None	Fibrillation only; nil ventricular contraction
3, 5, 6	250mls RS-I[1] + 250mls RS-I[2] / RS-I[2]	Adrenaline	Yes	Ventricular contractions/70mmHg *n4 nil activity*
7, 8	250mls RS-I[1] + 250mls UW[2] / RS-I[2]	Adrenaline, Ca gluconate	Yes	Ventricular contractions/90mmHg
9,11	250mls RS-I[1] + 250mls UW[2] / UW[2]	Adrenaline, Ca gluconate	Yes	Ventricular contractions/40mmHg *n10 nil activity*

1 - ambient room temperature; 2 - 4-8°C

Conclusions: Hearts sourced from DCD donors can be successfully reanimated. Factors influencing successful reanimation included adequate coronary flush, administration of adrenaline and DC cardioversion. Restoration of cardiac activity was achieved using both a conventional (UW) and novel perfusion solution (AQIX® RS-I). Further studies are needed before hearts procured from DCD donors can be incorporated into mainstream cardiac donation.

RO-153 **USING DIALYSIS FOR PROLONGED EX VIVO WARM REPERFUSION OF DCD HEARTS**

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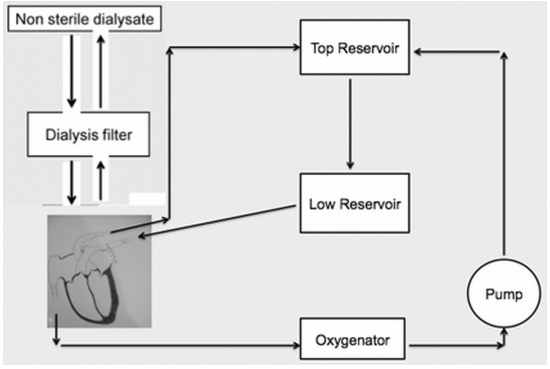
Background: *Ex vivo* reperfusion of organs sourced from Donors after Cardiac Death (DCD) offers the possibility of restoring organ function. However, prolonged reperfusion with warm blood can introduce waste metabolites and electrolyte imbalance into the *ex vivo* circuit. This potentially adversely affects the health of the organ.

Methods: Following 10 minutes of warm ischaemia, porcine hearts (n=6) were flushed and preserved using oxygenated, hypothermic machine perfusion for 2-4 hours. Subsequent warm blood (heparinised and leukocyte-depleted) reperfusion took place on our *ex vivo* circuit, with Aqix RS-I® (a novel perfusion solution) added to provide an adequate circulating volume.

A dialysis circuit was fashioned using a filter (Fresenius FX8 Capillary Dialyzer®) and two roller-pumps. This was placed in parallel with the reperfusion circuit.



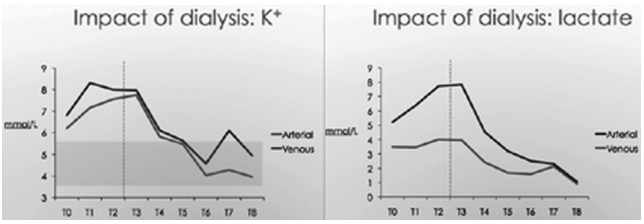
Circulating blood was diverted, using a pump, to the filter whilst dialysate was simultaneously pumped to run counter to the blood, allowing diffusion to occur. Blood was sampled for real-time acid/base and biochemical analysis.

The Fresenius A/5® dialysate used lacks phosphate due to its design for use with chronic renal failure patients. Therefore, phosphate was added to the dialysate.

Dialysate composition

	Composition of dialysate (mmol/L)		Composition of dialysate (mmol/L)
Na^+	138.0	HCO_3^-	35.0
K^+	2.00	Cl^-	105.5
Ca^{2+}	1.25	CH_3COO^-	3.0
Mg^{2+}	0.50	Glucose	1.0 g/L
Osmolality	291 mosm/L		

Results: After the commencement of dialysis, at T2, potassium and lactate levels were rapidly corrected. Dialysis was also seen to maintain arterial blood acid/base balance.



Discussion: Our dialysis circuit corrected potassium disturbance while rapidly reducing lactate levels. Our previous work has demonstrated that preservation followed by reperfusion is a technique which, when applied to a DCD-sourced heart, may lead to functional recovery and reanimation. Prolonged reperfusion, which may be necessary to achieve reanimation, would benefit from the dialysis technique we have described in order to protect the reperfusing organ from the deleterious effects of electrolyte and acid/base disturbance, as well as lactate accumulation.

RO-154 IMPACT OF DIFFERENT ATG DOSING PROTOCOLS ON LONG-TERM OUTCOME AFTER CARDIAC TRANSPLANTATION

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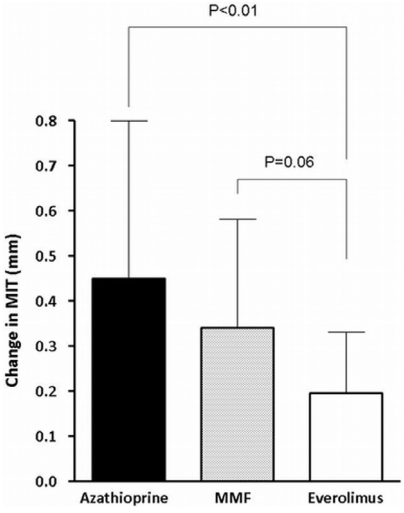
Background: ATG-Induction therapy after heart transplantation is still controversial and used only by less than 50% of centers. Moreover, there exist no data about the optimal dosage of ATG-induction. The aim of this study is to compare different doses of ATG induction.
Patients and Methods: Between 1996 and 2009 586 cardiac transplants were performed in our center. 523 (89%) patients with full data sets were included in the analysis. The median age was 56 years, 21% (n=112) were female. The median follow-up-time was 98 months. Patients were divided into 3 different groups according to total ATG dose: Group A: $\leq$4.5 mg/kg vs. Group B: 4.5–7.5 mg/kg vs. Group C: $>$7.5 mg/kg. Survival, incidence of rejection, infection, graftvasculopathy and cancer were compared by Kaplan-Meier-analyses (log rank test).
Results: There was better early (12m) and late (150m) survival in Group B (A: 80%, 43%; B: 90%, 65%; C: 88%, 58%; p= n.s.), however the difference was not significant. Freedom from treated acute rejection was better in group B (88%) compared to A and C (79, 80%, P=0.08). Signs of histological rejection were significantly different between the groups (A: 25%, B: 18%, C: 33%; p = 0.03). Group B had the lowest incidence of severe infection (A: 37%, B: 21%, C: 51%; p$<$0.01). CMV infection incidence was higher in group C (35%) compared to groups A, B (20%, 23%; p$<$0.01). There was no significant difference in freedom from graftvasculopathy between the groups (A: 91%, B: 85%, C: 79%; p=n.s.). The incidence of cancer was similar in all ATG groups (A: 3%, B: 7%, C: 11%; p=n.s.).
Conclusion: Different doses of ATG induction seem to have a significant impact on the outcome of heart-transplantation. There is a strong need for more studies on optimization of ATG therapy.

RO-155 EVEROLIMUS REDUCES CAV PROGRESSION AS COMPARED WITH AZATHIOPRINE AND MYCOPHENOLATE: A LONGITUDINAL IVUS-BASED STUDY

Marco Masetti, Luciano Potena, Paola Prestinenzi, Valeria Pece, Gaia Magnani, Francesco Saia, Paolo Romani, Nevio Taglieri, Fabio Coccolo, Marianna Nardozza, Teresa Ionico, Francesco Grigioni, Angelo Branzi. *Cardiovascular Department, University of Bologna, Bologna, Italy*

Coronary allograft vasculopathy (CAV) is the main cause of graft failure after heart transplantation (HTx). Besides its immunosuppressive properties, everolimus reduces CAV progression compared with azathioprine. However, whether this effect is reproducible in clinical practice and is retained also when compared to patients receiving mycophenolate mofetil (MMF) is unknown.
All consecutive patients receiving HTx between 2005 and 2009 treated with everolimus within the third month after transplant and in whom intra-vascular ultrasound (IVUS) study at month 1 and 12 after transplantation were feasible, represented the cases (n=17). Two cohorts of patients consisting in 24 patients receiving AZA and in 38 receiving MMF, matched for demographic and metabolic characteristics at baseline, and with IVUS data availability, represented the controls. All the 75 study patients additionally received cyclosporine and prednisone. Study endpoints were change in maximal intimal thickening (MIT), and occurrence of MIT change $\geq$0.5mm, a cut-off known as surrogate endpoint for subsequent cardiovascular mortality.
MIT increase was greatest in azathioprine, intermediate in MMF, and smallest in the everolimus treated patients (ANOVA=0.012). Bonferroni-adjusted comparisons showed a significant difference of everolimus vs. azathioprine (P$<$0.01) and a trend for everolimus vs. MMF (P=0.06). Similarly, frequency of MIT change $\geq$0.5mm was 46% in azathioprine, 26% in MMF, and 6% in everolimus patients (P=0.01). Use of statins varied between 81 to 95% of patients (P=0.3), and classic cardiovascular risk factors did not influence MIT progression in this population.



This observational case-control study shows that in a clinical practice setting everolimus may prevent CAV development as compared not only with azathioprine, but also with MMF. A larger number of patients is needed to elucidate the interaction between these immunosuppressive therapies and the other metabolic and immunological risk factors in determining CAV progression.

RO-156 FREQUENT OCCURRENCE OF DERMATOLOGIC COMPLICATION AFTER REPLACEMENT OF CALCINEURIN INHIBITOR WITH EVEROLIMUS LATE AFTER HEART TRANSPLANTATION

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Background: Efficacy and safety of everolimus (EVE) used in combination with cyclosporine-A as a primary immunosuppression after orthotopic heart transplantation (OHT) was established in prospective randomized trials, while the effects of late introduction of EVE are not explored yet.
Aim: Aim of the study was to describe the occurrence of dermatologic complication in OHT recipients after the late EVE introduction, used in combination with and without calcineurin inhibitor (CNI).
Methods: Study group consisted of 69 pts. (62M/7F, 53.5$\pm$11.3y/o) – 39 pts. receiving EVE without (Group I) and 30 pts. with CNI (Group II). Treatment was initiated at mean 97.21$\pm$54.76 (Group I) and 40.45$\pm$44.44 (Group II) months OHT. Predominant indication to use EVE was renal impairment in Group I, and recurrent acute rejection or coronary allograft vasculopathy in Group II. Follow-up was 12 months. At the end of observation 9 pts. from Group II were without CNI. All pts. were screened for the presence of skin lesions by the same experienced consultant in dermatology.
Results: Skin lesions were observed in 9 (23%) pts. from Group I and 1 (3%) pt. from Group II (p=0.021), and generalized itch in 8 (21%) pts. from Group I and 1 (3%) pt. from Group II (p=0.036, chi-square test). All complications were observed within the 1st month after EVE introduction, and none of them was noted in a group of 9 pts. in whom EVE was started in combination with CNI, and than CNI was discontinued. Predominant characteristics of the skin lesions was allergic or contact dermatitis and eczema. Therapy with anti-histaminic was sufficient enough to continue EVE in all pts.
Conclusions: Late replacement of CNI with EVE may cause dermatologic complications. Introduction of EVE with CNI seems to protect from the skin lesion appearance.

RO-157 IMPROVEMENT OR STABILIZATION OF RENAL FUNCTION AFTER LATE INTRODUCTION OF EVEROLIMUS IN HEART TRANSPLANT RECIPIENTS – 12 MONTH FOLLOW-UP

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Aim of the study: was to assess the efficacy and safety of late everolimus (EVE) introduction in combination with and without calcineurin inhibitor (CNI), with a special focus on renal function in heart transplant (OHT) recipients.
Methods: Study group consisted of 69 pts. (62M/7F, 53.5±11.3y/o) – 39 pts. receiving EVE without (Group I) and 30 pts. with CNI (Group II). Treatment was initiated at mean 97.21±54.76 (Group I) and 40.45±44.44 (Group II) months after OHT. Predominant indication to use EVE was renal impairment in Group I, and recurrent acute rejection (AR) or cardiac allograft vasculopathy (CAV) in Group II. Follow-up was 12 months. The additional analysis was performed according to CNI absence (Group IA, n=48) or presence (Group IIA, n=21) 12 months after EVE introduction. Renal function was evaluated by glomerular filtration rate (GFR) and plasma creatinine level (CRE). Safety profile of EVE was evaluated by a number of new incidence of CAV, AR, infection, myelotoxicity, lipid profile, and death rate.
Results: Highly significant improvement of renal function was observed in pts. without CNI (GFR0m 39±12/44±22; GFR12m 47±17/54±27mL/min, CRE0m 176±46/168±54; CRE12m 152±49/143±52umol/L in Groups I/IA) and remained stable in pts. on CNI (GFR0m 78±30/80±33; GFR12m 75±40/79±40mL/min, CRE0m 102±38/103±43; CRE12m 106±36/101±29umol/L in Groups II/IIA). Cholesterol and triglyceride levels did not increase, however statin dose was significantly higher in Group I. Only 1 clinically silent AR episode occurred (after CNI withdrawal). 10 deaths were observed (3/7 in Groups I/II, 4/6 in Groups IA/IIA), relation to EVE was considered in 3 cases: pneumonitis (n=2), and ileus/complication after surgery (n=1). CAV was a cause of 3 deaths.
Conclusions: Late CNI replacement with EVE improves renal function, and concomitant EVE/CNI use is possible without GFR deterioration.

RO-158 PRETRANSPLANT SOLUBLE CD30 (sCD30) FOR THE PREDICTION OF ACUTE CELLULAR REJECTION IN HEART TRANSPLANT RECIPIENTS

Olga V. Orlova[1], Alex V. Bugrov[1], Alex O. Shevchenko[2], Eduard N. Kazakov[1], Arkady J. Kormer[1], Igor M. Iljinsky[3], Olga P. Shevchenko[1]. *[1]Department of Heart Transplantation, Federal V. Shumakov Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation; [2]Department of Cardiology, Russian State Medical University, Moscow, Russian Federation; [3]Department of Clinical Pathology, Federal V. Shumakov Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation*

Despite the use of potent immunosuppressive agents, acute cellular rejection (ACR) affects early morbidity and mortality after heart transplantation (HTx). CD30, a cell surface glycoprotein, is a member of the tumor necrosis factor receptor superfamily. Pre- and post-transplant elevated levels of soluble form of CD30 (sCD30) have been shown to be associated with an impaired outcome in renal transplant recipients.
We have evaluated the pretransplant plasma levels of sCD30 with the aim of determining its value in predicting ACR in heart transplant recipients.
Methods: 75 heart transplant recipients, 70 men and 5 women, aged 44.5±9.5 years were followed for 36 months after HTx. The diagnosis of acute cellular rejection was made by endomyocardial biopsy performed either routinely or because of suggestive symptoms. Plasma levels of sCD30 were measured by ELISA.
Results: The concentration of sCD30 in patients before HTx was 6.9±3.4 ME/ml, in heart transplant recipient was significantly higher - 13.7±6.2 ME/ml ($p<0.01$). There was no significant correlation for sCD30 with age, gender, or plasma levels of C-reactive protein, interleukin-6, neopterin, and homocysteine.
During follow-up major study event defined as ACR grade 2R or more (ISHLT, 2004) occurred in 7 (38.9%) recipients with pretransplant sCD30 levels above median ($\geq$8 ME/ml) and only in 1 (1.75%) patient with low sCD30 ($<$8 ME/ml). Patients with high pretransplant sCD30 levels had $>$5-fold higher risk for ACR than patients with low sCD30 levels (relative risk, RR 5.3; 95% confidence interval 1.4 to 9.1). Event-free survival analysis showed significant difference in outcomes among patients with elevated and low levels of pretransplant sCD30 ($p<0.05$).
Conclusions: Measurement of pretransplant sCD30 plasma levels might offer a tool to recognize patients at high risk of acute cellular rejection after HTx.

RO-159 ANTIBODY-SENSITIZATION AGAINST HLA-A AND HLA-DR SPECIFICITIES AFTER IMPLANTATION OF VENTRICULAR ASSIST DEVICE

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Background: Patients who were bridged to heart transplantation (HTx) with ventricular assist device (VAD) have a higher incidence for the development of antibodies directed against human leukocyte (HLA) or against non-HLA antigens like major histocompatibility complex class I-related chain A (MICA). HLA and MICA antibodies have been associated with acute and chronic rejection leading to decreased survival after HTx. We monitored these clinical relevant antibodies to evaluate sensitization during the first year after VAD implantation.
Methods: Sera of 28 patients who underwent VAD implantation were analyzed by Luminex technology for anti-HLA and anti-MICA antibodies. Blood transfusion history, gender, age and panel reactive antibody (PRA) level before VAD implantation were reviewed.
Results: The mean age was 53.3±13.7 years and the group consists of 25 men and 3 women. 42.9% (n=12) of VAD-implanted patients showed HLA and/or MICA antibodies within the first year after VAD implantation, whereas 28.6% (n=8) with HLA-class I antibodies, 21.4% (n=6) with HLA-class II antibodies and 14.2% (n=4) with MICA antibodies were identified. Of these patients 10.7% possessed HLA antibodies in combination with MICA antibodies. An accumulation of antibodies with specificities against HLA-A or HLA-DR antigens was observed. In particular, antibodies against the specificities HLA-A68, -DR4 or -DR9 occurred in more than 14% of VAD implanted patients within the first year after implantation.
Conclusions: Patients with implanted VADs prior to transplantation have a higher risk to develop alloreactive antibodies within the first year after VAD implantation, mainly against HLA-A and HLA-DR antigens. Our data point out the necessity for monitoring HLA and non-HLA antibodies at VAD implanted patients prior to HTx, and future studies will focus on connecting these data with transplantation outcome.

RO-160 THE ROLE OF HLA COMPATIBILITY ASSESSMENT IN CURRENT CARE FOLLOWING HEART TRANSPLANTATION

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Introduction: Patient's life following the organ transplantation is about a fragile balance between the risk of graft rejection on one side and risk of infection or later malignancy on the other. Compatibility for the HLA-A, B, and DR loci was significantly associated with better outcome of heart transplantation. We postulate that HLA compatibility could be used for differentiation of immunosuppression treatment after heart transplantation (HTx).
Methods: We restrospectively analyzed 182 consecutive patients (153 men), who underwent HTx in our center from Jan/2001 to Apr/2010. Based on a model of Compatibility Index (CI) with a range from 0 to 26, the patients were divided into 2 groups; Group A (n = 83) with CI 0-17 and Group B (n = 99) with CI 17-26. All patients were treated according to the same post-transplant regime (dacluzimab, CNI, mycofenolate-mofetil and corticosteroids). Groups were compared for incidence of acute graft rejections (AR), infections, malignancies and death.
Results: There was a significantly lower incidence rate of AR grade 2 in Group A (12pt= 14%), compared to Group B (26pt= 26%), ($p\leq0,05$), no significant difference was found in incidence of grade 3 rejections, infective complications or malignancies. There was trend toward better survival (according to Kaplan-Meier) in patients with better HLA compatibility in Group A (1, 5, and 10 years survival was 96%, 91%, and 85%, respectively) compared to Group B patients (90%, 85%, and 82%, respectively).
Conclusions: Our data indicate that recipients with organs with better HLA matches could potentially require reduced immunosuppression leading to a reduced rate of infection and malignant conditions after transplantation. A randomized trial is warranted to prove this statement.

RO-161 CLINICAL RELEVANCE OF PREFORMED COMPLEMENT- AND NON-COMPLEMENT-FIXING HLA ALLOREACTIVITY IN CARDIAC TRANSPLANTATION

Stephane L. Mahr[1], Marcus Wahrmann[2], Farsad Eskandary, Arezu Z. Aliabadi[1], Andreas O. Zuckermann[1], Georg A. Böhmig[2]. *[1]Division of Cardiac Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria; [2]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria*

There is increasing evidence for a role of alloantibody-mediated rejection in organ transplantation. Solid phase HLA antibody detection using bead ar-

ray technology may help identify patients at risk of rejection and graft loss. In this retrospective monocentric cohort study we evaluated 229 consecutive heart transplant recipients (transplantation between 2000 and 2006; immunosuppression: ATG induction and calcineurin inhibitor-based maintenance therapy) for the presence of preformed (complement- and non-complement-fixing) HLA alloantibodies. Sera obtained immediately before transplantation were screened by FlowPRA, and test-positive sera were subjected to Luminex-based single antigen testing including a test modification for detection of in vitro C4d deposition. Seventeen recipients (7.3%) were found to have preformed IgG type donor-specific alloantibodies (DSA), five of them with C4d-fixing capability. The presence of DSA was related to retransplantation and previous pregnancies, but not associated with prior implantation of a ventricular assist device. Evaluating clinical endpoints, we found an association between DSA and acute rejection (>grade 1A according to the ISHLT 1990 grading system; no DSA: 17%; [IgG]DSA: 33%; [IgG/C4d]DSA: 60%). However, in our study cohort, sensitization had no effect on long-term survival rates (5-year transplant survival: 72% vs. 92% vs. 80%) or rates of chronic transplant vasculopathy (20% vs. 18% vs. 20%). Moreover, none of the DSA-positive patients was in need of extracorporeal membrane oxygenation, and the duration of post-transplant intensive care did not differ between groups. In conclusion, our data point to a relationship between preformed donor-specific alloreactivity and acute rejection. However, possibly as a result of our local immunosuppressive regimen, which also includes induction therapy with a depleting anti-lymphocyte antibody, such reactivity did not influence long-term allograft outcomes.

Infections

RO-162 PREVENTING DONOR DERIVED INFECTIONS THROUGH VIROLOGY SCREENING: REDUCING RISK AND INCREASING ORGAN AVAILABILITY

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Background: Expansion of the donor pool leads to utilisation of donors with risk factors for viral infections. Donor screening relies on serological and nucleic acid (NAT) testing.
Materials and Methods: The major issues relating to NAT testing for blood borne viruses (BBV) in donors are:

- Availability of NAT testing for all donors. This is addressed through national government-sponsored provision of testing services.
- Rapid turnaround time, in order to limit organ ischaemic times, and not affect the process of organ transplantation. This is addressed through 24-hour laboratory services, use of automated platforms, multiplexing of tests where possible, routine use of NAT assays, and use of parallel testing on two platforms to ensure maximum safety in minimum time.
- Technical limitations on the tests include: multiple transfusions in the donor resulting in haemodilution and free haemoglobin from deceased donors that may interfere with NAT assays. These technical issues are dealt with by laboratory assessments of the effects of these conditions on test results.

Results: NAT of HIV, HBV and HCV to detect blood-borne viruses in organ donors during the window period has further reduced the risk of donor derived infections and makes safer the use of organs from increased risk donors. In Australian services, this has contributed to ~4 additional (otherwise wasted) organs per month (2 donors pm) becoming available.
Conclusions: The use of single NAT testing enhances the risk-reduction through questionnaires. Additional issues that will need to be confronted include the risk of HBV infection from HBcAb positive donors, the continuing risk of introduction of exotic infections and the importance of viral infections such as EBV, and HHV8 in the rising incidence of post transplant tumours.

RO-163 CYTOMEGALOVIRUS INFECTION IS ASSOCIATED WITH EARLY TUBULAR INJURY AND LATE RENAL ALLOGRAFT DYSFUNCTION

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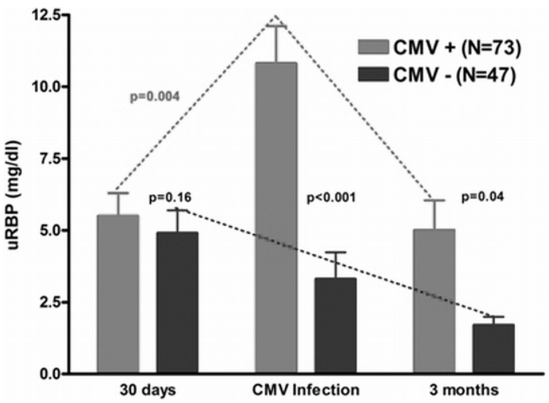
[2]*Laboratório de Imunologia Clínica e Experimental, Universidade Federal de São Paulo, São Paulo, SP, Brazil*

Background: Cytomegalovirus (CMV) is a risk factor for acute rejection and it could be associated with IF/AT as early as 3 month post kidney transplantation.
Aim: The aim of this study is assess the impact of CMV infection in early predictor of tubular damage (urinary Retinol Binding Protein), and risk of chronic allograft dysfunction.
Methods: We evaluated 194 renal transplants from deceased donor. All patients received Thymoglobulin and preemptive therapy to CMV. A subgroup of 142 patients with uRBP serial measurement were analyze in separate and compared patients with or without CMV.
Results: Cold ischemic time was greater among patients with CMV (22.8 vs. 20.9, p=0.04). Remain variables were similar. DGF, AR, graft loss and death were similar among both groups. Patients with CMV infection presented CrCL of 58.8 vs. 66.8 ml/min 1-year-after Transplantation (p=0.023) and 51.3 vs. 18.7 ml/min 3-years-after transplantation. Multivariable analyze demonstrated that AR (OR=1.46, p=0.04), CMV infection (OR=1.49) and donor age (OR=2.11) were related with risk of chronic allograft dysfunction (CrCl<60 ml/min 1-year-after transplantation). On the moment of CMV infection, uRBP level was high (<1.0 mg/L) in 80.6% of patients with CMV and in 38.8% among patients without CMV (p=0.026). According showed in figure 1, uRBP was similar in both groups 30 days after transplantation (5.5±6.8 vs. 4.9±5.5, p=NS). After than uRBP levels reduced progressively among patients who had not CMV infection, while among patients with CMV there is a significant increase on the moment of CMV infection (10.8±11.2 vs. 3.3±6.4, p<0.001) and in 3 months after transplantation (5.0±8.9 vs. 1.7±2.0, p=0.04).



Conclusion: CMV infection was related with worse graft function and a profile of early tubular injury, measured by urinary RBP.

RO-164 PREVENTION OF CYTOMEGALOVIRUS (CMV) INFECTION BY VALGANCICLOVIR (VGCV) IN SOLID ORGAN TRANSPLANT RECIPIENTS: THE ORVAL STUDY

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ORVAL, a French large cohort of SOT patients, is focused on the targeted population receiving VGCV. This descriptive analysis includes 441 patients and their 1 year follow-up, and consists of 245 kidney (55.6%), 87 liver (19.7%), 64 heart (14.5%), 36 lung (8.2%), 9 combined (2.0%) transplant recipients. 71.2% patients received VGCV prophylaxis, 20.4% recipients were initiated on pre-emptive therapy, and 8.4% recipients initiated VGCV as the treatment of CMV disease. Patients on prophylaxis comprise of 129 D^+/R^-, 175-D^+ or D^-/R^+ and 8-D^-/R^-. The mean prophylaxis duration (days) was 185.3±113 in D^+/R^-, 165.2±99.6 in D^+D^-/R^+. Prophylaxis duration in high risk patients was 159.9±84.7 in kidney, 196.4±129.7 in liver, 242.3±155.4 in heart and 279.8±126 in lung recipients. At inclusion, the mean dosage (mg) was 469.9±249.3 in kidney, 731.3±225 in liver, 741.2±261.0 in heart and 787.5±203.5 in lung recipients.
Data available showed that VGCV prophylaxis dosage was adapted to renal function at inclusion in 155/283 recipients (54.8%), at 1st follow-up visit in 138/262 (52.7%), at 2nd follow-up visit in 64/122 (52.5%), and at 3rd follow-up visit during the prophylaxis in 36/61 (59.0%). 69 patients on prophylaxis experienced a CMV event during the 1 year follow-up period and 16 (24.6%) of them received minidosing. Neutropenia (PNN < 1000/mm^3) was observed in 52 patients receiving prophylaxis and 12 (25%) of them were overdosed. 38.6% of neutropenia were treated by G-CSF.
Conclusion: The majority of SOT recipients were initiated on valganciclovir prophylaxis. Only in half of them VGCV dosage was adjusted to the renal function. Among the patients who received unadjusted dosage around 25% received dosage that could possibly increase the risk of developing a neutropenia or a CMV event.

RO-165 LEUKOPENIA & NEUTROPENIA IN KIDNEY TRANSPLANT RECIPIENTS EXPOSED TO 200 VS. 100 DAYS OF VALGANCICLOVIR PROPHYLAXIS: A SUBANALYSIS OF THE IMPACT TRIAL

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Background: Extending valganciclovir (VGCV) prophylaxis in kidney transplant (Tx) recipients to 200 days significantly decreases incidence of CMV-viremia/disease. This preliminary subanalysis (IMPACT study) assesses clinically relevant adverse events (AE) of leukopenia/neutropenia.
Methods: International, randomized, prospective, double-blind study, 318 CMV D+/R- pts. received VGCV prophylaxis (900 mg/d) to 200 days post Tx (200d), in comparison to 100 days followed by placebo to day 200 (100d). AE and serious AE (SAE) for leukopenia/neutropenia were assessed on (i) severity; (ii) occurrence in association to VGCV exposure; (iii) clinical relevance of toxicity grading.
Results: There were 57 and 81 AE of leukopenia/neutropenia in the 100d and 200d-groups, resp.; 19.3% (100d) and 20.9% (200d) of them were graded severe/serious, the rest classified as mild/moderate (Table 1).Overall incidence of severe/serious AE was similar during the first 100 days (Table 1). During the second 100 days, overall incidence/d for AE was 0.11 (100d) and 0.36 (200d), with severe/serious AE only occuring in the 200d-group (0.05).

Table 1. Leukopenia/neutropenia AE during study

Groups	Neutropenia/ leukopenia (n)	Severe/serious AE (%)	Days 0–100 (incidence/d)		Days 101–200 (incidence/d)	
			Total	Severe/serious	Total	Severe/serious
200 d	81	20.9	0.44	0.11	0.36	0.05
100 d	57	19.3	0.47	0.12	0.11	0

Severity (by tox. grading) for leukopenia (WBC) and neutropenia (ANC) was moderate at diagnosis and throughout most AE (Table 2).

Table 2. Toxicity grading leukopenia (WBC) & neutropenia (ANC) (%)

	Group 0	Group 1	Group 2	Group 3	Group 4
WBC					
@ diagnosis	34.6	28.6	20.3	15.8	0.7
Highest value during AE	13.4	26.9	34.3	22.4	3.0
ANC					
@ diagnosis	75.2	7.3	4.4	7.3	5.8
Highest value during AE	52.2	15.7	8.2	11.9	11.9

Conclusion: Most AE associated with leukopenia/neutropenia were mild/moderate, with a marked decline in frequency and seriousness throughout the second 100 days under VGCV. Clinical severity at diagnosis and during the AE-course were low, indicating that these events can be managed successfully during extended VGCV treatment.

RO-166 A QUANTITATIVE ANALYSIS OF CMV INFECTION IN SOLID-ORGAN TRANSPLANT RECIPIENTS MANAGED EXCLUSIVELY ON PRE-EMPTIVE THERAPY

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Human cytomegalovirus (CMV) is an opportunistic pathogen causing morbidity and mortality among patients undergoing solid organ transplantation. Natural history studies found that the amount of CMV DNA detected in whole blood among patients post-transplant correlates with the development of CMV end-organ disease. The monitoring of CMV DNA using quantitative real-time PCR (qPCR) is a sensitive method of detection and provides clinicians with a timely result for pre-emptive intervention.
We analysed pre-emptive CMV therapy in 692 prospectively-followed patients receiving a renal or liver transplant between July 2002 - Jan 2010. Routine monitoring for CMV DNA in whole blood using qPCR was performed for the first 90 days post-transplant, treatment begun once a viral load was detected above 3000 copies/ml, and discontinued following two consecutive negative PCR results. This strategy was also used for CMV seronegative recipients of organs from seropositive donors.
Post-transplant, CMV viraemia developed in 43% of all transplant recipients. Among those who developed viraemia, peak viral load was 10-fold higher in CMV seronegative recipients compared to seropositives. The duration of viraemia and number of patients requiring therapy was significantly greater in seronegative recipients. Although time to first detectable CMV DNA was not dependent on serostatus, the viral growth rate was found to be significantly faster in the seronegative recipients. 1.5% of liver transplant recipients and 0.8% of renal transplant recipients developed histologically confirmed CMV disease.
Although the risk factors associated with high level CMV replication were not affected by the use of aggressive pre-emptive therapy, in our experience, a pre-emptive treatment strategy guided by qPCR monitoring was found to be safe and effective with no increase in the development of CMV disease post-transplant.

RO-167 HUMAN HERPESVIRUS-6 IN DONOR BIOPSIES ASSOCIATED WITH HIGHER INCIDENCE OF CLINICAL CMV DISEASE AND HCV RECURRENCE

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The reactivation of cytomegalovirus (CMV) and human herpesvirus-6 (HHV-6) commonly occurs in the post-transplantation liver period as well as the recurrence of hepatitis C virus (HCV) causing a negative impact in the graft.
Aim: To analyze the presence of CMV and HHV6-DNA and its post-transplantation evolution correlation and its impact on CMV disease and HCV recurrence.
Methods: This study was prospective in which we observed the presence of CMV and HHV-6 DNA in liver biopsies, collected in a prospective database. CMV and HHV-6 were detected by N-PCR. CMV disease was characterized by the clinical symptoms. HCV recurrence was obtained by HCV PCR positive and liver biopsies. We verified using the Chi-square test if the presence of these viruses observed in liver donor biopsies (T1) remained at the post-transplantation period (T2).
Results: Four patients (9.7%) were positive for CMV DNA in T1 and three of them remained positive after transplantation. Eleven patients became positive in T2 liver biopsies (P=0.06). Fifteen (15/41=36%) patients were positive for HHV-6 DNA in T1 liver biopsies and 11 of these remained positive after transplantation (T2). The patients whose T1 biopsies were positive for HHV-6 DNA had a tendency (P=0.05) to remain positive in their T2 biopsies. CMV disease occurred in 41.4% and 58.8% were also positive for HHV-6 DNA in T1 biopsy and they continued positive after transplantation (T2) (P=0.0128). In this study 28 (68%) of the patients were transplanted for hepatitis C, 12 of them (42.8%) had recurrence of HCV and HHV-6 was positive in 9/12 (83.3%) (P=0.049).
Conclusion: HHV-6 DNA in T1 liver biopsies remained positive post-transplantation showing a possible risk for post-transplant allograft loss because of an association with HHV-6 and recurrent HCV and CMV disease.

RO-168 CLINICAL PHARMACOKINETICS OF VALGANCICLOVIR IN RENAL TRANSPLANT RECIPIENTS WITH OR WITHOUT RENAL IMPAIRMENT

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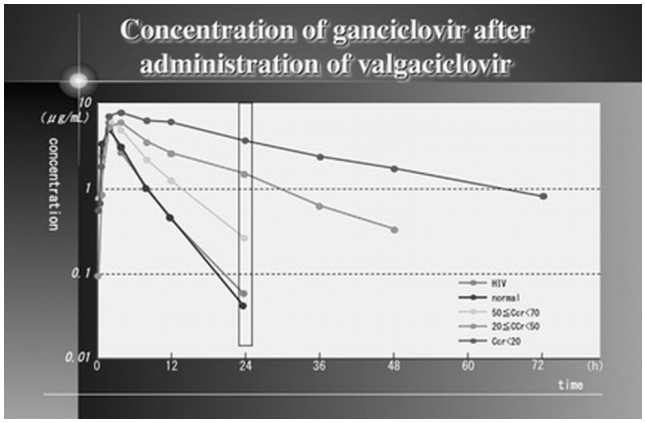
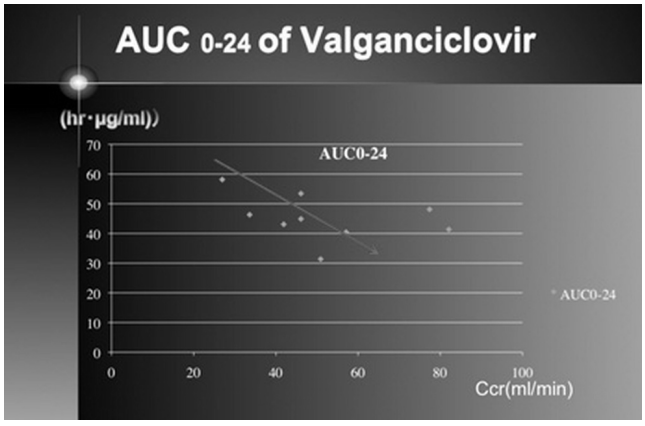
Background: Valganciclovir is the oral prodrug of ganciclovir, and is commonly used in the treatment of cytomegalovirus (CMV) disease in patients who are immunocompromised and for the prevention of CMV. The Pharmacokinetics of Valganciclovir in renal transplant recipients with renal impairment is no known. Furthermore, it is not known whether there are any pharmacokinetic differences between patients with and without renal impairment. We investigated the pharmacokinetics of Valganciclovirin renal transplant recipients to evaluate the validity of 50% reduction of drug information for mild renal impairment.
Methods: 32 renal transplant recipients with CMV-Ag were treated with Valganciclovir for renal impairment. 20 recipients with Ccr $<$40ml/min were treated 450mg/day (Group 1), 11 recipients with estimated Ccr 20-40ml/min were treated 450mg/2day (Group 2). Control is 12 renal transplant recipients, who were treated with 5-7mg/kg i.v. ganciclovir.

Table 1. Patients characteristics

	VGCV (Group 1)	VGCG (Group 2)	GCV
S-Cr(mg/dl)	1.28±0.8	1.68±1.0	1.78±1.3
Ccr(ml/min)	56.8±11.0	30.2±12.8	58.8±10.2
CMV-Ag (+) time	41 day (12–118)	39 day (15–89)	42 day (26–89)
Administer	450mg	450mg/2 days	5–7mg/day
Treatment time	8.1 days	9.7 days	18 days

Results: The success rate of viremia eradication at day 14 was 81.2% (26/32 cases) for Valganciclovir and 41.6% (5/12 cases) for i.v. ganciclovir, and at day 40 was 100% (32/32 cases) and 83.3% (10/12 cases), there was not significant difference between groups in treatment time. After oral administration of the prodrug Valganciclovir, ganciclovir bioavilability was 60% and ganciclovir concentration were higher (Cmax 8.9μg/ml vs 4.2μg/ml) and appeared later in patients with server renal impairment compared with normal subjects. The peak concentration was significantly higher in Group 1 (P=0.05). However, the decrease in the plasma ganciclovir concentration was slower in Group 2 (P=0.098), and AUC of all patients in both group was distributed within a narrow range (44.8±11.7 μg h/ml), that was higher than treating effective blood level (26.0μg h/ml).





Conclusion: Valganciclovir shows comparable safety, more convenient and effective to intravenous ganciclovir for treatment of cytomegalovirus disease in renal transplant recipients. The dosage of Valganciclovir has to be the degree of renal impairment.

RO-169 IDENTIFICATION OF PATIENTS AT HIGH RISK FOR INFECTIONS AFTER LIVER TRANSPLANTATION; DEVELOPMENT AND VALIDATION OF A NEW RISK MODEL

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Objectives: Infections are an important cause of morbidity and mortality in the early period after liver transplantation with a reported incidence up to 60%. Identication of patients at high risk for early post-operative infection could help in improving the outcome. This study was conducted to develop a model for predicting infections.
Methods: Medical records of 200 LTx recipients transplanted between 2005 and 2009 at the Erasmus MC Rotterdam were reviewed. We registered all infections according to CDC definitions during the first three months after LTx and noted potential risk factors for developing infections. Multivariate logistic regression was used to create a predictive model for infections in general. Subsequently, we validated this model in another cohort of 94 LTx recipients transplanted between 2007 and 2009 at the Ghent University Hospital.
Results: The model consists the following parameters: (1) preoperative haemodialysis; (2) preoperative Candida colonization; (3) history of abdominal surgery; (4) Sodium $<$ 130 mmol/l on day of LTx; (5) intubation $>$ 3 days after LTx; (6) relaparotomy within 5 days for intra-abdominal bleeding, anastomosis leakage, vascular insufficiency or (7) retransplantation.
In high risk patients 2 or more conditions were present. In the Rotterdam cohort 81% of high risk patients developed an infection versus 50% of low risk patients [OR 4.273 (2.1-8.9)]. Surgical site infections were the most frequent and 41 out of 109 bacterial infections (38%) were caused by 41 Enterococcus species. In the Ghent cohort 80% of the high-risk patients developed an infection compared to 48% of the low-risk patients [OR 4.3 (CI 1.3-14.2)]
Conclusion: This model based on 7 clinical parameters identifies patients at high risk for infections early after liver transplantation.

RO-170 TRANSPLANT PATIENTS UPTAKE OF INFLUENZA AND SWINE FLU VACCINATION: ARE THE "JABS" BEING GIVEN?

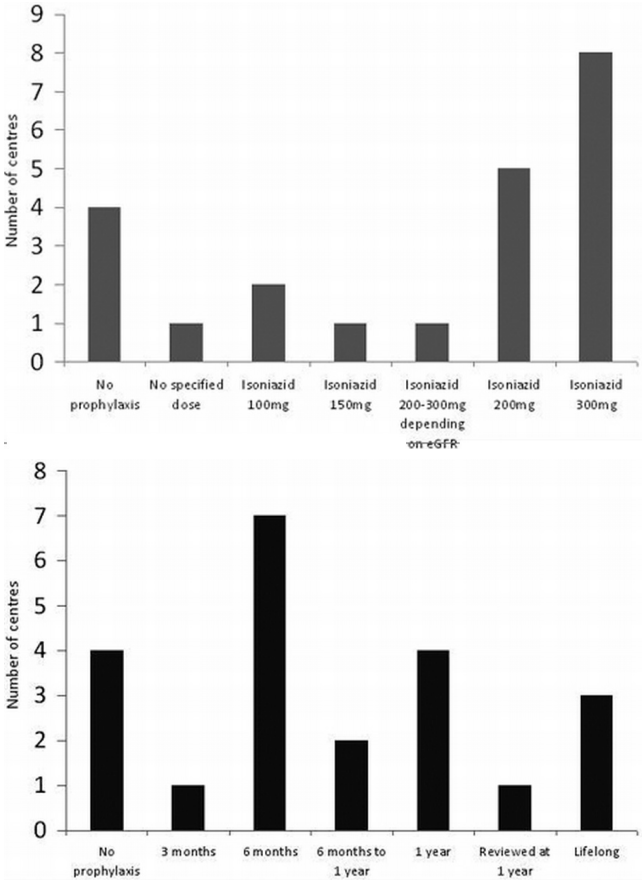
David van Dellen, Jay Nath, Marc Williams, Melanie Field, Hari Krishnan, Stephen J. Mellor, Ahmed Hamsho, Andrew R. Ready, Nicholas G. Inston. *Renal Transplantation, Queen Elizabeth Hospital, Birmingham, United Kingdom*

Introduction: Annual prophylaxis against influenza and swine flu (H1N1) is recommended in immunocompromised patients, including post-renal transplant. In addition, current United Kingdom guidelines support concurrent vaccination for household contacts. We aimed to determine the vaccination uptake against these two viruses amongst a cohort of renal transplant patients.
Methods: Patients who had a renal transplant over a 30 month period (January 2007 to July 2009) were included utilising a telephone based survey to determine vaccination status for influenza and H1N1 viruses for the 2009-10 flu season. In addition, the source of vaccination was established.
Results: 334 patients were transplanted over this period of which 201 were able to be contacted and included. There was a significantly greater uptake for the influenza vaccination compared to H1N1 vaccination (168 (83.6%) 144 (71.6%) respectively; $p<0.001$; McNemar's test.) General Practitioners (GP's) were significantly more likely to recommend the influenza vaccination when compared to hospital doctors (126 (62.7%) and 97 (48.3%) respectively; $p<0.005$.) although this finding wasn't mirrored for the H1N1 vaccination (95 (47.3%) and 102 (50.7%) respectively; p=0.55.) GP's were significantly less likely to advise patients to have the H1N1 vaccination compared to the influenza vaccination; (95 (47.3%) and 126 (62.7%) patients respectively; $p<0.005$.) Only 60 (29/9%) of the questioned patients had household contacts vaccinated against H1N1.
Discussion: In the United Kingdom, renal transplant patients are currently significantly less likely to be vaccinated against H1N1 as opposed to the influenza vaccine. In addition, few household contacts of transplant patients received the H1N1 vaccine. This appears to reflect a lack of awareness of guidelines amongst both health professionals and patients. There appears to be significant improvement possible in uptake of vaccination for both transplant patients and their household contacts.

RO-171 TUBERCULOSIS PROPHYLAXIS FOLLOWING RENAL TRANSPLANTATION: IS THERE CONSENSUS?

David van Dellen, Melanie Field, Andrew Clarke, Matthew Kelleher, Stephen J. Mellor, Ahmed Hamsho, Andrew R. Ready, Nicholas G. Inston. *Renal Transplantation, Queen Elizabeth Hospital, Birmingham, United Kingdom*

Background: Renal transplantation provides the optimal renal replacement therapy with the caveat of associated immunocompromised state. This places recipients at increased risk of infective complications. Tuberculosis is 20 – 70 times more common in renal transplant recipients resulting in significant adverse outcomes. Recent guidelines regarding routine Tuberculosis prophylaxis have recently been published in the United Kingdom (suggesting Isoniazid 300mg). We aimed to investigate prophylactic regimens in use amongst Renal Transplant units nationally.
Methods: All renal transplantation centres across Great Britain and Ireland were approached for tuberculosis prophylaxis protocols. This was achieved via the designated renal pharmacist for each centre who was approached by e-mail and telephonically sequentially with a standardised questionnaire. This enquired as to medication used, including dosage and duration of treatment as well as patient demographics warranting inclusion for treatment.
Results: 23/25 (92%) transplant centres in Great Britain and Ireland responded. All centres giving prophylaxis did so in the form of Isoniazid with variable dosages given across the majority of centres although a propensity for either 200mg or 300mg was noted.
In addition, duration of prophylaxis offered also varied, with many centres offering no prophylaxis and 6 months prophylaxis (highest incidence.)
In addition, lifelong anti-tuberculous treatment is currently offered in three cen-



tres. There appears to be no patient demographic standard for prophylaxis in the United Kingdom with great variance amongst individual units.
Discussion: Tuberculosis remains an important pathogen in the immunocompromised host. Prophylaxis therefore has plays a potentially crucial role in the post-transplant population. There appears to be no national consensus or adherence to recently published guidelines to ensure standardised "best practice". It is important that a rigorous approach to TB prophylaxis is undertaken to prevent unnecessary morbidity and mortality.

Islet / cell transplantation

RO-172 ARE YOUNG DONORS SUITABLE FOR ISLET ISOLATION?

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Backround: Donor variables have a significant impact on the outcome of the islet isolation. Importantly, young donor age is negatively associated with islet isolation yield. The aim of this study was to identify the outcomes of islet isolation from donors with $\leq$ 20 years of age and to compare the results with whole donor population.
Material and Method: We retrospectively analyzed 432 pancreas isolations performed from brain death donors between 2002 and 2010. Pancreases preserved using the two –layer method were excluded from analysis.We reviewed 23 donor charts from donors younger than 20 years of age and their islet isolation outcomes, and compared them with our whole donor pool. An identical enzymatic isolation procedure was used for donors $<$ or $>$ 20 years.
Results: Median age, BMI and cold ischemia time were 17.7$\pm$3, 23.1$\pm$4.6, 372$\pm$129 min, respectively. Avarage digestion time was 16$\pm$4 min. For two pancreases, isolation couldn't been performed due to technical failure. The mean islet recovery for 21 donors and transplanted preparations were 197$\pm$142 $\times 10^3$ IEQ, 326$\pm$82$\times 10^3$ IEQ, respectively. The islet isolation success rate (transplanted islet preparations and yield $>$ 250$\times 10^3$ IEQ) was 9/23 (39%). For the whole donor pool and transplanted preparations, mean islet yields were 252$\pm$125$\times 10^3$ IEQ, 341$\pm$97 $\times$ 10^3 IEQ, respectively and rate of transplanted preparations was 122/307 (39.7%)
Conclusion: In spite of the known difficulties in extracting islets from pancreas from donors $\leq$ 20 years of age, there was no difference in the transplant rates and islet yield for transplanted preparations between young donors and whole donor pool.

RO-173 QUANTIFICATION OF ISLET LOSS DURING IMMUNE REJECTION USING IRON-LABELED ISLET CELLS BY 3T MRI IN THE RAT MODEL

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Background: Monitoring the fate of transplanted islets remains a major challenge in clinical islet transplantation (IT). We developed a MRI imaging protocol (3D difference ultra-short echo-time = dUTE), resulting in positive contrast images of superparamagnetic iron-oxide (SPIO) nanoparticles-labeled islets transplanted in rat. Our aim was to compare the evolution of the MRI signal in 3 types of IT in the rat model.
Methods: Syngeneic and allogeneic SPIO-labeled islets (ferucarbotran, 280μg/ml iron) were injected intraportally into streptozotocin-induced diabetic Lewis rats. Xenogeneic human islets were transplanted into normoglycaemic rats and graft functionality was evaluated by serum human C-peptide levels. Images were performed on a 3T MRI, from day 0 up to day 106. An intensity threshold was applied within the liver region, giving automatically the number of dUTE-enhanced pixels, allowing quantification. Histological studies included insulin, CD4 and CD8 staining and iron detection.
Results: Decay rates for the 3 types of transplantation were different.

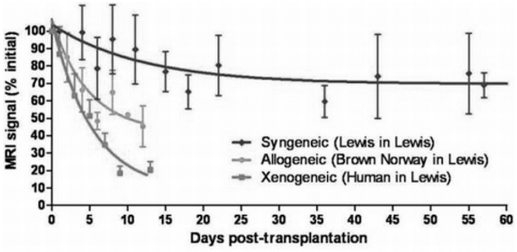

Figure 1: MRI signal after islet transplantation in syngeneic (n=6), allogeneic (n=9) and xenogeneic (n=6) models. Values are means and SD.

The syngeneic graft signal showed a 20% decrease during the first 2 weeks and remained stable up thereafter. For allogeneic transplantation, islet rejection (G$>$20 mmol/l) occurred at day 7.7$\pm$0.5 and 41%$\pm$12 of the initial signal was lost. In the xenogeneic model, 43%$\pm$8 of the initial signal was lost by day 3, when significant basal and stimulated human C-peptide levels were not detected any longer. Islet rejection was confirmed by islet CD4+ and CD8+ cell infiltration and loss of insulin staining.
Conclusion: After intra-portal IT and during immune rejection, the loss of SPIO-labeled islets can be monitored with clinical-grade 3T MRI imaging using a semi-automatic quantification method. The decay of the signal is correlated with the graft function and histological findings.

RO-174 PRE-TREATMENT WITH DONOR TOLEROGENIC DENDRITIC CELLS RESULTS IN ANTIBODY-MEDIATED, ACCELERATED GRAFT LOSS OF RODENT PANCREATIC ISLETS

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Background: Allogeneic islet of Langerhans transplantation as a curative treatment for type 1 diabetes is hampered in its success by the absence of potent specific non-toxic immunosuppressive drugs. Here we assessed whether donor bone marrow-derived, tolerogenic dexamethason-treated dendritic cells (dexDC), could prolong islet allograft survival in a full MHC mismatch rat model.
Methods/Materials: Rodent allogeneic islet of Langerhans transplantation was performed from DA to Lewis and vice versa. Tolerogenic DC were generated from bone marrow of DA and Lewis by treatment with dexamethason. Animals were either vehicle (PBS) or donor dexDC pre-treated. Serum was used to monitor glucose, C-peptide and donor-specific antibodies. Immunohistochemical analysis was performed on allograft tissue.
Results: Transplantation of DA islets into Lewis recipients showed direct graft failure, with even reduced numbers of insulin containing β-cells when rats were

pre-treated with donor dexDC. In the reverse model, dexDC-treated DA recipients showed significant accelerated rejection of Lewis islets.

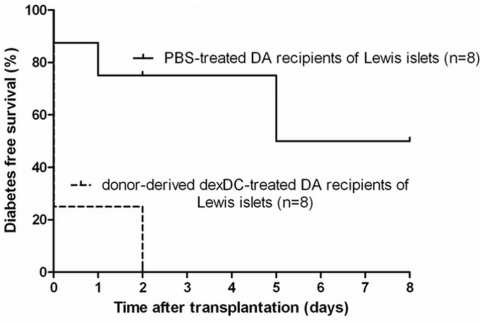

Fig.1 Time dependent allograft survival; percentage of rats developing diabetes after transplantation with or without dexDC pre-treatment.

The allograft tissue of the dexDC-treated recipients showed a predominant NK-cell infiltrate and presence of antibody reactivity through direct and indirect immunofluorescence in the absence of complement deposition. By FACS analyses, already before transplantation donor-specific antibodies were specifically found in the dexDC-treated recipients.

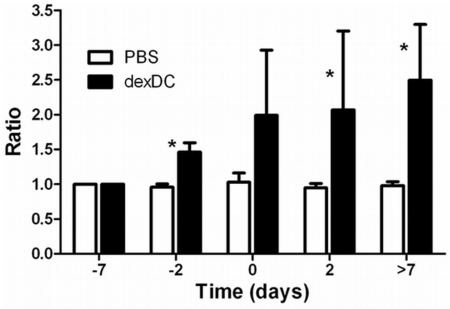

Fig.2 Detection of donor-specific antibodies in DA recipients
The ratio of the mean fluorescence of Lewis-DC incubated with serum of DA recipients, divided by the mean fluorescence when incubated with normal DA serum (mean ±SD, * p<0.05).

Conclusions: Treatment with donor-derived dexDC gives rise to an antibody-mediated rejection in this rodent model of islet transplantation. These results warrant a careful evaluation of employability of tolerogenic cell therapy in clinical transplantation settings.

RO-175 CO-EXPRESSION OF CD40LIG AND IKBA MEDIATED BY ADENOVIRUS PROLONGED ISLET ALLOGRAFT SURVIVAL

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Background: Interactions between CD40/CD40L represent a major costimulatory system that amplifies the immune response and promotes inflammation, and NF-κB activation plays a critical role in inflammation and apoptosis. The objective of this study was to investigate the role of simultaneous blockade of CD40/CD40L and IκB/NF-κB pathways in protection for islet graft
Methods: Streptozocin-induced diabetic Wistar rats were transplanted intraportally with 2000 IEQ islets isolated from Sprague-Dawley rats.Five groups were assigned according to the treatment: nontreated group,islet group, Ad-IκBα-transduced islet group, Ad-sCD40LIg-transduced islet group,and Ad-IκBα-IRES$_2$-sCD40L-transduced islet group.The islet graft mean survival time (MST), insulin expression of islet grafts, sustained gene expression of IκBα and sCD40L and the levels of cytokines in peripheral blood were measured.
Results: (97.69±0.94)% of the islets expressed EGFP at an MOI of 10 and the insulin stimulation indices at an MOI of 5 and 10 were preserved to the level of nontransduced islet ($P<0.05$).By MLIR, splenocytes cultured with Ad-IκBα-IRES2-CD40L-transfected islets demonstrated homospecific hyporesponsiveness.Compared to the islet graft mean survival time (MST) of non-treated group ((7.1±1.16) d) or Ad-sCD40L-treated group ((57.8±9.02) d), Ad- IκBα-treated group ((44.6±8.84) d), the islet graft MST was dramatically prolonged in the Ad-IκBα-IRES2-sCD40L-treated group (>100d); TNF-α, IL-6 and IL-1β were diminished commensurate with the reduced cellular infiltrate and in fact suggest a synergistic effect between the CD40/CD40L and IκB/NF-κB pathways ($P<0.01$).
Conclusion: Simultaneous blockade of the CD40/CD40L and IκB/NF-κB pathways via coexpression of sCD40L and IκBα mediated by adenovirus could synergisticly prolong the survival of islet grafts and reduce peripheral blood cytokine levels.

RO-176 BLOCKADE OF BOTH B7-H4 AND CTLA-4 CO-SIGNALING PATHWAYS ENHANCES MOUSE ISLET ALLOGRAFT SURVIVAL

Xiaojie Wang[1], Jianqiang Hao[1], Daniel Mertzger[2], Alice Mui[1], Ziliang Ao[1], Bruce Verchere[1], Lieping Chen[3], Dawei Ou[1], Garth Warnock[1]. *[1]Surgery, University of British Columbia, Vancouver, Canada; [2]Paediatrics, University of British Columbia, Vancouver, Canada; [3]Department of Oncology, Johns Hopkins University, Baltimore, USA*

Background: Costimulation blockade is an effective way for preventing allograft rejection. In this study, we tested the efficacy of two potent negative co-signalling molecules in protecting islet allograft function.
Methods: We used local expression of B7-H4 by adenoviral transduction of islets (Ad-B7-H4) and systemic administration of CTLA-4.Ig to investigate the outcomes of allograft survival. Five groups (n=12 each) of streptozotocin-induced diabetic C57BL/6 mice received 400 islets each from BALB/c donors. The groups consisted of virus control Ad-LacZ [group (G1)]; control without vector (G2); CTLA-4.Ig alone (G3); Ad-B7-H4 (G4) alone; and Ad-B7-H4 and CTLA-4.Ig combined (G5).
Results: All groups established euglycemia after transplantation, but G1 and G2 developed graft failure at 14.5±1.9 and 15±1.5 days, respectively. G3, G4, and G5 survived for 42.8±10, 56.5±15.5, and 74.7±10.5 days ($p<0.01$, G5 vs. G3; $p<0.05$, G5 vs. G4, by log-rank test), respectively. Activated T and B cells in the renal lymph nodes were significantly controlled by CTLA-4 treatment [($p<0.001$, G3 vs. G4; $p<0.002$, G4 vs. G5, in CD4+CD25+subsets), and ($p<0.001$, G3 vs. G4; $p<0.01$, G4 vs. G5, in CD19+CD69+subsets)]. Significantly reduced infiltrates were also detected in the allografts of G3 compared with G4 and G5. By contrast, B7-H4 significantly inhibited Th1 associated IFNg secretion ($p<0.001$, G4 or G5 vs. G3 in CD4+IFNg+subsets) in the allografts. Moreover, we found significantly increased Foxp3+ T cells in the grafts of both G4 and G5 but not in G4 in the long-term surviving recipients, suggesting that B7-H4–elicited T-regulatory cells play an important role in prolongation of islet allograft survival.
Conclusions: Our study suggests that CTLA-4 and B7-H4 inhibit alloimmune responses through distinct mechanisms and combination therapy which activates two negative co-signalling pathways, B7-H4 and CTLA-4, can further enhance islet allograft survival.

RO-177 BETA-CELL PROLIFERATION IN TRANSPLANTED ISLETS OVER TIME

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Background: Beta-cell replication is thought to play a significant role in maintaining pancreatic beta-cell mass. Nevertheless, it is still unknown whether a similar role could be attributed to cell replication in transplanted islets. The aim of this study was to determine the beta-cell replication rate in islets after their transplantation over time.
Methods: Five hundred rat islets were transplanted under the left kidney capsule of NOD/SCID mice. Animals were randomly allocated into experimental groups (8, 15, 22 and 29days post-transplantation) and BrdU was added to drinking water for 7 days before histology analysis of the grafts. Beta-cell replication was determined by double immunofluorescence staining for insulin and BrdU or Ki67. Apoptosis was determined by TUNEL staining. Percentages of positive BrdU, Ki67 and TUNEL positive beta-cell were determined in four experiments and data expressed as means±SEM.
Results: At 8 days post-transplantation, 5.95±1.11% beta-cell incorporated BrdU in the islet graft. At 15 days post-transplantation, the percentage of beta-cell incorporating BrdU gradually decreased (3.07±0.99, 1.34±0.48 and 1.94±0.59% at 15, 22 and 29days post-transplantation, respectively, $p<0.05$). Similar results were obtained with Ki67 staining (2.23±0.62, 0.59±0.16, 0.32±0.13 and 0.36±0.10% at 8, 15, 22 and 29 days post-transplantation, $p<0.05$). To determine whether the high number of replicating cell observed at 8 days post-transplantation was due to a compensatory effect of cell death in the graft, we analyzed the apoptotic rate of beta-cell in islet grafts. Apoptotic rates were very low at the different time points without any significant differences over time (0.12±0.06; 0.15±0.07; 0.13±0.05%, at 8, 15 and 29days post-transplantation).
Conclusion: Our results indicate that beta-cell proliferation continuously occurs within islet grafts. Proliferation rate is higher at the time of islet transplantation. These data suggest that beta-cell proliferation is important for engraftment and maintenance of long-term islet graft function.

RO-178 THE EXPERIMENTAL RESEARCH ON IMPROVING THE CURATIVE EFFECT OF AUTOLOGOUS BM-MSCs IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

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Background: To investigate the impact of oxidative preconditioning on the effect of mesenchymal stem cells (MSCs) in heart repair ability.
Methods/Materials: The models of myocardial infarction in swines were embolization by embolization left coronary artery with a gelation sponge through cardiac catheter. MSCs were exposed to H_2O_2 for 24 hours, and Bcl-2 protein expression was detected. Models were divided into four groups. Group A: control group, Group B: received MSCs (1×10^7/5 mL) transplantation without oxidative preconditioning in acute period after MI; Group C: received MSCs (1×10^7/5 mL) transplantation with oxidative preconditioning at the same period; Group D received untreated (1×10^7/5 mL) transplantation 4 weeks after MI. The changes of cadiac function were detected by Powerlab8SP + Millar catheter and ECT.
Results: 20μM H_2O_2 treatment of MSCs for 24 hours induced a increase in Bcl-2 expression ($p<0.05$). Compared group C with group B: (1) LVDP, $+dp/dt_{max}$, $-dp/dt_{max}$ was significantly improved($p<0.05$). (2) Left ventricular infarction area significantly decreased ($p<0.05$). (3) New vessels density in infarction junctional zone increased obviously after transplantation($p<0.05$). Compared group C with group D: (1) Left ventricular function, including LVDP, $+dp/dt_{max}$, $-dp/dt_{max}$ was significantly reduced ($p<0.05$). (2) The reduction of left ventricular infarction area decreased ($p<0.05$).
Conclusions: Low concentration of H_2O_2 could improve the effect for heart repir.

RO-179 EXPERIMENTAL STUDY ON ENHANCED THERAPEUTIC EFFECT OF COMBINING MESENCHYMAL STEM CELL TRANSPLANTATION WITH ERYTHROPOIETIN IN MYOCARDIAL INFARCTION MODEL

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Background: To assess the effects of mesenchymal stem cell (MSC) transplantation combined with erythropoietin (EPO) administration in the acute period after myocardial infarction and investigate the possible mechanisms.
Methods/Materials: Models of myocardial infarction of swines were established and divided into four groups: group A: control group, group B: EPO (1,000 U/kg) was administered subcutaneously by injection 3 times a week for 4 weeks, group C: MSC (1×10^7 cells) were group D: EPO was administered as in the group B and MSC were implanted as in the group C.
The serum levels of TNF-α and IL-1β, and proteins of MMP-2 and MMP-9 were detected, and echocardiography the cardiac function was assessed and capillary density was counted.
Results: Compared with other two groups, concentration of TNF-α and IL-1β in group B and group D decreased obviously at the different time points,. And compared with group A, the following changes were observed in the group B and group D: LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD) and posterior wall thickness (PWT) were decreased, LV ejection fraction (LVEF) was increased, the expressions of MMP-2 and MMP-9 proteins were inhibited and capillary density was enhanced, but there were no differences between group C and group A. The benefit in group D was more effective than group B.
Conclusions: Combination of MSCs transplantation with EPO treatment in acute period after MI results in better improvement of cardiac function and angiogenesis and attenuation of left ventricular remodeling than either of the monotherapy.

RO-180 MITOGENIC EFFECT OF HUMAN TISSUE FLUID/LYMPH ON KERATINOCYTE PROLIFERATION

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Background: Cultured keratinocytes (KC) are needed for covering large burn wounds and ulcers. They can be cultured in artificial media, however, the yield is always low and viability is limited. In our previous studies we found that human skin tissue fluid and lymph (TF/L) contain high levels of growth factors and cytokines. The aim was to study the effect of human TF/L containing IL-1β, IL-6, TNF-α, KGF, TGF-β on cultured human KC of human lower extremity skin and to show which cytokines and growth factors of human skin TF/L have influence on KC: proliferation, differentiation and expression of markers characteristic for epidermal stem cells
Material and methods: KC were isolated from lower limb skin and were cultured for 1 to 14 days in TF/L and standard medium. Neutralization of IL-1β, IL-6, TNF-α, KGF, TGF-β in TF/L and blocking their receptors on KC helped to estimate which cytokine could stimulated KC proliferation and differentiation.
Results: KC cultured in TF/L showed higher percentage of dividing and cells from basal layer and lower percentage of differentiated cells from upper layers vs control. Higher percentage of p63 (48 vs 8), CD29 (52.4 vs 41,4), Ki67 (57 vs 23,8), PCNA (63 vs 38), CK6 (15,5 vs 4,4), CK17 (10,6 vs 5,5), CK16 (26,4 vs 15,3) and decrease in percentage of CK 10 (52 vs 77,5), filagrin (19,6 vs 48,5) and involucrin (18,8 vs 45,3) positive KC was observed vs control. Neutralization of IL-1β, IL-6, TNF-α, KGF and blocking their receptors on KC caused decrease in percentage of mitotic cells. Quantitative growth of KC revealed higher proliferation after KC culture in TF/L vs control. Neutralization of selected cytokines and growth factors except TGF-β revealed lower total number of KC.
Conclusion: The investigated cytokines have a stimulating effect on proliferation of basal KC but not on their differentiation.

RO-181 EVALUATION OF THE CAPACITY OF MESENCHIMAL STEM CELLS MOBILIZED BY *Granulocyte colony-stimulating factor (G-CSF)* IN HEPATIC REGENERATION IN PATIENTS SUBMITTED TO HEPATECTOMY

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Introduction: G-CSF (granulocyte colony- stimulating factor) can stimulate growth factors of hepatocytic lineage (SDF1 and CXCR4), although this still needs to be affirmed by clinical trial.
Aim: To investigate cell mobilization by G-CSF and consequent migration of bone marrow stem cells, related to hepatocytic lineage, and assess whether mobilized cells to the liver (SDF1 and CXCR4) thus demonstrating the release of stem cells concerning hepatocytic lineage in patients undergoing hepatectomy.
Method: This was a prospective, double-blind, randomized study. Forty-four patients were selected.Laboratory tests and imaging were carried out on the day of selection (D0) and on the day of surgery (D5), and on other days (D15 and D30) only laboratory tests were performed. The patients were randomly chosen to be distributed into two groups: one with the use of G-CSF and the other with the use of 0.9% saline (Non G-CSF). The trial was based on CT scans performed by Toshiba multi-slice equipment - 64 channels to liver volumetry. Non-parametrical statistical tests were applied with $P<0.05$ as significant.
Result: We observed an increase in the production of MIF SDF1 and CXCR4 on D5 with a consequent reduction after D10 in the G-CSF group. In this period it was seen that the cells were mobilized for liver regeneration and concomitantly the volume on D60 and the delta volume (D60-D10) showed a statistical trend to increased liver remnant in patients who received GCSF.
Conclusion: There was an increase in the cellular mobilization present after D5 of stimulation by hepatotrophic factors that decreased after liver resection. This was seen as a consumption of mobilized peripherical stem cells which apparently increased the remaining liver volume in the group using G-CSF.

Clinical immunosupression I

RO-182 HIGH GRAFT PROTECTION AND LOW RATES OF INFECTIONS AND MALIGNANCIES BY INTRA-OPERATIVE HIGH-DOSE ATG INDUCTION IN KIDNEY GRAFT RECIPIENTS

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Background: Important adverse effects of the induction therapy are infections and malignancies, which occur in different frequencies depending on the type of agent and the duration of application. In 1990 we introduced the intraoperative high-dose induction (HDI) with ATG-F (ATG-Fresenius, 9mg/kg body weight) resulting in an improved 10-years kidney graft survival and in a re-

duced incidence of acute rejections. The aim of this study was to compare the rates of infections and malignancies in kidney graft recipients treated with standard triple-drug therapy (TDT) alone consisting of cyclosporine, steroids and azathioprine or with an additional intra-operative high-dose ATG-F induction.
Methods/Materials: A total of 760 renal transplantations from deceased donors performed in our clinic between 1987 and 1998 who initially received either TDT alone (n=238) or in combination with ATG-F induction (n=522) were included in this retrospective evaluation. Statistics: Kaplan-Meier survival analyses, pair-wise t-test, log rank test (Mantel-Cox), chi-square test.
Results: In contrast to the improvement of the 10-years patient (p=0.095) and graft survival ($p<0.001$) by TDT+HDI, the main adverse effects did not significantly differ between the two immunosuppressive regimens.

Table 1. Adverse effects

Variable	TDT+HDI, n=522	TDT, n=238	p value
Infections			
Bacterial, unspecified	106 (20.3%)	36 (15.1%)	0.089
Bacterial, pneumonia	16 (3.1%)	3 (1.3%)	0.139
Fungal	10 (1.9%)	9 (3.8%)	0.127
Parasitic	9 (1.7%)	1 (0.4%)	0.143
Viral			
CMV infections (asymptomatic)	234 (44.8%)	60 (25.2%)	<0.001
CMV disease (symptomatic)	97 (18.6%)	37 (15.5%)	0.308
Herpes zoster	15 (2.9%)	3 (1.3%)	0.175
Malignancies	234 (4.4%)	5 (2.1%)	0.118
PTLD	2 (0.4%)	1 (0.4%)	0.940

TDT, Triple-Drug Therapy; HDI, High-Dose-Induction; CMV, cytomegalovirus; PTLD, post-transplant lymphoproliferative disorder.

Conclusions: This single-centre analysis clearly shows the superiority of the single intra-operative high-dose induction with ATG-F compared to TDT alone in improving long-term graft survival without increasing the risk for infections and malignancies. Therefore this safe and effective type of induction can be recommended.

RO-183 IMMUNOSUPPRESSIVE REGIMEN BASED ON THYMOGLOBLULINE AND EARLY CONVERSION TO SIROLIMUS FOR TRANSPLANT RECIPIENTS WITH MARGINAL DONORS

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Background: During the past few years, there has been greater interest in the use of marginal donors for kidney transplantation. However, an ideal immunosuppressive strategy for this type of transplant has not been established.
Methods/Material: We retrospectively collected data on efficacy and safety of medical records of patients who received immunosuppressive regimen based on induction therapy with a single dose of thymoglobuline 3mg/kg, tacrolimus 0.1mg/kg/day, prednisone 0.5mg/kg/day and azathioprine 2mg/kg/day. Ten days after transplantation, azathioprine was converted to sirolimus (5mg loading dose followed by 2mg/day).
Results: Between July and November 2011, 60 patients were enrolled. The mean age was 50 years, 67% were male, 11 (18%) were diabetics and the mean time on dialysis before transplantation was 44 months. All patients were recipients of primary kidney transplants and had panel reactive antibodies less than 50%. Fifty (83%) donors were expanded criteria donors (ECD), 6 (10%) were standard donors (SCD) with renal failure and 4 (7%) were SCD with hypertensive nephrosclerosis demonstrated in pre-implantation graft biopsy. Delayed graft function occurred in 37 (62%), the incidence of acute rejection was 13% and serum creatinine at 3 months and 6 months was 2.2 ± 1.0 and 2.3 ± 1.2mg/dL, respectively. Cytomegalovirus infection was diagnosed in 9 (15%) patients. During the 6 month follow-up, one patient died and 10 patients lost the graft. Patient and graft survival at 6 months was 98% and 78%, respectively.
Conclusion: This immunosuppressive regimen seems to be effective in preventing acute rejection and ensure low incidence of cytomegalovirus infection in recipients of marginal kidneys, but there were no benefits for kidney function at 6 months.

RO-184 RABBIT ANTI-THYMOCYTE GLOBULIN (rATG)-BASED IMMUNOSUPPRESSION INDUCTION IN KIDNEY TRANSPLANTATION

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Introduction: Use of rabbit anti-thymocyte globulin (rATG) induction has increased in renal transplantation in recent years. rATG, when given prior to reperfusion, may reduce the incidence of delayed graft function (DGF). Potential complications of rATG therapy include increased risk of post-transplant infection and malignancy. This paper reports the use of intraoperative (pre-reperfusion) rATG in 707 consecutive kidney transplant patients with a minimum of 1-year follow-up.
Methods: Records of kidney transplant recipients at a single center from 2003 to 2009 were reviewed. Inclusion criteria included isolated kidney transplant recipients of any age who received intraoperative, pre-reperfusion rATG. Delayed graft function was coded according to UNOS definitions. Diagnoses of rejection, infection and malignancy required biopsy or culture confirmation.
Results: There were 242 living and 465 deceased donors. Twenty-five percent of patients had received a previous kidney transplant. Median follow-up was 52 months. Early graft loss at 7-, 30-, and 90-days was <1% for both living and deceased donor transplants. 1-year graft and patient survival for both donor groups was >97%. Measures of DGF included dialysis within 7 days (<1%), urine production (<40mL) in first day (<1%), and <25% decrease in serum creatinine within 1 day (17%). Median hospital stay was 5 days. The 30-day readmission rate was 24%. 1-year risk of rejection was 14% (antibody mediated 1%, cell mediated 11%, both 2%). 1-year risk of any infection was 38% (bacterial 30%, viral 13%, fungal 2%). 1-year incidence of CMV was 7%. BK virus 4%, and any neoplasm 6% (skin 2%, non-skin 4%, PTLD 1 case).
Conclusions: In this rATG-induction cohort, there was a low rate of early graft loss, patient death, DGF, and 1-year rejection. Immunosuppression-related complications were similar to those reported in the literature, with an overall risk of neoplasm of 6% and a 1-year risk of infection of 38%.

RO-185 RENAL FUNCTION OF AN EVEROLIMUS BASED THERAPY AFTER CALCINEURIN INHIBITOR WITHDRAWAL IN MAINTENANCE RENAL TRANSPLANT RECIPIENTS: 2 YEAR FOLLOW-UP DATA OF THE APOLLO TRIAL

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Objective: Assessment of renal function, safety and efficacy of an Everolimus regimen after Calcineurin-Inhibitor (CNI) withdrawal in maintenance kidney allograft recipients.
Methods: In an open-label, randomized, controlled, multi-center study 93 patients on a stable immunosuppressive therapy consisting of CNI, Enteric-Coated Mycophenolate Sodium (EC-MPS) with or without corticosteroids were randomized to either continue CNI treatment and EC-MPS or convert to an Everolimus/EC-MPS based regimen. After completion of the core study at Mo 12, patients were included in an observational 12-Mo follow-up study.
Results: 93 pts with a mean time since the most recent transplantation of 6.4 years were randomized to either Everolimus/EC-MPS (n=46) or CNI/EC-MPS (n=47), 79 (84.9%) pts completed the 24 month visit. Trough levels were 102.2 ± 38.4 ng/ml in CsA, 11.3 ± 15.0 ng/ml in Tacrolimus and 6.7 ± 2.6 ng/ml in Everolimus treated pts. At Month 24 after randomization mean calculated GFR (Nankivell) was higher by 5.0 mL/min/1.73m^2 for the Everolimus compared to the CNI group (63.9 ± 19.9 vs 58.9 ± 15.9 mL/min/1.73m^2; p=n.s.). The observed GFR slope from conversion to month 24 was +2.6 [-1.2,+6.3] for Everolimus/EC-MPS and -2.0 [-6.1,+2.1] mL/min/1.73m^2 for CNI/EC-MPS pts. Two deaths and one graft loss were observed in the CNI/EC-MPS group, one death in the Everolimus/EC-MPS group and no BPAR was observed in either group. The number of patients with infections was 13 pts (28.3%) in the Everolimus vs. 9 pts (19.1%) in the CsA group. Four (10.6%) malignancies occurred in the CNI group compared to one (2.2%) case in the Everolimus group.
Conclusions: The late conversion to an Everolimus/EC-MPS treatment in maintenance renal transplant patients after CNI withdrawal leads to a better renal function with a lower incidence of malignancies.

RO-186 EVEROLIMUS BASED/CNI FREE REGIMEN IN DE-NOVO RENAL TRANSPLANT RECIPIENTS

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Introduction: Everolimus is a potent immunosuppressive agent usually employed with low dose CNI. Few trials have been developed in de-novo Everolimus regimen with CNI avoidance. We report the results of a prospectical non randomized study on kidneys transplant recipients treated with CNI free/Everolimus based protocol.
Methods: 53 patients who received kidney transplantation between 2008 and

2010 has been assigned to a therapeutic protocol with m-TOR inhibitors (Everolimus), DNA inhibitors (MMF or EC-MPS), steroids and followed up. All patients received an induction therapy with Basiliximab. Everolimus was started from day 14 post transplant and doses aiming a trough blood level of 3-8 ng/mL.
Results: 19 patients with double kidney transplant and 34 single kidney recipients were investigated for an average time of 16,5 months. Recipients mean age was 60 years (range 41-72). 39 recipients received graft from marginal donor. Donors mean age was 66 years (range 38-86). Mean creatinine blood level at time of transplant, one, three, six and twelve months after transplant was, respectively: 750, 307, 141, 134 and 149 μmol/L. The rejection biopsy-proven rate was 20%. According to Banff classification at biopsy we found 5 type IA, 3 type IB and 3 antibody-mediated rejections. The overall drop-out was 4: 3 for surgical complications and one for antibody mediated rejection (converted to CNI). 12 patients displayed surgical complications: 8 wound healing complication and 4 lymphocele. At 1 year follow up mortality rate was 0% and graft survival 100%.
Discussion: Everolimus based/CNI free therapeutic regimen with DNA inhibitors and steroids resulted in acceptable rejection rate and good renal function at one year after transplant. This association provided good results in recipients of marginal donor kidneys. Based on these observations, Everolimus based/CNI free regimen has become the protocol of choice in our center for kidney transplantation from non-standard donors.

RO-187 CONVERSION TO EVEROLIMUS: EARLY VS LATE? A CASE-CONTROL STUDY

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Introduction: Several studies are shown that early conversion to everolimus is beneficial in graft function. The effects of late conversion are less well known.
Material and Methods: We have conducted a case-control study in 46 patients switched to everolimus in our center. In 18 patients with a mean age of 56±14 years and a men time of transplant of 12±11 months early conversion has been done, in 11 by renal function's preservation, in 3 by tumors and the rest for other reasons. In 28 patients, average age of 62.6±12.9 years and time of transplantation of 121.9±58.3 months late conversion has been done, most of them by tumors (25 patients). Controls were selected with the following criteria: Time of transplantation, renal function, age and sex. All patients are at least two years of following.
Results: On early conversion 4 patients discontinued due to adverse effects, however the reason for drop-out in late conversion were death with funtioning kidney due to tumors.
The key data are shown below in Table 1.

	Total (N=46)		Early (N=18)		Late (N=28)	
	Case	Control	Case	Control	Case	Control
Cr basal	1,6	1,5	1,7	1,4	1,58	1,55
Cr 6 months	1,4†	1,5	1,49†	1,56	1,46	1,60†
Cr 12 months	1,5†	1,69†	1,5	1,7	1,5	1,68†
Cr 24 months	1,44†*	1,7†	1,3†	1,6†	1,5	1,83*†
Prt basal	0,2†	0,4	0,33	0,3	0,17	0,19
Prt 6 months	0,3†	0,4	0,4	0,4	0,44†	0,26
prt 12 months	0,5†	0,3	0,47	0,43	0,0,53†*	0,26
prt 24 months	0,4†	0,5	0,5	0,5	0,47†	0,47†

Prt = proteinuria/creatinine, Cr = creatinine. †vs basal, *case vs control.

Conclusions Renal function improves both early and late conversion.
Late conversion slightly increased proteinuria. Proteinuria remained unchanged in the early conversion.
In late conversion there are not withdrawals due to adverse effects of medication.
The reason for conversion may influence the decision to withdraw everolimus.

RO-188 IMPROVED KIDNEY GRAFT FUNCTION AFTER CONVERSION FROM TWICE DAILY TACROLIMUS TO THE ONCE DAILY PROLONGED-RELEASE FORMULA

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Background: Tacrolimus once daily (Tac-QD) formulation has been recently introduced in order to improve patients' adherence to the immunosuppressive medication. A long-term effect of conversion from tacrolimus twice daily (Tac-BID) to Tac-QD on kidney graft excretory function has not been described yet. We have retrospectively analyzed the kidney graft function after the conversion from Tac-BID to Tac-QD during 24-month observation period.
Methods: Seventy-two kidney transplant recipients (including 19 simultaneous pancreas-kidney transplants) at least 9 months after transplantation and with stable graft function for 6 months were enrolled into the study. We have analyzed the kidney graft function (eGFR estimated according to MDRD equation), tacrolimus daily dose and tacrolimus blood trough level changes during a 24-month follow-up period after the conversion.
Results: All patients have completed the 12-month, and 47 patients the 24-month observation. eGFR increased significantly after the conversion from 57.1ml/min/1.73m^2 before to 60.0ml/min/1.73m^2 3 months later (p=0.004) and to 65.7ml/min/1.73m^2 24 months after the conversion ($p<0.001$). Tac-QD blood trough levels did not change throughout the whole observation, whereas Tac-QD daily dose decreased significantly not until the 24-month timepoint. There was no correlation between changes of eGFR during the first 12 months after the conversion and changes of Tac-QD blood trough levels (r = -0.157; p = 0.19).
Conclusions: 1. The conversion from tacrolimus BID to tacrolimus QD formulation is followed by the clinically significant improvement of kidney graft function in a long-term observation. 2. The improvement is not related to the changes of tacrolimus blood trough level.

RO-189 TACROLIMUS ONCE DAILY (Advagraf) VERSUS TWICE DAILY (Prograf) IN LIVER TRANSPLANTED PATIENTS: AN OBSERVATIONAL SINGLE-CENTRE STUDY

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Background: Advagraf is a once daily tacrolimus oral formulation approved in the European Union to prevent rejection in liver and kidney transplant recipients and to improve adherence to treatment.
The aim of our study was to evaluate the metabolic effects and tacrolimus plasma levels in liver transplanted patients treated with Advagraf compared to those treated with Prograf based regimen.
Methods: This was a retrospective single-centre study in patients with liver transplant using a database spanning 2008 – 2010. During the observation time, a 25 patients, (median age 60) transplanted from more than two years for liver cirrhosis and hepatocarcinoma were switched from Prograf to Advagraf based therapy. A subset of 22 patients, treated with Prograf served as controls. Mean follow-up was of twelve months. Whole blood tacrolimus levels were measured with Abbott Architect Tacrolimus assay that used a chemiluminescent microparticle immunoassay (CMIA) technology.
Results: No significant change during follow-up in renal or liver biochemistry values, and in carboidrate or lipidic profile was observed in patients treated with Advagraf after conversion from Prograf based regimens. The mean tacrolimus blood level during Advagraf therapy was 4,9±1,4 ng/ml versus 6,3±2,1 ng/ml during Prograf therapy. Tacrolimus levels in control group were 6,1±1,4 ng/ml. Tacrolimus blood levels were significantly more stable during Advagraf therapy than during Prograf therapy. This difference was observed both between treatment groups than in the same patient after switching from Prograf to Advagraf therapy. No significant adverse effects were observed in both groups.
Conclusion: Advagraf therapy in liver transplanted patients was safe and well tolerated. Advagraf therapy had no effect on carboidrate or lipidic metabolism, and as compared to Prograf therapy, has the advantage of maintainig more stable tacrolimus blood levels.

RO-190 THREE-YEAR RESULTS OF CONVERSION FROM CYCLOSPORINE TO TACROLIMUS IN RENAL ALLOGRAFT RECIPIENTS WITH CHRONIC ALLOGRAFT NEPHROPATHY

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Objective: This study evaluated the efficacy and safety of tacrolimus (FK506) as secondary intervention in cyclosporine A (CsA) treated kidney transplantation patients with chronic allograft nephropathy (CAN).
Methods: 176 patients who received a cadeveric kidney transplantation in our unit more than 3 months prior to study enrollment and who were being treated with CsA-based immunosuppressive treatment were included, all patients received allograft biopsy and were diagnosed as CAN. Patients were differentiated according to following regimen. Patients were either converted to tacrolimus (FK506 group,n=112) or remained on their initial CsA-based immunosuppression (CsA group,n=64).
Results: After 3-year of follow-up, Serum creatinine was markedly decreased from (160.7±46.3)umol/L to (149.8±49.8)umol/L,$P<0.001$.136 cases were subjected to repeated allograft biopsy. An evident pathological improvement

was achieved after conversion to FK506 treatment. Chronic allograft damage index (CADI) significantly decreased from 8.3±2.6 to 3.0±0.7 ($P<0.001$) in FK506 group.Repeated renal biopsy revealed that in FK506 group 56 cases (65.9%) became C4d negative in renal tissue and no case become positive, and 4 case (4.7%) showed steady C4d positive accompany with hepatitis C (renal graft biopsy showed membranous nephropathy); and in CsA group, no case became C4d negative, 7 cases (13.7%) showed steady C4d positive, and vice versa,there are 16 cases from negative to positive (31.4%). FK506 group significantly decreased PRA-II levels from 56±9%(36–88.5%) to 6.1±1.2%(3.9-7.3%),follow by C4d deposition from positive to negative in renal tissue. Graft survival rate was significantly increased in the FK506 group than in the CsA group,98.2% vs. 85.9% follow-up 3-year.

Conclusion: Our data suggest that a therapeutic approach combining FK506 and MMF rescue showed beneficial effects on the pathological changes with chronic allograft nephropathy, and showed high efficacy in the reversion of C4d-positive chronic rejection, and elevated long-term renal allograft survival.

RO-191 CLINICAL AND HISTOLOGICAL STUDY OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN SOLID ORGAN TRANSPLANT

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Background: Post-transplant lymphoproliferative disease (PTLD) is a serious complication of immunosuppressive therapy in solid organ transplantation (SOT), which causes high morbidity and mortality.

The Ebstein-Barr virus (EBV) plays an important role in the development of this disease.

The aim of our study was: to analyze the incidence of PTLD in SOT recipients in our centre; to study the demographic, clinical, histological, therapeutic and survival outcomes of patients with PTLD.

Material/Methods: We performed a retrospective study of 2114 SOT recipients in our hospital between 1998-2009. We collected demographic and laboratory data, histological findings, clinical course and treatment for patients diagnosed with PTLD.

Results: We analyzed 2114 SOT in our centre, 29 of those (1.37%) developed PTLD.

Table 1. Incidence of PTLD in SOT

Type of transplant	Nº transplants	Nº cases PTLD	%
Lung	283	10	3.5
Liver	793	7	0.8
Heart	456	4	0.8
Kidney	559	6	0.9
Liver-Kidney transplant	17	1	0.1
Heart-Kidney transplant	6	1	0.06
Total	**2114**	**29**	**1.37**

The clinical, histological and survival outcomes are shown in Table 2.

Table 2. Clinic and histological characteristics of PTLD in SOT

Type of transplant	Nº PTLD	Histology	EBER+ (yes/no)	I-II stages/ II-IV stages	CD20+ (yes/no)	Complete remission (yes/no)	Time between transplant and diagnosis (months)	Nº exitus
Lung	10	4 polymorphic + 3 LBDCG + 1 Burkitt lymphoma	2/4	0/10	4/0	7/10	28.94 (± 23.43)	4/10
Liver	7	2 polymorphic + 5 Burkitt lymphoma	1/3	3/4	5/2	2/7	48.80 (± 44.06)	3/4
Heart	4	3 LBDCG + 1 Burkitt lymphoma	1/2	3/1	4/0	2/4	153.16 (± 25.58)	3/1
Kidney	6	1 polymorphic + 2 LBDCG + 1 NHL-NK/T + 1 ALL	5/1	2/4	4/2	1/6	65.57 (± 41.90)	3/4
Combined transplants	2	2 LBDCG	1/1	1/1	2/0	1/2	70.06 (± 82.11)	1/2
Total SOT	29	7 polymorphic + 7 LBDCG + 7 Burkitt lymphoma + 1 NHL-NK/T + 1 ALL	10/16	9/20	19/4	13/29	58.81 (± 50.31)	14/21

NHL: non-Hodgkin lymphoma ALL: acute lymphoblastic leukemia DLBCL: Diffuse large B-cell lymphoma

We studied 8 renal transplant patients with PTLD. All of them received triple immunosuppressive therapy.

Seven patients were found to have EBV IgG+/IgM- pre-transplant serology. One patient sero-converted as shown by active replication of EBV on PCR.

Renal graft function remained stable after diagnosis but in all cases immunosuppression was reduced and five patients were converted into m-TOR.

The median survival for patients after diagnosis with PTLD was 15.1 months (range 89.9 months); in kidney transplant patients survival was 3.88 months (range 69.43 months).

Conclusions: The incidence of PTLD in SOT recipients in our hospital was 1.37% during 11 years of monitoring. The incidence in renal transplant was 1.07%.

This study confirmed a link between EBV and PTLD.

PTLD has a high mortality rate, regardless of the type of organ transplanted.

There are a wide range of histological features in renal PTLD; the majority are monomorphic, late onset and stage III-IV. These factors indicate poor prognosis.

Renal graft survival was 100% despite the reduction and/or change in immunosuppression.

Kidney V

RO-192 HEALTH RELATED QUALITY OF LIFE AND CLINICAL OUTCOMES IN KIDNEY TRANSPLANTED PATIENTS

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Background: Health-related quality of life (HRQoL) is an important outcome measure in patients with chronic kidney disease. It has also been repeatedly shown to predict mortality in various patient populations. In a prospective cohort study we assessed the association between HRQoL and long-term clinical outcome in kidney transplant recipients (Tx).

Methods: We collected socio-demographic parameters, medical and transplant history and laboratory data at baseline from 879 prevalent kidney transplant recipients (mean age 49 (SD=13) years, 58% male, 17% with diabetes mellitus). We assessed HRQoL with the Kidney Disease Quality of Life - SF™ (KDQOL-SF™) questionnaire and used the Center for Epidemiologic Studies – Depression (CES-D) scale to assess depressive symptoms. All-cause mortality and death-censored graft loss or death with functioning graft. Cox regression models and semiparametric competing-risks regression analyses were used to measure the associations between HRQoL scores and outcomes.

Results: Most of the examined HRQoL domains were associated with clinical outcome in the unadjusted models. After adjusting for several important confounders the SF36-Physical Composite Score, Physical Functioning and General Health Perception subscales remained independently associated with clinical outcomes. Every 10- point increase in the SF36-Physical Composite Score, Physical Functioning and General Health Perception scores was associated with 18% (HR=0.819; 95%CI:0.707-0.949), 11% (HR=0.889; 95% CI:0.837-0.944) and 7% lower risk of mortality (HR=0.934; 95% CI:0.875-0.996), respectively.

Conclusions: We demonstrated that the SF36-Physical Composite Score, Physical Functioning and the General Health Perception KDQOL-SF™ domains are independently associated with increased risk of mortality in kidney transplanted patients. Regular assessment of HRQoL may be a useful tool to inform health care providers about the prognosis of kidney transplant recipients. Additional studies are needed to assess if interventions aimed at improving HRQoL would improve clinical outcomes in this patient population.

RO-193 A COMPARISON OF TRANSPLANT OUTCOMES IN PERITONEAL AND HEMODIALYSIS PATIENTS – A PAIRED KIDNEY ANALYSIS

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Background: Studies examining the effect of pre-transplant dialysis modality on graft and patient survival have given conflicting results. Therefore, we studied the effects of pre-transplant dialysis modality on transplantation outcome. To minimize the donor variability and bias, a paired kidney analysis was used.

Methods: From December 1994 to December 2008, some 118 peritoneal dialysis (PD) patients received renal transplantation (RT). PD constituted 12% of all kidney transplantations performed in our centre at that time. 78/118 PD pa-

tients (42m, 36f) aged from 14 to 70 (mean 41) years had their hemodialysis (HD) pair (27m, 51f) aged from 16 to 69 (mean 42) years.
Results: Mean duration of RRT before transplantation was 19 months (PD) vs 33 months (HD), number of CABG/PTCA was 6/5 (PD) vs 1/0 (HD) ($p < 0.05$). The groups (PD vs HD) did not differ significantly with respect to: number of mismatches, type of immunosuppressive protocol, one year patient survival (97.4% vs 100%), and one-year graft survival (91% vs 90%). PD vs HD had lower incidence of delayed graft function (9% vs 28%; $p< 0.05$) and acute lower rejection incidence (14% vs 22%), graft thrombosis was more commonly listed as a cause of graft failure in PD group, also all types of infections occurred more frequently in PD patients (39% vs 30%). One year creatinine concentration was similar in PD vs HD group 1.53 mg/dl vs 1.68 mg/dl, respectively.
Conclusions: The outcome of RT is similar in patients coming from either PD or HD. Delayed graft was less common in PD patients by this potential benefit appears to be counterbalanced by other factors with are associated with graft loss.

RO-194 IMPACT OF INFLAMMATION AT 6 WEEKS ON INFLAMMATION AND FIBROSIS AT ONE YEAR IN KIDNEY GRAFT PROTOCOL BIOPSIES

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Background: Subclinical acute rejection is associated with subsequent graft fibrosis. The aim of this study was to assess if inflammation in protocol biopsies taken 6 weeks after kidney transplantation in low-risk patients predicts development of fibrosis and inflammation one year after transplantation.
Material and methods: All single kidney transplant recipients with a protocol biopsy at week 6 weeks and at year one were included. Biopsies were scored according to Banff. Recipients with preformed donor specific HLA antibodies, AB0 incompatibility and recipients with indication biopsies were excluded. The immunosuppressive protocol consisted of induction therapy with Basiliximab and maintenance therapy with calcineurin inhibitors, mycophenolate mofetil and steroids. Recipients with subclinical acute cellular rejection at week 6 received treatment with methylprednisolone and increased steroids.
Results: A total of 157 recipients fulfilled the inclusion criteria.
Of the 100 biopsies without inflammation at week 6, 69 were still negative at one year, 26 were borderline and 5 had subclinical acute cellular rejection. In the borderline-group at week 6 (n = 43), 20 were negative at one year, 19 remained borderline and 4 had subclinical acute cellular rejection. Fourteen recipients had subclinical acute cellular rejection at week 6, of whom 10 were negative at one year, 3 were borderline and 1 had Banff Ib subclinical rejection.
Conclusion: Inflammation in protocol biopsies at week 6 does not predict interstitial fibrosis or tubular atrophy at one year in low-risk single kidney transplant recipients. However, patients with subclinical rejection at week 6 had less tubular atrophy at one year compared to the other groups.

RO-195 DUAL KIDNEY TRANSPLANTATION FROM UNCONTROLLED DECEASED DONORS AFTER CARDIAC ARREST (uDDCA)

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Kidney grafts from uDDCA has been used in France to counteract the organ shortage. Some kidneys from uDDCA remained unsuitable for solitary transplantation and may be considered for dual kidney graft (DKG) transplantation. The aim of the study was to evaluate graft survival and outcomes in single (SKG) and DKG.
Five patients received a DKG and 24 patients a SKG from uDDCA. All kidneys were placed on MPP (pulsatile perfusion machine, RM3) and all patients received the same immunosuppressive treatment. Estimated MDRD and inuline clearance were analysed until 36 months after transplantation and systematic biopsies were performed at M3 and M12 to evaluate the chronic interstitial fibrosis (IF) by colour image quantification.
Our experience with RM3 perfusion machine leads us to perform a SKG when the resistance index (RI) is lower than 0.4 after 6 hours of perfusion and a DKG when the RI is between 0.4 and 0.6.
Donor's and recipient's characteristic (mean age, gender), mean numbers of HLA mismatch were not significantly different. The mean duration time of MPP and the mean warm ischemic time were higher in the DKG than in the SKG group (1319 vs 689 min, p= 0.05 and 105 vs 121 min, p=0.017). Patient and graft survivals were 100% in both groups. PNF (not observed in our cohort) and DGF rate were not statistically different between the 2 groups (100% vs 78%). Acute rejection rate was not different between the groups.
Graft outcomes and IF results are reported table 1.

Table 1. Evolution of graft function and histology

	DKG	SKG	p
eGFR M3	37.0 (6.8)	38.6 (7.6)	0.70
eGFR M12	42.0 (6.9)	44.3 (4.1)	0.81
eGFR M24	45.0 (3.3)	45.9 (14.0)	0.96
eGFR M36	40.3 (15.5)	45.1 (14.0)	0.52
m GFR M12	43.6 (5.0)	44.4 (13.0)	0.94
m GFR M36	36.7 (16.0)	42.5 (12.0)	0.60
IF score M3	37.8 (9.2)	29.2 (7.6)	0.25
IF score M12	34.6 (12.8)	36.2 (13.4)	0.92

eGFR: estimated by MDRD formula; m GFR: measured by inulin clearance; IF: interstitial fibrosis. All data are expressed as mean (SD).

Results between SKG and DKG are not significantly different. Kidneys from uDDCA with high resistance index should not be discarded and could be used as DKG with acceptable results.

RO-196 SWITCH FROM LAPAROSCOPIC TO RETROPERITONOSCOPIC HAND ASSISTED DONOR NEPHRECTOMY

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Retroperitonoscopic approach avoids entering into the peritoneal cavity and so offers the advantage of preventing intraabdominal adhesions and organ injuries. We present our series after switching our hand assisted donor nephrectomy technique from laparoscopic to retroperitonoscopic approach in our clinic.
Methods: We have performed 144 retroperitonoscopic nephrectomy procedures in between February 2009 and November 2010 at John F Kennedy Hospital. The average age was 45. Female ratio was 64%. Twenty eight nephrectomies were right sided (19,4%). Thirteen patients had more than one artery. All donors had hand assisted endoscopic nephrectomy requiring hand port and two trocar insertion. One donor with right nephrectomy required an extra trocar for liver retraction. Paramedian and Pfannenstiel incision (n=4) was performed. The retroperitoneal space was dissected by hand assistance.
Results: All retroperitonoscopic procedures were completed without transition to open nephrectomy. None of the donors had major perioperative complication. There was no organ injury and blood transfusion. Peritoneal opening was the most frequent complication (n=31). Seventeen donors had major peritoneal opening (opening more than 4 cm). One donor had deep vein thrombosis. Seven donors had superficial surgical site infection. Two donors had postoperative hernia. Eight donors complained about asymmetric appearance because of paramedian incision.
Conclusion: Centers using laparoscopic hand assisted donor nephrectomy can safely switch to retroperitonoscopic approach. Peritoneal tears were frequent especially at the beginning of the learning curve but it did not cause any technical difficulty during the procedure. We used liver retraction only at our initial right nephrectomy case with retroperitonoscopic approach. Avoiding liver retraction was an important advantage of right retroperitonoscopic approach. There was more stress to surgeon's arm during retroperitonoscopic hand assisted technique. The stress to arm was minimal with paramedian incision but some of the donors were unsatisfied from this incision.

Abstract RO-194 – Classification at 6 weeks and fibrosis/atrophy at one year

Variables at one year	Classification of biopsies at 6 weeks			p (neg vs. bord)	p (neg vs. rej)	p (bord vs. rej)
	Negative (n=100)	Borderline (n=43)	Rejection (n=14)			
Interstitial fibrosis	0.80 (0.71)	0.91 (0.43)	0.71 (0.47)	0.36	0.66	0.17
Tubular atrophy	1.03 (0.63)	0.98 (0.34)	0.71 (0.46)	0.60	0.073	0.028

Mean (SD).

RO-197 CORTICOSTEROIDS WITHDRAWL IN STABLE MAINTENANCE RENAL TRANSPLANT PATIENTS

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Corticosteroids are powerful antiinflamatory with immunosuppressant effects utilized in maintenance therapy following kidney transplantation and are associated with a higher rate of side events in comparison with protocols involving early corticosteroid withdrawl. The present paper reports the results of cessation of steroids in stable maintenance renal transplant patients.
One hundred forty four deceased kidney grafted patients (51% men), aged 55.6±12.3 years, with follow-up of 62 months (1-247) and steroids withdrawl period of 36.6 months (1-198) follow-up steroid free were studied. Etiology of end stage renal disease was secondary to Glomerulonephritis 31%, Diabetes 22%, Policystic disease 14%, Tubulointerstitial nephropathy 13%, Vascular 5%, Unknown 17%. The patients were on Prednisone 5-10 mg dairy combined with Cyclosporine 50-150 mg/Tacrolimus 0.5-6 mg, associate to Mycophenolate Mophetyl 250-2.000 mg, Sodium Micophenolate, 360-900 mg or Azatioprine 50-75 mg, and Everolimus 1-4 mg. Steroids were diminished gradually in three months period and some patients receibe monotherapy only.
Basal serum creatinine was 1.5±0.6mg/dl and after five years followup 1.35±0.5 mg/dl. Basal blood glucose concentration was 128±11 mg/dl and after five years 110±0.9 mg/dl. Weight was maintained. At 5 years, graft and patient survival were 100%. There was no acute rejection after steroids withdrawl. After withdrawl blood pressure control was achieved with less antihypertensive drugs. Lipids diminished slightly with less cholesterol-lowering drugs.
Conclusion: Corticosteroids could be withdrawn safely in stable renal transplant patients and avoid morbidity and adverse events related to chronic utilization improving survival and quality of life.

RO-198 IS "SINGLE STAPLER TECHNIQUE SAFE" IN LAPAROSCOPIC DONOR NEPHRECTOMY?

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Aim: Although laparoscopic donor nefrectomy (LDN) has gained a worldwide popularity. Use of a single vascular stapler instead of 2 seperate staplers for the renal artery and vein and hand removal of the graft through a pfannenstiel incision may decrase both warm ischemia and the overall operative time. However there is still an ongoing debate considering the AV fistula formation with the use of a single stapler. We report here a series of 120 LDN cases with the use of a single stapler and hand removal of the graft.
Material and Method: LDN cases were rewieved retrospectively and all the patients were invited for physical examination and doppler USG considering the AVF formation. Demographic data, operation time, warm ischemia time, follow up period, and complications were rewieved.
Results: Between December 2005 and June 2010, 120 (48 male,) patients were operated for LDN. Median age of donors were 48 (25-71). Median operation time was 87 min (range: 64-135). Median warm ischemia time 38 s (range: 22-148). There was no conversion to open surgery and no peroperative or postoperative mortality. None of the patients needed dialysis. Only 40 patients were available re-examination for AV fistula. Color doppler ultrasound was performed to these patients and AV fistula was not detected. Overall morbidity rate was 10% (12 patients). Four patient had haematoma, 3 patient had urinary tract infection, 3 had wound infection, and 2 patient had atelectasis.
Conclusion: LDN is the best choise for living-donor renal transplantation today. The operation time and warm ischemia time are decreased with single stapler and hand removal technique when compared with the literature. Furthermore, this technique is safe, and cost effective.

RO-199 FEASIBILITY TO MAINTAIN TRIPLE BLOCKADE OF RENIN ANGIOTENSIN SYSTEM IN RENAL TRANSPLANT PATIENT WITH SEVERE PROTEINURIA

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Experimental and clinical data suggest that aldosterone may contribute to proteinuria and progressive renal disease. In fact, an aldosterone antagonist seems to be effective for controlling proteinuria in native kidneys. However, there is little information about this approach in renal transplant patients, in whom the presence and amount of proteinuria represent risk factors for graft loss, cardiovascular disease and death. The aim of our study was to evaluate whether addition of spironolactone provided an additional antiproteinuric effect to the angiotensin-converting enzyme inhibitor (ACEI) and angiotensin type I receptor antagonists (ARB) and if possible to keep these three drugs chronically. We evaluated the effects on severe proteinuria at 24 months after prescription of spironolactone (25 mg/day) among 11 renal transplant patients with serum creatinine values less than 3 mg/dL who were under treatment with an ACEI plus an ARB. Patients were examined in the renal transplant outpatient clinic every week. Nine patients showed a more than 50% reduction in proteinuria not only early, but also sustained at 6 months with a mild, nonsignificant deterioration in renal function.

Table 1. Twenty-four month follow-up of the patients treated with triple blockade of the Renin-Angiotensin System (RAS)

Variable	Baseline	6 mo	12 mo	24 mo	p
Patients in follow-up	11	11	6	5	NS
SBP (mm Hg)	133±9	136.8±16	137±16	137±14	NS
DBP (mm Hg)	79±7	80±12	80±12.3	81±11	NS
Weight (kg)	79.5±16.7	80.5±19.8	80.5±19	81.5±18.7	NS
Serum creatinine (mg/dL)	1.6±0.32	1.7±0.54	1.8±0.65	1.9±0.45	NS
eGFR (mL/min)	52±12.7	48±14.2	44.4±14.2	42.3±16	NS
Proteinuria (g/d)	4.4±1.4	2.3±1.1	1.23±0.86	1,9±0,75	0.01
Potassium (mEq/L)	4.6±0.4	5±0.62	5±0.6	4,6±0,48	NS

SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; NS, not significant.

Five patients (45%) showed sustained response at 24 months, but 6 patients had to drop out the treatment because of the side effects (hyperkalemia in 4 cases, increase fo serum creatinine in 1 case and gynecomastia in 1 case).
This study showed that spironolactone decreased severe proteinuria among patients treated with an ACEI plus an ARB. This therapy is not recommended for patients with GFR below 40 mL/min. Therefore, it is suggested that using triple blockade of RAS could be feasible in selected renal transplant patients to reduce proteinuria in the medium term, although caution is required to avoid severe hyperkalemia.

RO-200 THE USE OF RITUXIMAB IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Background: To review the indication, treatment and subsequent outcomes with rituximab in all paediatric renal transplant recipients (RTR).
Methods: Retrospective case-note analysis of all RTR who received rituximab in a single renal transplant centre.
Results: 19 patients aged 5.7-17.5 (median 13.3) years (y) with 20 rituximab treatment episodes identified from 2002-2011.
5 received rituximab at 43-90 (median 65) days with other treatments for post-transplant recurrence of focal and segmental glomerulosclerosis. 3 cases were treated with a single dose of 750mg/m^2, 1 received 2 doses and 1 given 4 weekly doses of 375mg/m^2. 60% responded (one with Stage V(T)-CKD and another requiring graft nephrectomy) with resolution of proteinuria and estimated glomerular filtration rates (eGFR) of 20-76mls/min/1.76m^2 at 0.75-1.25y post-transplant.
6 cases received rituximab for biopsy proven rejection with donor specific antibodies at 0.04 - 12.5 (median 6.3) y post-transplant. 5 patients have functioning grafts (eGFR = 30-76mls/min/1.76m^2 with time from transplantation of 3.7-9.9y).
3 patients received rituximab for rejection without donor specific antibodies at 15days, 2y and 8y post-transplant.
4 weekly doses of rituximab at 375mg/m^2 were used to treat post-tranplant lymphoproliferative disease (PTLD) in 5 cases presenting 0.5-7 (median 0.8)y post-transplant. 2 patients have resolution of disease at 0.8 and 1.3y post diagnosis, 1 patient responded to treatment and transitioned to adult services. 2 patients died; one had B-cell Burkitt phenotype non-Hodgkin's lymphoma receiving two doses of rituximab before care was withdrawn. The other had atypical HUS and developed PTLD 0.5y post-transplant requiring chemotherapy but was unresponsive to therapy.
One case of ABO incompatible transplant received rituximab (375mg/m^2) 4 weeks prior to transplantation. At 1.3y follow up graft function is stable (eGFR 52mls/min/1.73m^2).
Conclusion: Rituximab therapy has been given for a variety of indications in paediatric RTR. Further analyses need to be performed on larger groups patients to determine its indications and benefits.

RO-201 BORDERLINE REJECTION IN RENAL ALLOGRAFTS – MANAGEMENT AND OUTCOMES FOR KIDNEY TRANSPLANTS IN 2008

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Background: Borderline changes are frequently identified in renal allograft

biopsies. The relationship between borderline change and acute renal allograft rejection is unclear and optimal clinical management remains uncertain.
Method: We retrospectively studied patients who received a kidney allograft at our centre between January 1st and December 31st 2008 and who underwent an allograft biopsy within the first year. We identified 40 renal allograft biopsies that showed borderline change as the principal finding. We assessed the degree of allograft dysfunction pre-biopsy and the change in graft function post biopsy, quantified as a percentage change in serum creatinine. We arbitrarily defined a significant change in graft function as a percentage change in serum creatinine greater than 10% above or below pre-biopsy baseline. Treatment was allocated to one of 3 categories: "Anti-rejection therapy", "No Treatment" and "Treatment for other diagnoses". Outcomes for each category of treatment were assessed in terms of the percentage change in serum creatinine above or below the pre-biopsy baseline.
Results: 27 biopsies (68%) were for allograft dysfunction, 7 (18%) were protocol biopsies and 6 (15%) were for delayed graft function (DGF), and these were excluded from further analysis. 4 patients subsequently developed unequivocal T cell mediated rejection between 1 and 4 months later.

Outcomes - excluding those with DGF

	Improved function	Stable	Continued dysfunction	Total
No treatment	4 (50)	4 (50)	0 (0)	8
Anti-rejection therapy	10 (50)	9 (45)	1 (5)	20
Treatment for other diagnoses	0 (0)	4 (66)	2 (33)	6

Number of cases (percentage).

Conclusion: In this single centre observational study, borderline change was non-progressive in the majority (91%) of cases, though some patients (12%) later developed unequivocal T cell mediated rejection. A favourable outcome was seen both in patients who received anti-rejection therapy and in those who did not. This demonstrates that our individualised treatment strategy based on clinical assessment of each case is successful. The favourable outcomes seen in those patients not treated for rejection suggests that a more conservative approach may be appropriate.

Kidney VI

RO-202 EARLY ULTRASOUND SCAN AFTER LIVING DONOR RENAL TRANSPLANTATION ALLOWS IMMEDIATE CORRECTION OF PERFUSION PROBLEMS AND MAINTAINS GRAFT FUNCTION IN ADULT AND PAEDIATRIC POPULATIONS

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Introduction: Our protocol states that live renal transplant recipients should receive a post op ultrasound (US) assessment of graft perfusion before leaving recovery.
Since introduction, 278 adult and 70 paediatric transplants have been performed.
The purpose of this study was to assess whether this scan identified perfusion problems & allowed immediate surgical correction and maintained graft function.
Methods: We collected data from our database & notes on whether the transplant was pre-emptive and native urine output (UO). We looked at the reports of the scans performed to see whether any abnormality was found and what action was taken.
Results: Of the adult population, 272/278 (98%) had an US and of these 29 (11%) were abnormal. Of the abnormal scans, 21 showed suboptimal perfusion which were not re-explored. 8 showed global poor perfusion or abnormal flow in the main vessels of which 6 re-explored: 1 had a negative re-exploration; 3 had poor flow secondary to position and were re-positioned in theatre; 2 had arterial thrombus and underwent surgical thrombectomy.
Of the paediatric population, 63/70 (90%) had an US. 2/63 (3%) of cases had abnormal graft perfusion and were immediately returned to theatre.
Case 1: large renal artery thrombus was identified requiring thrombectomy and re-implantation.
Case 2: minimal intra-renal blood flow which improved following exploration and repositioning of the graft.
All of the patients with positive operative findings had native UO and so malperfusion was occult. All left hospital with a functioning graft.
Conclusion: Early postoperative US identified perfusion problems in 2% of adult and 3% of paediatric live donor renal transplants allowing immediate graft saving intervention. We recommend immediate post-op US as a non-invasive potentially graft saving procedure in all live renal transplant recipients.

RO-203 DISLIPIDEMIA IN KIDNEY TRANSPLANT RECIPIENTS: PREVALENCE IN A NATIONAL COHORT AND THE EFFECT ON GRAFT FUNCTION

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Background: Dislipidemia is a risk factor for cardiovascular disease and allegedly for long-term kidney graft dysfunction. Little information exists regarding prevalence and treatment of dislipidemia in kidney transplant recipients. This historic cohort study aimed to assess the prevalence of dislipidemia in a national cohort of kidney transplant recipients and to analyze whether dislipidemia influences the kidney graft function.
Methods: At the beginning of 2011, 574 patients represented the Slovenian national cohort of kidney transplant recipients with a functioning graft. Lipid data (total serum cholesterol, LDL, HDL, and triglicerides) and serum creatinine were collected for 561 recipients in the period between 1.1.2009 and 1.1.2011. A geometric mean for the last three values of each of these entities was calculated. Geometric mean values of all patients were averaged and presented as mean ($\pm$standard deviation) and median (minimal-maximal) values. Geometric means of cholesterols were correlated with serum creatinine.
Results: The average total cholesterol was 5.1 ($\pm$0.9) mmol/l, median 5.0 (2.9-9.3) mmol/l, LDL 2.9 ($\pm$0.7) mmol/l, median 2.9 (1.4-7.2) mmol/l, HDL 1.4 ($\pm$0.4) mmol/l, median 1.3 (0.7-3.5) mmol/l, and the average triglyceride value was 1.7 ($\pm$0.8) mmol/l, median 1.5 (0.5-7.1) mmol/l. A total of 410 recipients (73.1%) had total cholesterol $\geq$4.5 mmol/l, 411 (73.3%) had LDL $\geq$2.5 mmol/l, and 315 recipients (56.1%) were treated with a statin. The average serum creatinine was 116.8$\pm$54.8 mmol/l. There were no significant correlations between serum creatinine and total cholesterol, LDL, HDL, and triglicerides (r = -0.01, 0.01, -0.18, and 0.10, respectively).
Conclusions: In our national cohort of kidney transplant recipients, approximately 75% of the patients have dislipidemia. Dislipidemia, however, was not associated with kidney graft function. Lipid profile will have to be optimized for lowering cardiovascular risk.

RO-204 PROTEINURIA IN KIDNEY TRANSPLANT RECIPIENTS: PREVALENCE IN A NATIONAL COHORT AND STUDY DESIGN OF THE EFFECT OF PARICALCITOL FOR REDUCTION OF PROTEINURIA

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Introduction: Kidney transplant recipients with proteinuria are at high risk for further progressive graft dysfunction. Treatments that decrease proteinuria have been linked with renal protection. This study aimed to assess the prevalence of proteinuria in a national cohort of kidney transplant recipients. Study design and baseline characteristics of the trial to investigate the effect of paricalcitol for reduction of proteinuria in kidney transplant recipients are presented.
Methods: Urinary protein/creatinine ratios (UPCR) were measured from three consecutive second morning void urine samples in all prevalent kidney transplant recipients at least three months post-transplant. After the screening phase, recipients with proteinuria, defined as a geometric mean of UPCR $>$200 mg/g ($>$22 mg/mmol), estimated glomerular filtration rate (eGFR) $>$15 ml/min/1.73 m2, serum calcium $<$2.6 mmol/l, and intact parathyroid hormone (iPTH) $>$35 pg/ml were candidates for entering the treatment phase. Randomization in this double-blind trial is equal allocation to paricalcitol 2 μg/day, or placebo. The primary endpoint is the percentage change in UPCR form baseline to last measurement during 24 weeks of treatment.
Results: Proteinuria was present in 190 out of 572 recipients (33.2%). Baseline characteristics of the 190 recipients are: 58.9% men, mean age 53$\pm$12 years, eGFR 52$\pm$20 ml/min/1.73m2, median UPCR (interquartile range) 403 mg/g (272–710 mg/g) or 44 mg/mmol (30–78 mg/mmol), serum calcium 2.33$\pm$0.14 mmol/l, and median iPTH (interquartile range) 83 pg/ml (51–156 pg/ml). A total of 96 recipients (50.5%) were treated with renin-angiotensin-aldosterone system inhibitors.
Conclusion: In a national cohort of kidney transplant recipients at least three months post-transplant, approximately one third of the patients have proteinuria. This trial will be the first clinical test of the hypothesis that paricalcitol safely lowers proteinuria after kidney transplantation.

RO-205 CHRONIC RENAL REJECTION: THE POSSIBLE ROLE OF VEGF, TGFβ-1 AND POST-TRANSPLANT HLA ALLOANTIBODIES

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In contrast to acute reactions, characterized by vascular changes, fibrosis typically results from chronic inflammation and in subset is associated with anti-HLA antibodies correlated to bad long-term survival. Following tissue injury activated leukocytes secrete profibrotic cytokine, transforming growth factor beta-1 (TGFβ-1). A cross-sectional analysis humoral immunity and cytokines renal allograft recipients with or without deteriorating function was performed. The prospective study of possible risk factors for CR is based on 6, 73, and 7 years (form 1-19 years).
Methods: Enzyme-linked immunosorbent assay (ELISA) of VEGF and TGFβ-1 are used to quantify endothelial activation, comparing the relationships between released cytokines in sera of 48 kidney recipient, before and after transplantation (at least ≥1yera). Recipients were dividing in four groups; 1) PRA neg. (-) class I, II (12), 2) PRA pos. (+) class I, (12) 3) PRA pos. (+) class II, (12) 4) PRA pos. (+) class I, II (12). For statistical difference Cox and logistic regression was used.P values are two sided and considered statistically significant if less than 0.05.
Results: Allogeneic stimulation of host cells is activated with secreting of cytokines which up regulate VEGF and TGFβ-1. In group 3) PRA neg. (-) class I, pos. (+) class II, were statistically higher level both molecules but specially TGFβ-1 (P≤ 0, 05) opposite to other groups. Anti-HLA I antibodies induce increase VEGF production but not statistically significant. Between patients CR (+) and CR (-) control P=0.032.
Conclusion: The results demonstrate that tested cytokines released in circulation could be indication for incoming chronic rejection. Cytokines in combination, especially with class II abs is mirror of the surface expression on EC and final results is fibrosis. Repeated biomarkers sampling reflect actual disease processes, instead of measurement errors or other incidental variations.

RO-206 TRANSITION OF ADOLESCENT RENAL TRANSPLANT RECIPIENTS TO ADULT NEPHROLOGY UNITS

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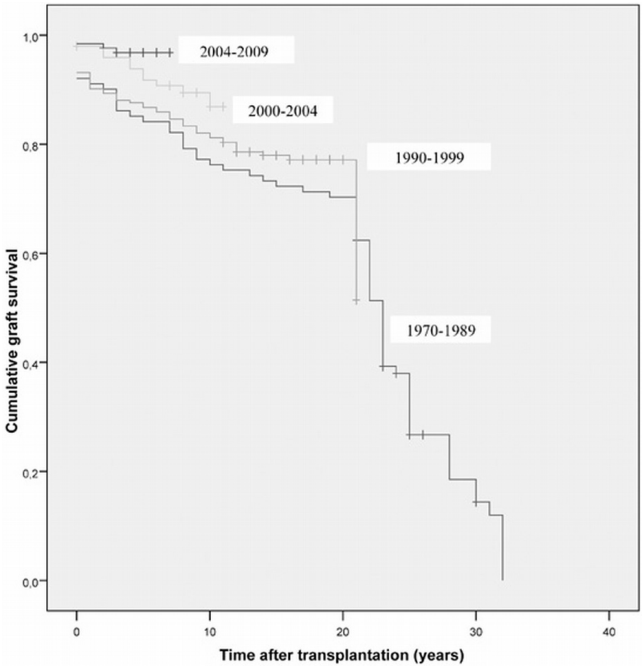
Background: The literature states that 30% of renal allografts are lost when patients are transferred to adult nephrology units.
Aim: To report the patients and renal allograft survival in paediatric renal transplant recipients when they are transferred into the care adult nephrology units.
Methods: Retrospective review of the patient and renal allograft survival and influencing factors in the 496 children transplanted between 1973 and 2008 and the 159 transferred into adults at Great Ormond Street and Royal Free Hospitals, with a minimum of one year follow-up.



Results: 496 children had received a total of 579 transplants; 172 were living-related donations. The median age at transplantation was 12.34 (range 2-17) years. 63 children required a second and 10 a third transplant before transfer to an adult unit. 101 transplant patients are currently under paediatric follow-up. 159 patients have been transferred to adult nephrology units. The median age when they were transferred was 17.43 (range 16-19) years. 64.2 percent had congenital structural abnormalities of the urinary tract.
The outcome for successful transplantation is improving in the last decade as shown in the figure.
The overall patient and renal allograft were 97.5% and 86.5% at follow up of 5-266 (medium 84.34±53.87) months after transfer to adult nephrology unit.
Conclusions: The outcome for successful transplantation is improving in the last decade.
We note that 13: 5% (21.4) renal allografts were lost and the overall patient and renal allograft were 97.5% and 86.5% after transferred to adult nephrology unit.

RO-207 REMOTE ISCHEMIC CONDITIONING IN A PORCINE KIDNEY TRANSPLANTATION MODEL – POSITIVE IMPACT ON GFR AND RENAL BLOOD PERFUSION

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Delayed graft function occurs in 20-30% of kidney transplantations using brain dead donors. Remote ischemic conditioning (rIC) involves brief, repetitive, non-damaging ischemia in distant tissue prior to ischemia in the target organ. rIC is hypothesized to induce systemic protection against ischemia/reperfusion injuries. Using a porcine kidney transplantation model we investigated the effects of rIC on early glomerular filtration rate (GFR) and intrarenal blood perfusion.
Method: Brain death was induced in donor pigs (65 kg, n=8) and kidneys were removed and kept by cold storage until transplantation. Recipient pigs had native kidneys removed and were randomized to rIC (15 kg, n=8) or non-rIC (15 kg, n=8) with one kidney from the same donor in each group. rIC consisted of 4×5 minutes clamping of abdominal aorta separated by 5 minutes periods of free flow.
GFR was determined with constant ^{51}Cr-EDTA infusion and collection of blood and urine samples. Cortical and medullary renal blood flow were measured by MRI scanning technique.
The data were analyzed using a repeated measurement ANOVA.
Results: Mean GFR was significantly higher in the rIC group than in the non-rIC group (3.7 ml/min, 95%-CI: 0.3 - 7.2 ml/min, p=0.0379). Mean renal blood flow in both cortex and medulla was significantly higher in the rIC group compared to the non-rIC group (medulla p=0.0467, cortex p=0.0006).
Findings and conclusion: In this experimental model of high risk of delayed graft function, rIC improved GFR and renal blood flow just after graft reperfusion and the effect lasted the full 10 h observation period. Even small improvements in GFR may avoid dialysis after kidney transplantation, and a potential long term beneficial effect of rIC on graft survival should be studied.

RO-208 SIROLIMUS IN RENAL TRANSPLANT: ANALYSIS OF SAFETY AND EFFICACY IN A CONVERTION GROUP

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Background: Immunosuppresion conversion to Sirolimus (SRL)-based immunosuppression in renal transplants is an alternative for chronic allograft dysfunction (CAD), cancer and viral infections. In order to analyze the indications, safety and efficacy of SRL converting protocol in a group of renal transplant patients, a retrospective study was performed.
Methods/Materials: Medical records from renal transplant recipients older than 18 years that had the immunosuppressive regimen converted to SRL-based were selected, and data collected include: indication for conversion, transplant/conversion time (TCT), serum creatinine and protein/creatinine ratio (at the conversion and 6 months after), death, graft loss and indication for SRL withdrawal.
Results: From 1821 renal transplants performed between January/1984 and

February/2011, in 112 (6%) immunosuppressive regimen was changed to SRL. Indications for conversion were infection (n=32 – fungal, polyomavirus or CMV), chronic allograft dysfunction (CAD, n=30), cancer (n=21), rejection (n=3) and others (n=26). The mean time from transplant to conversion was 41±57 (0-273) months, later in cancer. Nineteen grafts were lost (graft survival of 88% e 80%, 1 and 3 years after conversion, respectively), and 6 patients died during follow up. In remaining 87 patients with functioning graft, protein/creatinine ratio increased from 0.28±0.3 (conversion) to 0.63±0.09 (after 6 months) (p<0,001), while renal function improved (serum creatinine 2.24±0.13 mg/dL (conversion) *vs.* 1.89±0.75 mg/dL (6 months), p<0,001). SRL was discontinued in nine patients due to adverse events, such as edema, proteinuria, mucositis and pneumonitis.

Sirolimus in functioning graft

Functioning graft	Infection (n=22)	Cancer (n=19)	Imunological (n=3)	CAD (n=21)	Others (n=22)
Proteinuria conv	0.20±0.19	0.25±0.35	0.16±0.07	0.40±0.36	0.32±0.35
Proteinuria 6m	0.45±0.51	0.53±0.91	0.71±0.74	0.77±0.86	0.67±1.02
Creatinine conv	2.23±0.62	1.61±0.65	1.82±0.93	2.87±1.48	2.24±.1.52
Creatinine 6m	2.23±0.65	1.52±0.53	1.78±0.72	2.24±0.83	1.52±0.68
TCT(months)	15.9±12.7	114±80	28.3±27.1	24.4±34.3	27.7±47.8
Suspension SRL	2	1	0	3	3

Conclusion: In this study, conversion to SRL resulted in graft function improvement. There was a slight increase of proteinuria after conversion and SRL was well tolerated.

RO-209 RIGHT-SIDED VERSUS LEFT-SIDED LAPAROSCOPIC DONOR NEPHRECTOMY: EQUIVALENT IN SAFETY AND EFFICACY

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Introduction: Laparoscopic donor nephrectomy (LDN) is accepted as a standard method of living donor nephrectomy. Left sided LDN (L-LDN) is preferred to right sided LDN (R-LDN) due to longer length of the left renal vein. The purpose of this study was to establish the safety and efficacy of R-LDN at a single transplant centre.
Methods: Laparoscopic nephrectomies performed from December 2004 to October 2010 were analysed using a prospectively maintained database. The decision on laterality was based on renal anatomy and split renal function determined by CT-angiography and DMSA renography. R-LDN was compared with L-LDN for donor and recipient outcome measures.
Results: 167 LDN were performed comprising of 65 (39%) R-LDN (group 1) and 102 (61%) L-LDN (group 2). The groups were matched for age, gender, BMI, pre-operative creatinine and GFR.
Peri- and postoperative complications occurred in 3 (5%) and 6 (6%) patients of group 1 and 2 respectively. Two cases in group one required open conversion and one case in group 2. Blood transfusion was necessary for two patients in group 1 and for one patient in group 2. None of the patients required re-operation.
There was no significant difference between R-LDN and L-LDN in terms of initial warm ischaemic time (mean 3:36 vs 4:09 min, p=0.099), operation time (215 vs 221 min), inpatient stay (3.7 vs 3.3 days, p=0.13) or 6-week postoperative creatinine (118 vs 117, p=0.70).
When compared for recipient outcome, there was no significant difference between the two groups in 6 months postoperative creatinine (138 vs 131, p=0.44), incidence of rejection or graft failure at one year.
Conclusion: In our experience R-LDN is equivalent to L-LDN in donor safety and outcome, and does not affect recipient outcome measures. R-LDN should be offered routinely when pre-operative imaging demonstrates that the right kidney is the preferred donor organ.

RO-210 EXPANDED CRITERIA DONORS (ECD) – IS IT THE TIME TO CHANGE THE CRITERIA

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Background: The study presents the outcome of ECD renal grafts which were transplanted over a 5 year period (2004-2008) in our centre and their comparison with one year transplants from standard (deceased) donors (2008-2009).
Methods: 57 ECD transplants included fit into following criteria: Donor age > 60 years, or age between 50 and 60 years plus one or more associated risk factors, Serum Creatinine >132 mmol/L and/or hypertension and/or cause of death was Cerebrovascular accident. The outcome measures were delayed graft function (DGF), rejection/s and 1 and 5 year graft survival. SPSS 15.0 was used for statistical analysis.
Results: In ECD group: Mean donor age was 61±7 years. There were 8 donors with serum creatinine >132 mmol/L (mean 156±30 mmol/L) before retrieval. 60% (n=34/57) donors were hypertensive. The cause of death was Subaracnoid haemorrhage in 56% (n=32/57) and Intracranial haemorrhage in 44% (n=25/57) donors. Mean cold ischaemia time was 14±3 hours and warm ischaemia time 30±4 minutes. The incidence of DGF was 44% (n=25/57) and biopsy proven rejection 28% (n=16). Overall 1 and 5 year graft survival was 91% (CI 95% 90-92) and 88% (CI 95% 86-90) respectively (Figure 1). There were seven deaths (12%), none within one year after transplant. 4 patients died due to myocardial infarction, one with infective endocarditis and two because of septicaemia. In standard group (n=44): 1 year graft survival was 93% (CI 95% 91-94, p=NS, Figure 2) and DGF 27% (p=0.001).

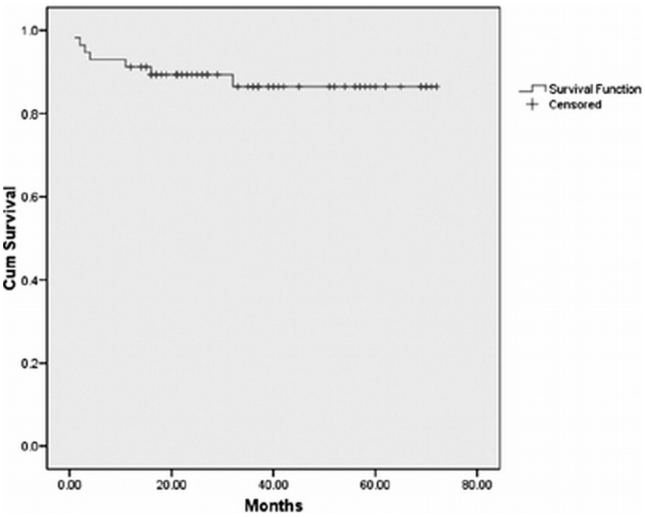

Figure 1. Graft survival in ECD group.

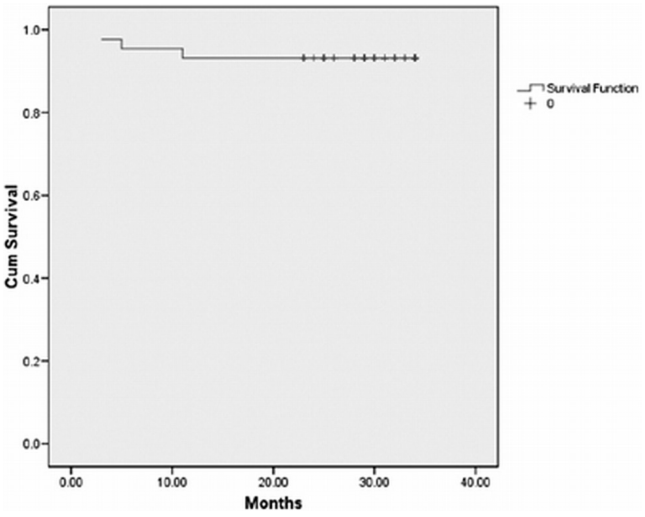

Figure 2. Graft survival in standard group.

Conclusion: ECD are a reliable source of deceased donor renal grafts with satisfactory 1 and 5 year survival but relatively higher incidence of DGF. It may be the time to revisit the traditional definitions/criteria of ECD in order to expand the donor pool.

RO-211 EFFECT OF STATINS ON RECURRENCE OF IgA NEPHROPATHY AND GRAFT LOSS

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Background: Recurrence of IgA nephropathy (IgAN) after renal transplanta-

tion is common and there is no documented preventive treatment. This retrospective study evaluated the effect of general medical treatment on rate of recurrence of IgAN and graft loss.
Methods/Materials: Data from patients having received a renal transplant due to IgAN was collected from the transplantation registries at the University Hospital of Uppsala, Sweden and at the Oslo University Hospital, Rikshospitalet, Norway.
Results: Of 4976 transplantations 402 (8.1%) were due to IgAN and 373 were included in the analyses. The median follow-up time was 60 months (range 12-288 months). Biopsy verified recurrence of IgAN was diagnosed in 59 transplants (15.8%). Death censored graft loss due to recurrence was seen in 29 transplants (7.8%). Death censored graft loss for any reason was seen in 71 transplants (19.0%).
Recurrence was seen in 14% of transplants among patients on statins compared with 19% of transplants among patients without statin treatment. The median time to recurrence was >180 months vs 148 months; hazard ratio 0.61, p=0.08. Also median time to death censored graft loss (any reason) was longer in patients using statins: 182 months vs 129 months; hazard ratio: 0.33, p<0.0001. 12% of transplants resulted in graft loss among patients on statins compared with 24% among patients without statin treatment.
A multiple Cox-regression analysis on time to IgAN recurrence showed that use of ACE inhibitor/ARB and use of statins were independent risk factors. Similar analysis of time to graft loss (any cause) showed that time from diagnosis to first transplantation, use of statin and serum creatinine after one year were independent determinants.
Conclusion: Use of ACE/ARBs and statins were associated with recurrence and statins also with graft loss in kidney transplant recipients with IgAN.

Islet / cell transplantation

RO-212 PREOPERATIVE CARDIAC EVALUATION IN LIVER TRANSPLANT (OLT) CANDIDATES: LESS IS ENOUGH!

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In OLT candidates, CAD rates vary (3–27%.) At our institution, preOLT cardiac evaluation includes clinical history (METs and RCRI), EKG, TT echocardiogram and, with 1 major/2 minor risk factors, Stress Myocardial Perfusion Scanning (SMPS) test. Coronary angiography (SCA) is performed in patients with positive SMPS and known CAD.
Methods: We retrospectively studied 93 consecutives cirrhotic candidates to OLT to assess the incidence of CAD and to evaluate the appropriateness of our screening approach.
Results: 68 were males, 25 females (MELD score < 19 in 64 pts; >19 in 14; >25 in 15 pts). Median age was 52 y. RCRI score was ≥ 3 in 4 pts. Median EF was 60%. Diabetes mellitus was present in 20%, arterial hypertension in 16%, known CAD in 3 pts (3.2%), no new cases were diagnosed. All the 93 candidates underwent OLT: 1 year mortality rate was 7%. 60 candidates (65%) underwent SMPS (85% due to 2 minor criteria, one being age > 50): positive SMPS test was present in 3 pts (all falsely positive according to SCA, performed in 7 pts and not providing further relevant information). In 4/7 SCA cases, CT coronary artery calcium score (CAC) was also performed (3 negative; 1 inconclusive with negative SCA). No CAD related perioperative death was recorded and no acute coronary event occurred in 1 y FU.
Conclusions: SMPS has to be reserved to asymptomatic pts at high risk (diabetes, renal dysfunction/failure, pts with RCRi >2). In this series, SMPS could have been used in <30% of the pts without increased risks or prognostic disadvantages but with significant cost containment and pts exposure. CAC needs further studies.

RO-213 LIVER TRANSPLANTATION IN PATIENTS WITH PREVIOUS NON-HODGKIN LYMPHOMA: REPORT OF A SINGLE CENTRE EXPERIENCE

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Introduction: The published relative risk to develop a non-Hodgkin lymphoma (NHL) among HCV and HBV positive population is 2.5. Moreover, HCV account for more than 60% of OLT indication.
Materials and methods: Between 1997 and 2009, we transplanted 6 patients with previous NHL. Indication was HCV cirrhosis in 2, hepatocarcinoma on HCV cirrhosis in 3, HBV cirrhosis in 1. Two of them had accidental diagnosis during OLT (one hepatic lesion, one mesenteric lymph node; in both cases the histology showed low grade NHL). Four patients undergoing OLT after a careful evaluation of NHL low recurrence risk (2 cases of complete relapse after therapy, 2 cases of low grade disease activity).
Results: Two patients are alive. Of them, one, who had former low grade NHL and a gastric MALToma, experienced NHL recurrence (time to recurrence 149 days), controlled with Rituximab, and a chronic rejection leading to re-OLT after 241 days. Thereafter the patient undergoes an early HCV recurrence (50 days). The 2nd patient, who had former incidental LHN low-grade stage I, developed a de novo lung tumor after 3487 days.
Four patients died: Median survival time was 345 days (min 215, max 1210 days). In all cases death was due to a relatively early and aggressive HCV recurrence (median to recurrence of 87.5 days, range 50-444).
Conclusions: Coexistence of disorders as NHL in HCV/HBV cirrhotic patients is a fact. As the reported rate of NHL recurrence is relatively low (5.9% in OLT, 10% in kidney-transplant, 6-50% in general population), a careful candidates selection and an aimed immunosuppression can provide a survival not affected by NHL. Nevertheless, HCV recurrence seems to worsen in this group of patients.

RO-214 LIVER TRANSPLANTATION AFTER RADIOEMBOLIZATION FOR HEPATIC METASTASES OF A PANCREATIC NEUROENDOCRINE TUMOR

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Background: The most common metastatic site of neuroendocrine tumors (NET) is the liver. Since the primary frequently eludes for years, liver metastases are often extensive upon diagnosis.
Methods: We here report on a rare treatment approach in a 54-year-old female patient with a pancreatic NET and synchronous liver metastases.
Results: Diagnosis was made by Gallium 68-Dotatoc-PET/CT scan, demonstrating a NET primary in the pancreatic tail and multiple liver metastases. At first the patient underwent left pancreatectomy, lymphadenectomy and splenectomy. Histopathological assessment revealed pT2 pN1 G1 L0 V0 R0, Ki67: 3%. After discussion in our interdisciplinary tumor board, the patient was evaluated for liver transplantation (LT) and scheduled for bridging treatment with radioembolization. Two months after initial surgery radioembolization with Yttrium 90-microspheres was performed. Two months after bridging treatment the patient underwent LT and lymphadenectomy of the liver hilum. Histopathological assessment revealed extended tumor sclerosis and necrosis (G1, pN1 (2/3)). Glass microspheres were detected within the tumor as well as within the lymph nodes. The postoperative course was uneventful and the patient was discharged on postoperative day 14 on immunosuppression consisting of tacrolimus and prednisone. A PET/CT scan three months after LT did not reveal any tumor reccurrence.
Conclusion: This is the first report detecting glass microspheres not only in the tumor itself but also in the explanted lymph nodes. New therapeutical issues may be raised.

RO-215 REGENERATION OF CAUDATE LOBE IN EXTENDED LEFT LOBE GRAFT INCLUDING CAUDATE LOBE AFTER LIVING DONOR LIVER TRANSPLANTATION

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Background and Aim: An extended left lobe graft including a caudate lobe is known to be a useful method for increasing the graft volume in living donor liver transplantation (LDLT). Reconstruction of short hepatic vein remains to be controversial. The aim of this study is to clarify regeneration of caudate lobe in case of no reconstruction of short hepatic veins after LDLT.
Methods: Eleven extended left lobe grafts with a caudate lobe were included in this study. Neither short hepatic vein was reconstructed. Graft volumetry of both the transplanted caudate lobe and other segments (segments II-IV) were done before LDLT and 1 month and 6 months after LDLT, using SYNAPSE VINCENT (FUJIFILM Corp., Japan)
Results: The addition of the caudate lobe increased the graft volume by 28±5 ml, corresponding to a 2.5% increase in graft volume/standard liver volume ratio. Three cases showed 10% or more of volume decrease of the caudate lobe after LDLT, and their preoperative volumes were all over 30 ml in volume. The median regeneration rate of other 8 cases 1 month and 6 months after LDLT were 39%, and 35%, respectively. On the other hand, those of other segments in the left lobe graft 1 month and 6 months after LDLT were 120% and 178%, respectively.
Conclusions: These data suggest that regeneration of caudate lobe differed

from other segments in the extended left lobe graft, and that reconstruction of short hepatic vein may be taken into consideration in case of over 30ml of preoperative caudate lobe volume.

RO-216 RESULTS OF LONG-TERM FOLLOW-UP INCLUDING PROTOCOL BIOPSY OF THE FIRST 500 LIVER TRANSPLANT RECIPIENTS IN IKEM PRAGUE

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Background: Since 1995 till 2005, 500 liver transplantation were performed in 476 patients at the Institute of Clinical and Experimental Medicine, Prague. The most common indications were alcoholic liver cirrhosis (23%), hepatitis C cirrhosis (17%), and cholestatic cirrhosis (PBC and PSC, 9% each). Ten-years patient survival was 79,1%, graft survival 74,1% respectively. Best survival was achieved among patients with autoimmune diseases, the worst in alcoholic cirrhosis. Malignancies were the most common cause of death during the follow-up (17 patients).
Material and methods: Patients were followed longitudinally at the institution according to prospective protocol including liver biopsies.
Results: Hypertension (71% of recipients), and overweight or obesity (56,3%), were the most prevalent medical complications among long-term survivors. Diabetes was found in 28,6%, of which 14,7% was de-nove after transplantation. Renal insufficiency (s-creatinin > 150 umol/l) was present in 61 of 348 (17,6%) survivors. Out of these, 16 needed chronic hemodialysis, and 12 underwent kidney transplantation subsequently.
Protocol biopsy at 5 years after transplantation was evaluated. Normal liver was found in 4% of recipients, minor non-specific changes in 36% of them. Disease recurrence was present in all of 16 recipients transplanted for HCV cirrhosis, in one third of them graft cirrhosis was already present. Disease recurrence was found in patients transplanted for autoimmune disease frequently, PBC in 40%, PSC in 25%, and autoimmune hepatitis in 60% of recipients. Graft steatosis greater than 33% was present in 13% of recipients.
Conclusions: Liver transplantation is highly effective method of treatment of end stage liver disease. Despite frequent medical complications, and disease recurrence on histological examination almost 80% of recipients transplanted in the liver transplantation program in IKEM survived more than 10 years after procedure.

RO-217 IMPACT OF VASCULAR COMPLICATIONS IN LIVER TRANSPLANTATION: A COHORT STUDY

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Background: Vascular complications after liver transplantation are the most common cause of graft loss. The aim of this study is to evaluate the incidence of these complications and to determine its effect on survival and development of further complications.
Materials and Methods: Historical cohort study, prospective database of liver transplant program since its inception in 1994 until 2010 was reviewed. We included all transplants in adult recipients. Variables of the donor, graft surgery and receptor were recorded. We performed univariate and multivariate analysis to determine factors associated with vascular complications. We performed a Kaplan-Meier analysis to determine the effect of vascular complications in graft survival after transplantation.
Results: The study series comprises 114 transplants in 110 patients. The median follow-up was 45 months (IQR 26-61). Eleven patients (9.6%) had a complication of hepatic artery (thrombosis 7.9%, stenosis 0.9%, posterior segments branch injury 0.9%). Portal vein complications occurred in 7.9% of patients (thrombosis 5.3% and stenosis 2.6%). One year graft survival was significantly lower in patients with portal complications than without it (44% vs 78%, p = 0.027). Graft survival was similar in patients with and without arterial complications (73% vs 75%). In multivariate analysis, patients undergoing retransplantation had significantly higher risk of developing arterial complications (OR 11.7, p = 0.039). The only variable associated with portal complication was a female donor (OR 14.9, p = 0.002). Patients with complications of hepatic artery developed significantly more biliary complications (73% vs 27%), OR 4.2, p = 0.05.
Conclusion: Portal vein complications significantly reduced graft survival. Liver retransplantation was independently associated with development of arterial complications and these patients had significantly more biliary complications.

RO-218 LOW INCIDENCE OF HEPATIC ARTERY THROMBOSIS IN ORTHOTOPIC LIVER TRANSPLANTATION: TECHNICAL TRICKS IN A 16-YEARS EXPERIENCE OF A SINGLE TRANSPLANT CENTRE

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Background: Hepatic artery thrombosis (HAT) is the worst complication after liver transplantation, potentially leading to graft loss.
Patients and methods: Data of 280 OLT were reviewed retrospectively to report a single centre experience. Among the surgical factors considered to be associated with HAT, arterial reconstruction skill can be considered the most important.
After cavo-caval and portal anastomosis, the liver is reperfused and rotated to the right in the hypochondriac region. The artery of the recipient is prepared down to the splenic artery emergency and both the common trunk and the gastroduodenal artery are clamped.
The celiac trunk of the graft is placed upwards, the splenic artery being thorn straight up. This position re-establishes the more physiological angle of the celiac trunk when the liver is finally in its definitive position. The anastomosis is the performed termino-laterally by a continous running suture bothsides 6-0 Prolene.
Results: 4 patients (4/280=1.4%) with HAT were identified. Two patients underwent emergency Re OLT due to Early-HAT (1 died, 1 alive). Two patients with a Late-HAT are currently asymptomatic.
Conclusions: The literature reports HAT incidence ranging from 1.9% up to 9.2%. Our low figures are the results of a standardization, easy and wide of this surgical procedure. This technique, based on a meticulous array of the anastomotic rhymes, prevents twisting of the vascular-axis eventually responsible for a turbulent flow.

RO-219 LIVER TRANSPLANTATION IN PATIENTS OVER 60 YEARS OLD: 6 YEAR FOLLOW-UP EXPERIENCE

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Introduccion: Some Series have reported similar results inortohotopic liver transplantation (OLT), independtly of recipient age, even taking into account sexagenarian liver recipients. At present time, due to donor scarcity and increasing mortality in waiting list, indications of OLT for patients older than 60 years is controversial.
Patients and Methods: Between April 1996 and December 2004 we performed 650 OLT. We select a sample of 353 patients who underwent OLT that was divided in 2 groups according to recipient age: a group A (cases) with 127 patients older than 60 years old and a group B (controls) with 226 patients younger than 60 years old.
Results: Mean recipient age was 63,48+2,8 years (range 60-74) in group A, and 45,57+10,2 years (range 15-59) in group B (p=0,00). The gender was 80 males and 47 females in group A versus 152 males and 74 females in group B. The etiology was in group A: HCV cirrhosis 51,2% and alcoholic cirrhosis 29,6%, whereas it was in group B: HCV cirrhosis 22,1% and alcoholic cirrhosis 29,6% (p=0,02). Acure rejection rate was in group A 40,8% versus group B 39,6% (p=ns). Chronic rejection rate was in group A 11,3% versus group B 8%. Actuarial patient survival at 1, 3, 5 and 10 years were: group A 79,5%, 70,1%, 63% and 46,7% versus group B 84,1%, 78,3%, 71,2% and 60,1% respectively (p=0,009). Actuarial graft survival at 1, 3, 5 and 10 years were 79,5%, 70,1%, 62% and 30,5% versus group B 83,1%, 78%, 66,3% and 40,5% respectively (p=0,013).
Conclusion: Either we have differences, in the short and long time outcomes, we have to be cautious because there are important differences in the grafts we implant in both group.

RO-220 THE PROGNOSTIC VALUE OF THE MELD SCORE

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Introduccion: Ideal system for distributing organs don't exist. Most of trans-

plantation groups use clinical and biological classifications such as the MELD score for optimizing the time for transplantation. This score considres only objective parameters and it is alo used by some groups for giving priority in relation to severity of the disease among patients in the waiting list.
Methods: Between January 2003 and December 2010, 608 liver transplantations were performed. We excluded children, retransplantation, and OLT for hepatocarcinoma. A sample of 407 liver transplantation ramained after exclusion criteria.
Results: Mean age was 52,5+ 12,13 years (RANGO) with a ratio male:female of 3:1. Mean MELD score was 16,5+ 6 (RANGO). The most frequent indications of OLT were: HCV cirrhosis 42,9% (NUMERO DE PACIENTES), alcoholic cirrhosis 28,8% (NUMERO DE PACIENTES). Liver grafts were considered suboptimal in 22,1% cases. Increase of MELD score was associated with significantly higher transfusion of hemoderivates (red blood cells concentrates (p=0,026), fresh frozen plasma (p=0,043), platelets (p=0,00) and fibrinogen (p=0,007)); and also with significantly higher hospital stay (p=0,001). Relation of MELD score with overall patient survival was significant too (p=0,000).
Conclusion: MELD score has proven to be a good parameter for estimating hospital stay, long survival and the neccesity of intraoperative hemoderivates transfusion.

RO-221 FEASIBILITY EVALUATION OF SUBCUTANEOUS ADMINISTRATION OF IMMUNOGLOBULIN FOR POST LIVER TRANSPLANT HBV RECURRENCE PROPHYLAXIS

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Background: The HBIG prophilaxis modifies Quality of Life due to necessity to go in hospital, in the case of the endovenous administration or for the necessity of someone that injects the drug and the pain, in the case of the intramuscular administration. HBIG for subcutaneous administration (SCHBIG) introduce the concept of home and self treatment that could decrease the impact on patients quality of life independently of their social or cultural background.
Methods: 20 patients in prophylaxis anti HBV were included in the analysis. Socio-cultural features were diversified and were recorded. Before first administration, patients have been informed about the right way to self inject. The first 5 weekly injections have been done under the control of a medical tutor that recorded the time to perform them. Patients over than 75kg need 2 vials, those under 75 only one.
Findings: For the 12 patients injecting twice, the time for the procedure at the first week was 9 minutes and 6 at the fifth week, that means a reduction of 33% of the time required for the procedure in just one month. For the other 8 that injecting a single dose weekly, the reduction was of 40%, from 5 minutes at the first injection to 3 minutes at the end of the observation. According to those results the tutoring was suspended and the patients started the self-therapy at home.
Conclusions: Let patients self-manage therapy with SCHBIG, increases awareness of their active role after OLT and adherence to all prescribed therapies. Be independent of someone who injects, is not something to underestimate: SCHBIG could increase the awareness that liver transplanted patients are the main drivers of their recovery, of their health, of their quality of life.

Paediatric transplantation

RO-222 THE IMPACT OF LIVER TRANSPLANTATION DURING CHILDHOOD ON THE COURSE OF LIFE AND TRANSITION INTO ADULTHOOD

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Background: In general, the course of life of adolescents and young adults having grown up with a chronic disease is delayed. Gaining insight into the course of life and factors associated with a delay in course of life is important, since impediment in the course of life during childhood may affect participation in social and professional activities in adulthood. The aim of this study is to examine the course of life of young adults who underwent a liver transplantation in childhood by comparing their course of life to healthy peers and to investigate factors possibly related to course of life.
Methods: A total of 39 young adults (response 59%) who underwent a liver transplantation in their childhood at the University Medical Center Groningen completed the Course of Life Questionnaire which assesses the achievement of developmental milestones (autonomy, psycho-sexual, social and anti-social development) and risk behavior (substance use and gambling).
Results: Young adults who underwent liver transplantation in their childhood, reported having achieved fewer milestones with regard to autonomy, psychosexual and social development, compared to healthy peers. However, they reported less risk behavior. In young men, differences with the comparison group were found in autonomy and psychosexual development, and in risk behavior. In women, differences with the comparison group did not reach significance. Age at time of study and of transplantation, nor time since transplantation significantly correlated with any of the course of life subscales. Young adults who had undergone re-transplantation(s) reported a delay in psycho-sexual development as compared to their peers in the comparison group.
Conclusions: Young men who underwent liver transplantation in their childhood achieved fewer milestones compared to healthy peers during the transition into adulthood. In addition, those who received a re-transplantation are prone to psychosexual developmental delay.

RO-223 METABOLIC AND CARDIOVASCULAR RISKS AFTER PEDIATRIC LIVER TRANSPLANTATION

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More than 500 pediatric liver transplants (OLT) have been performed in our hospital since the begining of the program.
Aims: Assess prevalence of cardiovascular and metabolic risks in pediatric OLT patiens (p).
Methods and Patients: Descriptive study with OLT p performed at Hospital of Pediatrics J. P. Garrahan with more than a year of follow up during the period 2008-09.
Statistical Analysis: SPSS program Poll statistic: continuous variables were described using mean, standard deviations (SD). Analysis of differences t-test.
Results: 133 pediatric liver transplant (OLT)p were studied for cardiovascular and metabolics risks after OLT.Mean age at study 12.8±4.4 (SD) years, mean age at transplant 5.2±4.2 (SD)years. Mean time after transplant 7.7±3.6 (SD) years. As ims all received corticoids. At study 12 p were receiving corticosteroids, 85 cyclosporine, 27 patients FK, sirolimus 25 p and mycophenolate 71 p.Mean BMI Zscore -0.27±0.9 (SD). Mean Height Zscore 0.02±1.24 and mean weight Zscore -0.3±1.07. 6 p were stunted, 36 p low weight for height, 4 p obese, 12 p overweight. 80 p normal weight/height. The mean basal glucose 79.9 mg% ±12.8. Basal insulin 9.5 U/ml ±12.4. The homeostasis model assessment of insulin resistance index (HOMA IR) 2.14±5. Mean total cholesterol was 145 mg% ±54.8, and triglycerides 94 mg% ±43. 3% for obesity, 9% of overweight, the prevalence of impaired fasting glucose 3.9%, the prevalence of diabetes 1.6%.
Conclusions: A high prevalence of abnormal glucose metabolism 13.4%, compared with previous data from healthy children in our country of 2.5% was found.There was strong statistically significant association between alterations in glucose metabolism and insulin resistance. No association was found between the different immunosuppressive regimens.

RO-224 CHRONIC ALLOGRAFT NEPHROPATHY AND PERITUBULAR CAPILLARY C4d DEPOSITION IN PROTOCOL RENAL ALLOGRAFT BIOPSIES

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Recently, the role of humoral damage has been underlined not only in acute but also in chronic allograft rejection. During 7th Banff conference the positive staining of C4d, a degradation product of complement-factor C4, on Peritubular Capillary (PTC) was suggested as a new marker of humoral rejection. Later studies conducted on biopsies made for clinical indications showed an association between PTC-C4d positivity ($C4dPTC^+$) and a faster decline in graft function.
We analyzed the prevalence $C4dPTC^+$ on protocol biopsies performed 12 and 24 months after transplantation (Tx) presenting histological features of Chronic Allograft Nephropaty (CAN). Among 365 available biopsies, 54 biopsies with histological features of CAN, performed on 45 paediatric recipients, were evaluated. Patients m.age (M/F 30/15) was 13,62±6,3y. (range 1,8-26,2). 27 patients received an induction based on anti-CD25-Mab, while 18 received only corticosteroid pulses. Manteinance immunosuppression was based on CsA/FK506±MMF/AZA±steroids.

10/30 biopsies (33,3%) at 12 and 10/24 biopsies (41,6%) at 24 months post-Tx showed a rate of C4dPTC$^+$>10%; in 6/10 (66.6%), both at 12 and 24 months post-Tx, the positivity rate was >30%. C4dPTC$^+$ was not correlated to induction received or to maintenance therapy (CsAvsFK506, MMFvsAZA). CrClearance at 12 and 24 months post-Tx was compared among three groups: C4dPTC$^+$<10%*vs*10-30%*vs*>30%. We found no differences between the groups. Furthermore, we observed no differences comparing the CrCl at 3 and 5 years post-Tx between patients who showed C4dPTC$^+$>30% at 12 and 24 months post-Tx and the other patients. In conclusion we found a high incidence of C4dPTC$^+$; indeed, about 30% of patients showed a C4dPTC$^+$>30%. However, this find does not seem to be associated with a worse graft outcome early after transplantation. The role of C4dPTC$^+$ as a predictive marker of kidney function late after transplantation remains to be understood.

RO-225 INVOLVEMENT OF NUCLEAR RECEPTOR SXR SNPs IN CYCLOSPORINE PHARMACOKINETICS VARIABILITY DURING THE FIRST YEAR POST KIDNEY TRANSPLANTATION

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Introduction: In this study we investigated the relationships between CyA exposure and CyP3A5, MDR1 and the steroid X receptor (SXR) SNPs, to rule out any possible pharmacokinetics effect on CyA profile during the first year after kidney transplantation (kTx).
Materials and Methods: The study involved 65 pediatric kidney transplant recipients (32 females and 33 males, mean age 13.26±6.2 years). All the patients were genotyped for CYP3A5, MDR1 (C3435T, C1236T, G2677T and IVS21+49) and SXR (-200GAGAAG/- and A7635G) SNPs. CYA trough level (C0), weight normalized CyA dose (nDose) and normalized C0 (C0/nDose) were recorded at 30, 90, 180 and 360 days after kTx and compared between different genotypes.
Results: ANOVA test for repeated measures corrected for age, rejection episodes and steroid doses, didn't show any significant difference in nDose, C0 and nC0 for CYP3A5 and MDR1 polymorphisms. In patients with homozygous deletion of 6bp in SXR gene, a significantly lower CyA nDose and nC0 was observed when compared to heterozygous or wild groups ($p<0.05$).
Discussion and Conclusion
According to our observation SXR represents the only SNPs affecting CyA metabolism. Since SXR is a central regulatory mechanism of CYP3A enzymes and transport proteins like the permeability-glycoprotein, the high inter and intra-individual variability of CYA levels could be potentially related to its genetic polymorphism.

RO-226 CLINICAL AND HISTOLOGIC EFFICACY OF INTERLEUKIN 2 RECEPTOR ANTAGONISTS IN PAEDIATRIC KIDNEY TRANSPLANTATION

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Basiliximab is a non-depleting recombinant chimeric murine/human IgG1 monoclonal anti-interleukin-2 receptor antibody indicated for the prevention of acute organ rejection in renal transplant recipients.
Aim of our study was to compare two consecutive groups of paediatric kidney recipients, the first including patients with Basiliximab and corticosteroids induction, the second including recipients transplanted during the previous 4 years, who exclusively received corticosteroid pulses induction. In both groups, immunosuppression was based on CsA or FK506± MMF ± corticosteroids.
We conducted a retrospective analysis in 130 paediatric kidney recipients: 78 (60%) patients were treated with Basiliximab (recipient mean age 12.36±7.19 years, recipient gender M/F 44/34, donor mean age 15.41±8.68 years, donor gender M/F 58/17, HLA mismatches 3.64±0.96), and the others 52 (40%) received only corticosteroid pulses (recipient mean age 15.12±5.73 years, recipient gender M/F 32/20, donor mean age 13.97±10.38 years, donor gender M/F 36/12, HLA mismatches 3.14±1.06).
We observed a lower incidence of acute clinical rejections in patients who received IL-2 receptor antagonist induction (p=0.0049). Furthermore, corticosteroids withdrawal at 12 and 24 months after transplantation was possible in a larger number of patients treated with Basiliximab, compared to patients receiving only corticosteroid pulses (p=0.0015 e p=0.0001, respectively). We found no differences between the two cohorts regarding organ survival, creatinine clearance, acute or chronic subclinical lesions detected by protocol biopsies, mean corticosteroids dosage, CsA and FK506 blood through levels, statural growth at 6, 12 and 24 months after transplantation.
Our results highlight that the use of IL-2 receptor antagonists allows an early corticosteroid withdrawal and confirms a higher efficacy of Basiliximab in preventing clinical acute rejection. We found no differences in terms of prevalence of acute and chronic histological lesions at short or long term after transplantation.

RO-227 INTERVENTIONS FOR PRE-EXISTING BLADDER DYSFUNCTION IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS; WHEN IS BEST?

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Background: Lower Urinary Tract Dysfunction (LUTD) is responsible for 20% of End Stage Renal Disease (ESRD) cases in paediatric patients. It was previously believed that these children should not be offered a renal transplant. Recent surgical advances mean that bladder reconstruction or drainage may permit transplantation. It is however unclear when to intervene for LUTD. This study compares outcomes of renal transplantation in children with dysfunctional bladders, and considers when is the most appropriate timing of such interventions.
Methods: We reviewed the outcomes of children receiving a renal transplant due to LUTD at two major London hospitals between 01/2002-12/2010. Of the 75 children with LUTD 47 (62.7%) underwent intervention. Depending on clinical/urodynamic assessment they received a Mitrofanoff, augmentation, or diversion (vesicostomy/ureterostomy). Graft and patient survival, perioperative complications and follow-up serum creatinine were recorded.
Results: 65 (86.7%) children were male. Mean age at transplant was 9.2 years. Mean follow-up was 2.9 years after transplantation. 8 (17.0%) children received a Mitrofanoff only, 17 (36.2%) received Mitrofanoff plus augmentation, 4 (8.5%) received Mitrofanoff plus diversion, 13 (27.7%) received Mitrofanoff plus augmentation plus diversion and 5 (10.6%) received diversion only. 38 underwent intervention pre-transplant and 9 post-transplant, mean follow-up serum creatinine was 112.7umol/l and 87umol/l respectively.
Significant surgical perioperative complications (within 30 days) requiring intervention included 2 cases of hydronephrosis and 3 of lymphocele with 1 of these occurring in the intervention group and 4 in the non-intervention group, with 1-year graft survival rates of 97.7% and 100% respectively. There was 1 patient death.
Conclusion: Outcomes of renal transplantation in children with LUTD are excellent. There is no difference in complication rate in children who underwent intervention pre-transplant or post-transplant, and therefore timing of intervention should be based on clinical/urodynamic assessment.

RO-228 RISK OF SEVERE BACTERIAL INFECTIONS AFTER ANTI-CD20 TREATMENT IN PAEDIATRIC PATIENTS WITH IDIOPATHIC NEPHROTIC SYNDROME AND KIDNEY TRANSPLANT RECIPIENTS

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Rituximab (RTX), an anti-CD20-Mab used in B-cells lymphoma and rheumatoid arthritis, showed an increased incidence of serious bacterial infections mainly in patients with cancer. In kidney transplant (KTx) RTX is used for EBV-related-PTLD, acute humoral rejection and de-novo/recurrent glomerulonephritides. Recently it has been suggested for the treatment of idiopathic nephrotic syndrome (INS).
We analysed the incidence of bacterial infections in a 6-months-period after RTX in 25 paediatric patients: 10 KTx and 15 INS.
Tx group: m.a ge 7,8±5,5y; M/F: 9/10. Indications for RTX therapy were chronic EBV-infection 3/10, PTLD 2/10, humoral rejection 1/10, recurrent FSGS 3/10, de-novo glomerulonephritis 1/10. The median time between transplant and RTX infusion was 8m (range 0,4-60); the mean number of doses was 2.4. Ongoing immunosuppression was based on steroids + CsA/FK506±MMF.
We observed 8 severe infections in 7 patients at an average time of 60 days after RTX infusion (range 30-180): 5 pneumonias (4 bacterial, 1 P.Carinii), 1 sepsis after E.Coli pyelonephritis, 1 peritonsillar abscess, 1 St.Aureus bacteriaemia.

INS group: m. age 11±4y; M/F: 11/4; 11/15 patients had steroid-dependent and 4 steroid-resistant INS. Average time between INS onset and RTX infusion was 69m (range 8-204); mean number of infused doses was 1,5. Immunosuppression, based on steroids + CsA/FK506/MMF, was progressively reduced after RTX infusion. Two patients developed localized bacterial infections (paronychia, dental abscess) 30 days after RTX.
In KTx group we observed more frequent and serious infections than in INS group, despite a longer immunosuppressive treatment before RTX infusion (>5 years) in INS patients; moreover, 73% of INS patients were still on a double therapy 6 months after RTX. We suppose that the level rather than the duration of immunosuppression expose patients treated with RTX to a higher risk of bacterial infections.

RO-229 LUNG TRANSPLANTATION IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Background: Lung transplantation is an uncommon procedure in children. According to the registry of ISHLT in 2006 the overall number of paediatric lung transplantations worldwide was 75.
Method: From November 2002 to December 2010 we performed 11 lung transplantations in 9 children (median age 13,5 years, range 5,8 – 17,4). The indication for transplantation was cystic fibrosis in 8 children and idiopathic bronchiolitis obliterans in 1 child. Pre transplant median FEV1 was 30% (range 14%-37%). Eight patients underwent a sequential bilateral single lung transplantation (SBSLTx). Five patients received a whole size lungs; 1 a reduced size lungs; two patients received a left split lung grafts due to a donor/recipient mismatch. One patient, who have previously undergone a right pneumonectomy, received a lower left lobe for a single lung transplantation. Immunosuppression was based on basiliximab, tacrolimus, azathioprine and steroids.
Results: Median waiting time was 134 days (range 17-461). Median ischemia time was 280 minutes for the first and 405 for the second lung. Cardiopulmonary by-pass was used in all but two children. The patient who received a left lower lobe was re-transplanted on the 46th post-operative day with a reduced left lung for a primary lung dysfunction but eventually died a few hours later of pulmonary edema and hemodynamic instability. Another child developed a severe bronchiolitis obliterans syndrome with a severe hypercapnia that required ECMO support and was re-transplanted 3,2 years after first transplant. Another patient developed a severe BOS and has been listed for re-transplantation. Overall patient and graft survival at 1 and 5 years of 89%/89% and 89%/76%
Conclusion: Paediatric lung transplantation can be performed in a large volume paediatric transplant center with good results. The limited number of paediatric donor organs can be overcome by using reduced-size, lobar and split grafts.

RO-230 PHARMACOKINETICS FOR ONCE DAILY TACROLIMUS FORMULATION IN CHILDREN WITH DE NOVO KIDNEY TRANSLANTATION

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Background: Tacrolimus, a cornerstone immunosuppressant, is widely available as a twice-daily formulation (progart BID). A once-daily prolonged-release formulation (Advagraf QD) has been developed that may improve adherence and impart long-lasting graft protection.
Tacrolimus has a narrow therapeutic index and its oral bioavailability is highly variable between individuals. Systemic exposure to tacrolimus (area under the curve, AUC) is a significant efficacy variable especial in children.
Tacrolimus pharmacokinetics (PK) have been compared between Advagraf QD and prograf BID in adult stable kidney. However, the PK in children of Advagraf QD in newly transplanted kidney recipients has not been previously investigated.
This study compared the PK of Tacrolimus in de novo kidney transplant pediatric patients treated with Advagraf QD or prograf BID.
Methods: A single 0.2 mg/kg/Day dose orally of advagraf qd or prograf 0.2 mg/kg/dose twice daily was given to 12 new paediatric renal transplant patients. Tacrolimus plasma levels were measured for 24h post-dose.
Results: Advagraf had a lower C_{max} and AUC than those of the prograf capsules. Interindividnal variability was noted in our study. We found that there were two PK patterns in Advagraf. One showed similar results to prograf. Another showed a lower AUC level. There was slightly lower but without difference in t_{max} and $t_{1/2}$ between the two groups.
Conclusions: Advagraf had improved absorption and bioavailability. However, interpatient variability still existed. Careful drug monitoring and dose adjustment should be performed during treatment to avoid nephrotoxicity.

RO-231 RENAL FUNCTION IN CHILDREN AND TEENS WITH LIVER TRANSPLANT. ONE SINGLE CENTER REPORT

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Liver transplantation (OLT) is the alternative for patients with acute or chronic end stage liver disease.
Aims: Assess incidence of renal disease in long term follow up through the glomerular and tubular evaluation in patiens with OLT.
Methods and Patients: Descriptive cross study with patients under 18 years with OLT performed at Hospital of Pediatrics J. P. Garrahan with more than a year of follow up during the period 1992-2008.Were excluded patients whose disease was associated with prior damage of the renal parenchyma.
Statistical Analysis: Data was analyzed on a database designed SPSS program version 11.0. Poll statistic: continuous variables were described using mean, standard deviations (SD) and range (r). Analysis of differences by t-test, was considered significant $p<0.05$.
Results: Were evaluated 187p, women 52%, males 48%. Age at olt = 5.1 x 4.2 years ±SD, range: 6 months - 17.3 years. OLT etiology: 80 p due to Acute liver failure, 72 p biliary atresia, 19p with cirrhosis, 16p others. Cadaveric 68% and living related 32% donors. Were retransplanted 4%. Mean time follow up and monitoring 7.5 (SD±3.4 years) and range 1–15.2 years. 82% p received triple therapy as initial immunosuppression with CsA, azathioprine or mycophenolate mofetil in combination with steroids. Tacrolimus was used in 22% p. Glomerular Filtration Rate was normal 72%p, hyperfiltration with significant proteinuria in 16% and falling in glomerular filtration in 12%.Tubulopathy isolated or complex with normal renal function in 57%. Arterial hypertension was not found.GFR was studied using Schwarts formulae a non renal biopsy was performed.
Conclusions: Kidney damage in our patients was presented with similar characteristics to those described in adults OLT patients.Minimization and avoidence of neprotoxic drugs ims and using non nefrotoxic alternatives still pending when good long term survival of the pediatric olt has already been proved.

Lung

RO-232 IMPACT OF "SUPER URGENCES" ON THE ACCESS OF THE O LUNG RECIPIENTS IN FRANCE

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Introduction: In 2007, the "Super Urgences" (SU) were implemented to allocate lungs preferentially to the patients who are at high-risk of dying, with deteriorating medical conditions and specific indications: the objective of these new rules was to decrease deaths on the lung waiting list by favouring the patients who had the worse medical status while, in the same time, not penalizing the other patients.
Two years after its implementation, the impact on the access of O group patients has been assessed.
Method: Patients registered for the first time on the French lung waiting list (WL) between 2004 and 2009 were included. Kaplan Meier curves stratified by blood group were used to assess the waiting time. The cumulative incidence (competing risks) was used to assess incidence of death on the WL.
Results: Of the 1324 patients registered, 980 recipients were transplanted. Of those patients 5% (11/205) of O donors were used for other blood group recipients before 2007 and 14% after (33/233).
Among the O donors, 13% (58/438) were used for SU recipients. This rate was 6% (29/448) for A donor 3% for B (n=2) and 0% for AB donors (0/19 donors).
The waiting time duration increased from 4.4 months (3.8- 5.1) before 2007 to 6.1 months (4.6- 7.2) after and this rise only concerned this blood group.
The incidence of death on the WL decreased: after 2007, it represented 9% at 1 year (11% before 2007). This diminution was particularly important for O groups.

Conclusion: One impact of the SU was to increase the O patients waiting time but it didn't increase the mortality rate on the WL. The use of O donors for A recipients has to be monitored carefully.

RO-233 EMOTIONAL EXPERIENCE IN PATIENTS AWAITING LUNG TRANSPLANTATION: A QUALITATIVE ANALYSIS

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Emotional reactions in the course of transplantation are often explored through negative emotions (e.g. stress, guilt) or depression and its evaluation. However the emotional reactions in the course of transplantation describing positive and negative emotional experiences have not been comprehensively described.
Qualitative semi-structured interviews were conducted shortly after registration on the waiting list with 15 lung patients waiting for an organ coming from a deceased donor.
In a qualitative analysis, focussing on the emotional experience of transplantation, a very rich discourse was underlined.
The described emotions in the interviews of the patients were related to specific situations, stakes and existential questions. All these emotions help to describe more precisely the very intimate experience of a difficult and stressful situation while awaiting transplantation.
It also helps to better understand the impact of the paradoxical situation of transplantation when a person is waiting for an organ, which will improve quality of life and will allow to survive, but which also depends on the end of the life of a donor.

RO-234 LUNGS FROM SMOKING DONORS CAN BE SAFELY USED FOR TRANSPLANTATION

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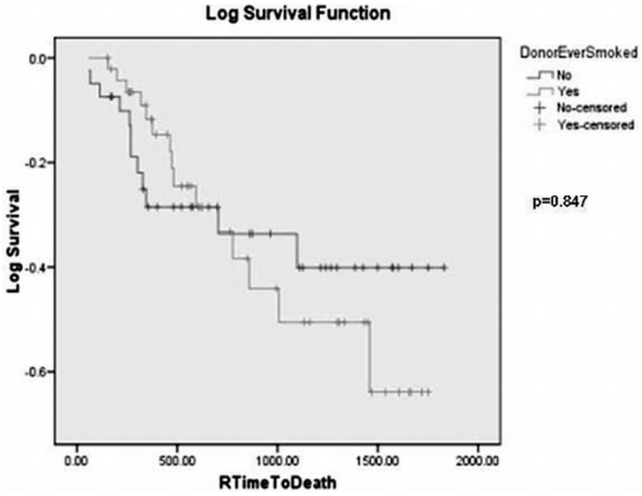
Introduction: The decline in the number of suitable donor lungs has led to an increasing use of previously unacceptable donors. This study aimed to evaluate the outcome of recipients of lungs from smoking donors in our centre.
Methods: We retrospectively reviewed 92 medical records for donor and recipient lung transplants from April 2005 to December 2009.
We classified the donors into distinct groups: pack year history (PYH) greater than or less than 20 years, current or non-smoker at time of death and past history of smoking vs. lifelong non-smoker.
The main outcome was survival which was calculated using the Kaplan-Meier survival curve. Other outcomes were ventilation time, stay in intensive care unit, hospital stay, number of infections in the first 30 days and time on the waiting list.
All data was analysed using SPSS vs.16.
Results: The groups were comparable in donor and recipient characteristics apart from donor age, which was higher in the smoking donors.
The survival was not significantly different in recipients of lungs from smoking and non- smoking donors.



There was no statistical difference in ventilation time, length of ICU and hospital stay or number of infection episodes within 30 days of transplant or time on the waiting list between the groups.
Conclusion: Our results showed that recipients of lungs from smoking donors had comparable outcome to standard donors. Although the numbers were relatively small, we recommend the use of lungs from smoking donors after careful assessment.

RO-235 SINGLE LUNG TRANSPLANTATION AS THE FIRST CHOICE IN EMPHYSEMA

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Introduction: Single (SLT) or double (DLT) lung transplantation in pulmonary emphysema patients is a topic of current debate. We retrospectivaly review unilateral (group 1) and bilateral (group 2) lung transplantation and analize survival, the incidence of surgical complications, postoperative infections and development of bronchiolitis obliterant (BOS).
Materials and Methods: From 1999 to 2009, 273 patients were transplanted in our department, 71 (26%) with pulmonary emphysema. Prior to 2003 we ussually did DLT and from 2003 most cases were SLT. In case of broncopulmonary colonization DLT were always done. The same inmunosupresive protocol was used in both groups. All SLT patients receive aerosolized amphotericine 50mg once a week during waiting list time. We used Kaplan-Meier method for survival, log-rank test and Pearson's chi-square test for stadistical analisis.
Results: The mean age was 56±7,15 years (range 30-65). 84,5% were man. The mean preoperative FEV1 was 22±8.04. Cumulative 5-year survival, was 56% and 54% (p=0.98). BOS was 39,7% and 41,2% (p=0.31). The relative risk (RR) for BOS was 1,38 (IC 0,73-2,62). At least one acute rejection episode occurred in 43,2% and 50% (p=0.0,56; RR 1,15 IC 0,7-1,9)). Bacterial infections were experienced by 43,2% and 55,9% (p=0.28; RR 1,29 IC 0,80-2,07). Fungal infections affected 19,8% and 17,6% (p=0.89 RR 0,93 IC 0,34-2,5). CMV infections were 24,3% and 17,6% (p= 0,49; RR 0,72 IC 0,28-1,82). Intraoperative complications were recorded in 27.6% and 54%, and this difference was statistically significant (p=0.032).
Conclusions: The study results support the decision of our group to consider single lung transplant the treatment of choice in empysema, which may be complemented with volume reduction surgery in the native lung if necessary. This option permit better donnor lung optimization.

RO-236 COMBINED SEQUENTIAL BILATERAL SINGLE LUNG-LIVER TRANSPLANTATION WITH EVEROLIMUS AND LOW DOSE STEROIDS: A LONG TERM FOLLOW-UP

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Background: Renal failure is a concern after solid organ transplantation. Patients with cystic fibrosis, after transplantation of the lungs or liver, are at particular risk of renal failure due to a long lasting history of massive antibiotic therapy and renal toxicity of calcineurin inhibitors (CNI). In the recent years use of mTor inhibitors, such as everolimus and sirolimus, have been advocated to reduce the nephrotoxic effect of CNIs.
Material and Method: A 22.7-year-old man affected by CF with end-stage lung and liver disease (FEV1 32%, hypersplenism, secondary biliary cirrhosis, esophageal varices and a previous episode of gastro-esophageal bleeding) underwent combined sequential bilateral single lung-split liver (segments I, IV–VIII) transplantation (SBSL-LTx). Immunosuppression was based on basiliximab, tacrolimus and steroids. On the 9th postoperative day he developed an acute renal failure (tacrolimus trough level 18.4 ng/mL). Azathioprine was added and the tacrolimus dosage was reduced (5,5 mg bid, trough level 8-10 ng/ml). Patient was discharged on the 27th postoperative day. On the 7th postoperative month he was switched from azathioprine to everolimus (trough level 6-8 ng/ml). On 15th post-transplant month tacrolimus was stopped and patient was maintained on everolimus 3 mg bid (trough 5-9 ng/ml) and prednisone 20 mg. The course was uneventful for 5 years. Prednisone was reduced to 10 mg and everolimus was maintained at trough level of 5-9 ng/ml). After 6 years the creatinine is in normal range, no episodes of lung or liver acute rejection and no bronchiolitis obstructive syndrome were observed.
Conclusion: In this case of SBSL-LTx a long term immunosuppression with everolimus and steroids appeared to be safe and effective in preventing acute and chronic rejection of the grafts, allowing a recovery and maintainance of a normal renal function.

RO-237 INTERVENTIONAL TREATMENT OF BRONCHIAL ANASTOMOTIC STENOSIS AFTER LUNG TRANSPLANTATION

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Background: Despite advances in surgical techniques and introduction of modern immuno-suppressive drugs, stenosis of the bronchial anastomosis remains a frequent and severe complication after single- and double lung transplantation (sLTX, dLTX) implying considerable morbidity. Aim of this retrospective single-center study was to evaluate short- and long-term results of interventional laser treatment with/without combined application of self-expanding nitinol stents.
Methods: Between 01.01.2005 and 01.06.2010, 57 sLTX (mean recipient age 55.4 ys.) and 115 dLTX (mean recipient age 42.6 ys.) were performed in our center. 1.8% of the patients after sLTX and 10.4% after dLTX developed significant ($\geq$ 80%) anastomotic stenoses requiring bronchoscopic intervention. 5 patients were treated by NdYAG laser only, 4 patients received laser therapy for recanalisation prior to stenting. 6 patients underwent primary stent implantation (self-expanding nitinol grafts). Repetitive stent application had to be performed in 4 patients.
Results: Clinical follow-up ranged between 1.2 and 65 months. An average of 2.0 reinterventions/patient after sLTX and 9.6 reinterventions/patient after dLTX had to be performed. Overall technical feasibility of a successful intervention amounted to 95%. In the postinterventional course, 2 patients developed pneumonia requiring iv. antibiotics, one patient showed a mucus-associated in-stent stenosis, and one patient required reintervention due to stent breakage.
In 98% of patients treated, successful bronchoscopic intervention resulted in immediate improvement of respiratory complaints. Patients treated with a nitinol stentgraft only and patients receiving stent application after prior laser recanalisation showed a significantly prolonged reintervention-free interval (39.3 vs. 34.3 days) when compared to patients undergoing laser therapy only (17.6 days).
Conclusion: Flexible interventional bronchoscopic application of self-expanding nitinol stents with facultative prior laser recanalisation provides an effective and safe treatment option for anastomotic airway stenosis after lung transplantation with favorable short- and long-term results.

RO-238 THE CROSSED WIRING TECHNIQUE, ESPECIALLY THE PARASTERNAL TECHNIQUE, IS ASSOCIATED WITH LESS STERNAL DEHISCENCE AFTER BILATERAL LUNG TRANSPLANTATION

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Background: The transverse thoracosternotomy (clamshell incision) is a widely used approach in bilateral lung transplantation. The closure technique is associated with sternal dehiscence, a condition that might need surgical intervention. Several methods are used to close the sternum. The objective of this study was to assess the incidence of sternal dehiscence and to compare the crossed and uncrossed closure technique.
Methods: A group of 149 patients underwent transplantation through the clamshell incision since 2001. There were 20 (13,4%) peri-operative deaths leaving 129 patients for evaluation. The sternum was evaluated on the lateral chest radiograph and scored as normal, override or separation. This outcome was compared to the crossed or uncrossed closure method.
Results: Of the 129 patients (66 male, mean age 43 years), the uncrossed method was used in 79, the crossed method in 50 patients. Of all patients, there were 38 overrides and 18 separations.
There was significantly less override (6/50) and separation (6/50) in the crossed group compared to the uncrossed group (32/79 overrides and 12/79 separations, $p<0,001$).
The crossed closure technique was subdivided in two groups: 33 patients were sternally crossed, 17 patients parasternally crossed. There were no sternal separations and 1 override in the parasternally closed group, compared to 6 separations and 5 overrides in the sternally crossed group (p=0,08).
Of all 129 patients, surgical correction was only performed in patients with a separation (10/18). No surgical correction was performed in the parasternally crossed group.
Conclusion: Crossed closure of the sternum after bilateral lung transplantation reduces the incidence of sternal dehiscence, compared to the uncrossed closure technique. Parasternally crossed closure probably reduces the number of patients that need corrective surgery.

RO-239 LUNG CANCER COMPLICATING LUNG TRANSPLANTATION: INCIDENCE AND OUTCOME – THE VIENNA EXPERIENCE

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Background: Long-term immunosuppression, longer survival times and underlying end-stage pulmonary disease might be contributing factors for the development of lung cancer (LC). Aim of the study was to determine the incidence and outcome of LC in a single-center cohort of lung transplant (LuTx) recipients.
Material/Methods: Retrospective review of the records of 962 consecutive patients who underwent LuTx between 1989 and 2009 at our institution to identify patients diagnosed with LC.
Results: 10 patients were identified with an unexpected LC in the explanted lung and 10 patients with LC developing after LuTx (6 women and 14 men, mean age 55$\pm$14 years (range 19-69), 8 single LuTx and 12 bilateral LuTx). Mean follow up was 2405$\pm$1052 days (range 672-4346). Reasons for LuTx were fibrosis (4 cases), COPD (11 cases) and others (5 cases). 12 patients had adenocarcinoma, 6 squamous cell carcinoma and 2 others. In patients developing LC after LuTx, 6 cancers occurred in the native and 4 in the transplanted lung. Mean time from LuTx to diagnosis of LC was 1859$\pm$809 (range 264-2797) days. Late stage LC (IIIB-IV) was diagnosed in 7 and early stage (Ia-IIb) in 3 patients. Median overall survival after detection of LC was 198 days (SE 144, range 0-2800 days).1 year and 3 years survival after diagnosis were 34% and 11%, respectively.
In patients with unexpected LC in the explanted lungs, all neoplasms were detected at early stage (I). No recurrence was found in these patients. 9 patients are still alive.
Conclusion: Unexpected LC in explanted lungs at LuTx, with an incidence of 1,03%,was found in an early stage and did not affect survival. In the case of diagnosis of LC after LuTx, rapid progression to locally advanced disease or metastatic disease was common.

RO-240 INCIDENCE OF SOLID DE-NOVO MALIGNOMA AND POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD) AFTER LUNG TRANSPLANTATION – EXPERIENCE IN VIENNA

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Background: A factor limiting the survival after lung transplantation (LuTx) is de-novo malignancy. The immunosuppressive treatment, the increasing longtime survival and the capacity to reactivate viruses like Epstein-Barr virus (EBV) are risk factors for the development of malignancies in LuTx recipients. The aim of this study was to determine the incidence and outcome of patients suffering from de-novo solid tumors and PTLD in a single center cohort.
Material/Methods: Between 1989 and 2009 962 patients underwent LuTx at our institution. 50 patients (5,2%) developed a solid tumor or PTLD. All data were collected and retrospectively analysed.
Results: 19 (38%) patients were female, 31 (62%) were male. At the time of incidence patients were on average 51$\pm$15,9 years (13-73) old. 16 (32%) patients suffered from PTLD, 10 (20%) from lung cancer, 12 (24%) from tumors of the gastrointestinal tract, 7 (14%) of the urinary tract. 2 female patients (4%) were detected with breast cancer, 3 patients (6%) with other neoplasms. Overall survival after solid neoplansms and PTLD was 53% at 1 year, 32% at 3 years and 29% at 5 years. The median time to cancer diagnosis was 1378$\pm$1272 days after LuTx (45-5003). 16 patients with de-novo neoplasms or PTLD underwent surgery, 21 were treated with chemotherapy and/or radiation. 5 patients received no therapy and therapy in 7 patients was unknown. The underlying illness, the status of Cytomegalie-Virus infection, immunosuppressive regimen and induction therapy had no influence on the incidence of neoplansms after LuTx. The only risk factors identified were the age at time of LuTx (p=0,005) and sex ($p<0,05$).
Conclusion: Immunosuppressant drug-induced neoplasms and PTLD as a late complication after LuTx are an important cause of mortality.

RO-241 CYSTIC FIBROSIS, LUNG TRANSPLANTATION AND CLOSTRIDIUM DIFFICILE ASSOCIATED DISEASE

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We present the case of a 26-year-old woman with cystic fibrosis (CF) who underwent a single sequential lung transplant and received peri-operative prophylaxis with intravenous meropenem and colomycin. She was commenced on metronidazole on day 2 and initially had an uncomplicated post-operative period in the intensive care unit (ICU). However on day 6, she vomited undigested food after four days of absent bowel movements.
Over the ensuing days, the patient developed mild abdominal tenderness maximal at the right iliac fossa and deteriorating renal function, a marked neutrophilic leukocytosis of 104×10^9/L and a delayed rise in C-reactive protein count to 350mg/L. She had started to open her bowels following the administration of laxatives and gastrograffin, but her abdominal symptoms persisted.
We had a high index of suspicion for the presence of *Clostridium difficile* colitis, given our previous experience (Yates B et al. Thorax 2007;62:554-56), and the patient's stool sample was positive for *C difficile* toxin. An abdominal CT scan showed wall thickening throughout the colon, consistent with colitis. Oral vancomycin was commenced but despite maximal medical therapy, she developed a septic response and an emergency subtotal colectomy was performed. The patient remains in the ICU at present on ventilatory support.
Up to 50% of patients with CF are colonised with *C difficile*. This case illustrates the need to risk-stratify patients in order to identify patient sub-groups at higher risk of developing fulminant colitis. The presentation of *C difficile* colitis in CF patients post-transplant is often atypical, with absence of diarrhoea. A high clinical suspicion for *C difficile* colitis is needed in post-transplant CF patients with abdominal symptoms, and early, prompt surgical intervention is recommended if severe *C Difficile* colitis confirmed.

Tissue injury / preservation II

RO-242 THE ANTIOXIDANT DOGMA IN HUMAN ISCHEMIA-REPERFUSION INJURY: NO EVIDENCE FOR FREE RADICAL MEDIATED DAMAGE

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Background: Oxidative stress has traditionally been considered the primary initiator of ischemia-reperfusion (I/R) injury. Remarkably, while antioxidant therapy has been highly effective in animal studies, patient trials fail to show a clinically relevant benefit of antioxidant therapy. This challenges the role of reactive oxygen species (ROS) as a major contributor to human I/R injury.
Methods: Using an unique method of clinical arteriovenous measurements, various markers of oxidative damage were measured during planned reperfusion in human kidney transplantation and cardiac surgery. Arterial and venous samples were compared in their concentration of oxidative stress markers (i.e. malondialdehyde (MDA) and 15(*S*)-8-*iso*-prostaglandin F2α (15(*S*)-8-*iso*-PGF2α)) and markers of nitrosative stress (i.e. nitrite, nitrate and nitrotyrosine) during the early reperfusion phase.
Results: None of the markers of oxidative and nitrosative stress were released upon reperfusion, with the exception of a small, transient release of 15(*S*)-8-*iso*-PGF2α. Urinary measurements during kidney transplantation were in conformance with plasma findings, showing no release of oxidative or nitrosative stress markers.
Conclusion: Results of this study show no evidence for damage caused by oxidative or nitrosative stress in early clinical I/R injury in humans. This finding suggest that endogenous antioxidant systems are sufficiently equipped to handle the excess ROS load during reperfusion; thus preventing damage.

RO-243 CHANGES IN BIOMECHANICAL FUNCTIONALITY AND STRENGTH FOLLOWING CRYOPRESERVATION OF HUMAN ILIAC VESSELS

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Purpose: The purpose of the study is to investigate the effect of cryopreservation on mechanical functionality of the vessels after long period of cryopreservation.
Method: Twelve pairs of iliac vessels were harvested from cadeveric donors. The vessels are divided into two groups. One group underwent biomechanical assessment immediately and another cryopreserved for a variable period of time, maximum being one year. The changes in functionality were studied quantitatively by matching stress and strain curve of cryopreserved and fresh vessels.
Result: Of the twelve pairs of vessels collected, seven (60, 120, 150, 240, 300, 330, 364-day cryopreserved vessels) showed good matches with their fresh controls on the stress-strain curve beyond 1.3 stretch ratio and only one sample (270-day cryopreserved vessel) failed to display good match within 1.3 stretch ratio. When the inter-tissue variation is taken into account, display of similar trend within elongation of 30% strain is considered a good match. The remaining four pairs had severe local calcification and therefore their functionality cannot be properly characterized by strain-stain curve. When the pairs of the vessels (cryopreserved and fresh) which showed good matches in functionality are compared with the pair of vessels which did not, the latter was found to have poor strength in the fresh control as evidenced by exacerbated elongation with little force.
The histologies of the cryopreserved vessels were analyzed. All the vessels, except one which had good match (300-day cryopreserved vessels), showed no or mild fragmentation in lamina elastica interna and externa. The 300-day cryopreserved vessel showed moderate fragmentation in lamina elastica interna and externa.
Conclusion: There is no apparent change in material strength up to 1 year of cryopreservation. Weak vessel is more likely to deteriorate with cryopreservation and seriously calcified vessels are not suitable for cryopreservation as calcification caused stiffening of the vessels and compromised elasticity.

RO-244 WARM HTK DONOR PRE-TREATMENT REDUCES ISCHEMIA REPERFUSION INJURY AND MATRIX METALLOPROTEINASE TISSUE ACTIVITY IN AN ORTHOTOPIC RAT LIVER TRANSPLANT MODEL

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Improved outcomes after liver transplantation have led to "organ shortage" and use of extended critiria donor (ECD) livers. ECD organs are more susceptible to ischemia-reperfusion injury. Thus improvement of preservation is needed. A new concept is pre-treatment of donors with 21°C warm HTK-solution.
Male inbred Wistar rats (bodyweight 230-260g) served as donors and recipients (n=6/group). Donors of treatment groups received i.v. 0.01 ml/kg BW warm HTK 15 min. prior to perfusion, control groups 0.01 ml/kg BW warm NaCl 0.9%.
Following pre-treatment, perfusion was performed with 4°C cold HTK solution as well as storage for 6 hours. Thereafter orthotopic liver transplantation was performed. According to three different groups animals were harvested four hours, two and five days after reperfusion and blood and liver tissue samples were stored. Blood samples were analyzed for AST, ALT, Bilirubin and LDH, liver tissue was analyzed for proMMP-2, MMP-2 and pro-MMP-9, MMP-9 using zymography.
Warm HTK pre-treatment proved to be feasable and easy to perform. Treatment groups showed significant lower values vs. control groups concerning ALT and LDH four hours post transplantation as well as a trend to lower values of AST at for hours, two and five days. Moreover in treatment groups significantly lower activities of pro-MMP2 at two and five days as well as of MMP-2 and proMMP-9 at two days were detected. A trend to lower activities was found for MMP-2 at four hours and five days as well as for proMMP-9 at five days. Histological analyses revealed a trend to minor damage in pre-treated groups. Warm HTK donor pre-treatment leads to a better preservation. Further studies using marginal donors may underline our thesis and might contribute to an extension of the donor pool.

RO-245 PREVENTION OF ISCHEMIA REPERFUSION INJURY FOLLOWING KIDNEY TRANSPLANTATION: A PILOT STUDY USING A PIG AUTOTRANSPLANTATION MODEL

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Introduction: Ischemia-reperfusion-injury (IRI) is known to adversely affect kidney graft survival. Recently we were able to show abrogation of IRI

by tetrahydrobiopterin in different murine transplantation models. Herein we present the results of a pilot study using a porcine kidney autotransplantation model.
Methods: Common house pigs (60kg) were used. To avoid alloimmune reactions an autotransplantation model was chosen. Left kidneys were explanted and stored on ice for 24h. Before implantation, contralateral nephrectomy was performed. Pigs were either pre-treated with tetrahydrobiopterin (BioMarin, Novato, CA, USA) 20mg/kg b.w. i.v. (n=3) or were untreated (n=3). Intraoperative urine production was recorded; serum creatinine and urea levels were analyzed during the entire observation period (7d). Parenchymal damage was analyzed by H&E histology and nitrotyrosine western blots, tetrahydrobiopterin tissue levels by HPLC.
Results: Compared to untreated animals, tetrahydrobiopterin-treated pigs displayed higher creatinine (1.8±0.6mg/dl vs 4.3±2.4mg/dl; p=0.15) and urea levels (32.3±2.7mg/dl vs 74.0±32.1mg/dl; p=0.09) before autograft implantation. However, only tetrahydrobiopterin-treated animals showed urine production immediately following reperfusion. Of the untreated group one animal survived for the entire observation period, its creatinine and urea levels still rising at day seven post transplantation. The other two animals died anuric. In contrast, two out of three tetrahydrobiopterin-treated animals survived throughout the observation period. Peak serum creatinine and urea levels were reached by day 3 to 5 and decreased afterwards. One animal died due to a gastrointestinal bleeding. Two hours post reperfusion histopathology and nitrotyrosine western blots revealed no differences. Significantly higher tetrahydrobiopterin tissue levels were measured in treated animals before autograft recovery ($p<0.05$).
Conclusion: Immediate urine production and better survival confirm the protective effect of tetrahydrobiopterin. However, further studies investigating optimal tetrahydrobiopterin dose and administration are required due to altered kidney parameters following application of the compound.

RO-246 COMPARISON OF REPERFUSION BIOPSIES FROM LIVERS PRESERVED WITH THE HISTIDINE-TRYPTOPHANE-KETOGLUTARATE VERSUS THE UNIVERSITY OF WISCONSIN SOLUTION IN LIVER TRANSPLANTATION

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Aim: To compare reperfusion biopsies and graft survival in histidine-tryptophane-ketoglutarate (HTK) and university of Wisconsin (UW) preservation solutions in patients undergoing orthotopic liver transplantation (OLT).
Material and methods: We reviewed the prospective database of all adult patients undergoing deceased donor OLT from March 1994 to July 2010 (114 transplants). We excluded transplants without reperfusion biopsy (21 patients). Variables of the donor, graft surgery and receptor were recorded. We categorized the preservation damage in minimal changes or minor injury and moderate or severe injury. Biopsies were compared between both groups by univariate and multivariate analysis. We used the Kaplan-Meier method to calculate graft survival and Cox regression model to compare the two groups.
Results: The study series comprises 93 patients (mean age 51±13 years, 61% men), UW was used in 48 transplants and HTK in 45. The median follow-up was 45 months (IQR 24-61). One year overall and graft survival were 84% v/s 79% (p=NS) and 77% v/s 79% (p=NS) in the HTK and UW group respectively. There were no differences to have a moderate or severe preservation injury between the two groups in reperfusion biopsies: HTK 20% v/s 20.8% UW (adjusted OR 0.85, 95% CI 0.28 to 2.59). Marginal grafts and a over 60 minutes warm ischemia time had a greater risk of moderate or severe preservation damage, adjusted OR 3.55 and 4.31 respectively.
Conclusions: There were no differences in graft survival at year and in preservation graft damage between the HTK and UW groups. Marginal grafts and warm ischemia time exceeding 60 minutes were independent predictors of preservation damage.

RO-247 PROTECTION FROM I/R DAMAGE WITH ANTI-T LYMPHOCYTES ANTIBODIES (THYMOGLOBULIN) DURING LIVER TRANSPLANT (LT)

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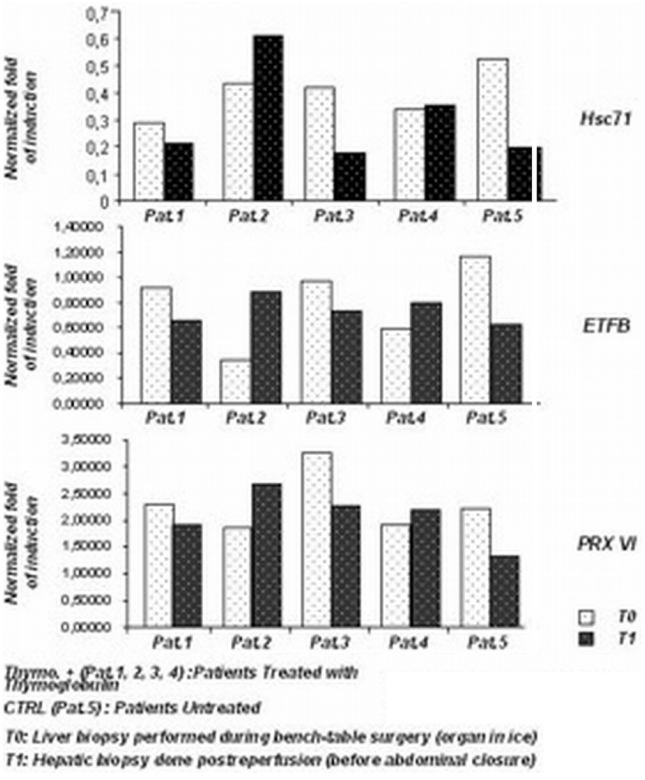
Ischemia reperfusion injury (IRI) in a major cause of graft failure after LT. Thymoglobulin (TG) seems to offer potential benefits to minimize graft damage associated with IRI. TG is a T-cell depleting polyclonal antibody which blocks multiple antigens related to IRI. Recent studies have highlighted the role of specific proteins whose expression level was significantly altered in response to liver cell damage by IRI. The differential expression of target proteins observed in liver biopsies performed during cold ischemia and postreperfusion, seems to be associated with the extent of cell damage. This aspect might have important consequences for understanding the molecular basis of IRI. Five cadaveric LT recipients were randomized to receive either TG (1mg/Kg/dose) during surgery or no TG. A tru-cut (16-gauge) biopsy (T0) was obtained during bench-table surgery at 4° C. A tru-cut (16-gauge) liver biopsy was performed at the end of the transplant after reperfusion (T1). To analyze differential protein expression of specific target proteins such as Hsc71, ETFB and PRX VI, total protein extracts from the biopsies were subjected to Western blot. These protein factors are involved into protein folding as molecular chaperone, energetic metabolism and redox mediated processes respectively. The increased expression levels of the analyzed proteins observed in 50% of TG-treated patients may be due to the importance of ROS in the pathophysiology of the damage associated with IRI.



Thymo. + (Pat.1, 2, 3, 4): Patients Treated with Thymoglobulin
CTRL (Pat.5): Patients Untreated
T0: Liver biopsy performed during bench-table surgery (organ in ice)
T1: Hepatic biopsy done postreperfusion (before abdominal closure)

TG treatment may be able to reduce the expression levels of protein factors having a crucial role in the regulation of the oxidative cell responses. Although it is necessary to extend the analysis to a larger number of cases, TG may allow for liver grafts from extended criteria donors to be transplanted with less clinical evidence of IRI and improved function.

RO-248 PROLONGED RAT KIDNEY PRESERVATION WITH ET-KYOTO SOLUTION: COMPARISON WITH HISTIDINE-TRYPTOPHAN-KETOGLUTARATE AND UNIVERSITY OF WISCONSIN SOLUTIONS

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ET-Kyoto (ET-K) solution is an extracellular-type trehalose-containing organ preservation solution. We here report the efficacy of ET-K on prolonged kidney preservation by comparison with histidine-tryptophan-ketoglutarate (HTK) solution and University of Wisconsin (UW) solution, using a rat kidney transplantation model.
Methods: Lewis rats were randomly assigned to three groups according to the preservation solution used: ET-K, HTK and UW. The kidneys were stored for 24 h and orthotopic kidney transplantation was performed after bilateral nephrectomy. Survival and graft function were assessed over a 14-day period. Pathological changes were evaluated at 3 h after reperfusion and day 14.
Results: After prolonged preservation for 24 h, no rats in HTK group survived

for 2 weeks post-transplant. The death was caused by renal failure as demonstrated by an irreversible rise of serum creatinine. The survival of ETK group was significantly better than that of HTK, and not different from that of UW (6/8, 0/8 and 6/8, respectively). Preservation in ET-K resulted in a significant reduction to 50% in serum creatinine level at post-transplant day 1 as compared with that in HTK, while the creatinine level was comparable to that in UW. In ET-K group, graft ATP level was significantly higher than that in HTK and not statistically different from that in UW. Consistently, at 3 h after reperfusion, the grafts of HTK group demonstrated severe tubular necrosis and apoptosis in the outer medulla. Graft ICAM-1 mRNA level was also highest in the HTK group. At 14 days after transplantation, both ET-K and UW groups showed normal serum creatinine level, while the pathological changes were mild and comparable.
Conclusion: ET-K is superior to HTK and comparable to UW in rat kidney preservation. This solution offers a novel alternative for cold storage of kidney.

RO-249 ORGAN VIABILITY ASSESSMENT IN THE PRESERVATION PERIOD UTILISING RAPID SAMPLING MICRODIALYSIS

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Viability assessment of the marginal allograft during the preservation period is imperative. We have therefore developed a system that allows continuous tissue monitoring with rapid measurements of the metabolic markers of ischaemia, based on a rapid sampling microdialysis analyser that has been validated in clinical studies monitoring tissue viability in brain injuries and bowel ischaemia. We aim to develop a tool that allows accurate organ viability assessment in the preservation period.
Kidneys were retrieved from pigs after termination. 12 unperfused kidneys were monitored at room temperature for 48 hours in the control group. In the preservation group 4 kidneys have been monitored to date. These kidneys were flushed with cold UW solution after retrieval and stored on ice, followed by continuous tissue monitoring for 48hrs. A microdialysis probe was tunneled into the renal cortex in each kidney. Each probe was connected directly to the novel analyser producing a real-time, on-line measurement of lactate concentration of the target tissue every 60 seconds. The system samples dialysis fluid and is injected into the enzyme biosensor system, resulting in a current peak at the electrode proportional to the lactate concentration.
On commencement of monitoring stable levels were achieved, with quantifiable lactate concentrations in the control group. The mean extracellular lactate concentration was 212.2±48.8 μM at 100 min post termination. We successfully identified a fall to 135.1±47.4 μM at 300 min. In the preservation group there was no detectable concentration of lactate within the extracellular fluid.
This fall in concentration reflects a reduction in anaerobic metabolism as ischaemia worsened and cells died. The absence of identifiable lactate within the parenchyma of the kidneys in the preservation group is due to a reduction in anaerobic metabolism secondary to hypothermia.

RO-250 THE OUTCOME OF USING MACROSTEATOTIC GRAFTS IN HUMAN LIVER TRANSPLANTATION AND MECHANISMS OF ISCHEMIA/REPERFUSION INJURY

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Introduction: Presence of liver macrosteatosis has increased in the general population. This study was performed to better understand the mechanism involved in ischemia/reperfusion (I/R) injury in macrosteatotic grafts.
Purpose: To analyze the clinical and histopathologic factors associated with I/R injury in human LTx, when macrosteatotic grafts were used.
Patients and methods: This is a prospective study performed between May/02 and Fev/10 in 119 cadaveric LTx performed in 117 patients. The liver biopsies were assessed for the following histological features (HE): *parenchymal neutrophilic infiltration*, *portal inflammation*, *hepatocellular necrosis*, *ballonization* and *presence of apoptotic cells* (TUNEL and Caspase-3 cleaved assays). It was included in this study *macrosteatotic grafts* (>10% of macro and <10% of microvesicular) and, they were classified in 4 degrees: *absent*, *mild*, *moderate* and *severe*. Also, it was analyzed the donors' and recipients' demographic parameters, body mass index (BMI), cold (CIT) and warm (WIT) ischemic time, LTx indications, MELD score, waiting time on list, hospital stay, blood transfusion, preservation solutions' and patient and graft survival rates. Grafts functions were assessed during the 7 days after LTx by serum levels of AST, ALT, Bilirubine, and Protrombin time. Results significant when $p<0.05$.
Results: There were no significant difference regarding donors' and recipients demographics parameters, with the exception of those present at the table. Primary Non Function occurred in 1/81 - *absent*, 2/24 - *mild* and 1/14 - *moderate/severe*.

Macrosteatosis Degree	Absent (n=81)	Mild (n=24)	Mod + Severe (n=14)	P
Donor BMI	25±3	26±3	27±5	0.01
Hepatocellular Necrosis				
I+II	17(21%)	7(29%)	8 (57%)	0.03
Mean	3.5±11	7±14	12.5±16	0.04
Apoptotic index (TUNEL)	0.235±0.109	0.221±0.106	0.167±0.09	0.2
Patient Survival (1,3,6mths)	90,86,85%	83,67,67%	86,79,72%	0.3
Graft Survival (1,3,6mths)	90,85,84%	79,67,67%	79,72,64%	0.1

Conclusion: The pathway of I/R injury in human liver transplant grafts that had >30% steatotis macrovesicular occurred due to high rates of hepatocellular necrosis and low apoptotic index. However, new research must be done to better investigate I/R injury in these grafts and to bloc the process of hepatocellular necrosis, and consequently to transplant them, safely expanding this large donor pool.

RO-251 MECHANISMS OF COLD ISCHEMIA/WARM REPERFUSION INJURY AFTER HUMAN LIVER TRANSPLANTATION

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Introduction: Apoptosis is a key mechanism of reperfusion injury in normal liver; however, the pathway of cell death in steatotic grafts after liver transplant (LTx) is unknown.
Purpose: To analyze the mechanisms and the evolution of the cold ischemia and warm reperfusion injury (CI/WR) in human LTx, when macrosteatotic grafts were used.
Patients and Methods: This is a prospective study performed between May/02 and Feb/10 in which 182 liver biopsies were collected: 91 on back table (*pre reperfusion*) and other 91 at 2 hours after graft reperfusion (*pos reperfusion*). Donors' data analyzed: demographics, cold (CIT) and warm ischemic time (WIT) and preservation solutions. The liver biopsies were assessed for the following histological features (HE): *parenchymal neutrophilic infiltration*, *portal inflammation*, *hepatocellular necrosis*, *ballonization* and *presence of apoptotic cells*; *steatosis* was classified in macro and/or microvesicular, and its degree classified as: *absent, mild*, *moderate*, *severe*. Apoptosis was assessed by the apoptosis index (TUNEL and Caspase-3 cleaved assays). Results significant when $p<0.05$.
Results: There was no statistical difference among 3 groups (*absent* vs *mild* vs *mod+sev*) regarding donors' age, causes of death, days in ITU, ALT and sodium serum; except body mass index: 24±3.5, 26±3, 27±4 (p-0.01); CIT (p-0.5) and WIT (p-0.3). After reperfusion the mean of hepatocellular necrosis was in *absent* – 2.5±5, *mild* – 7±11, *moderate/severe* – 16±19, ($p<0.001$).

Macrosteatosis Degree	Absent (n=61)	Mild (n=21)	Mod + Severe (n=5+4)	P
Pre Reperfusion				
Neutrophil Infiltration (I)	27 (44%)	12 (57%)	6 (67%)	<0.001
Hepatocellular Necrosis (I+II)	1 (1.6%)	2 (9.5%)	1 (11%)	0.02
Pos Reperfusion				
Hepatocellular Necrosis (I+II)	18 (29.5%)	9 (43%)	6 (67%)	0.006
Apoptosis index(TUNEL)	0.23±0.10	0.20±0.12	0.13±0.07	0.2

Conclusion: Before graft reperfusion, there was exponential raise of neutrophil parenchyma infiltration and hepatocellular necrosis increased as the macrosteatosis degree increased. Also, after reperfusion the grafts (>30% macrosteatosis) presented significant enlarging of hepatocellular necrosis and impairment of apoptosis index (TUNEL). However, additional research must be done to better understand the mechanisms of I/R injury in human macrosteatotic grafts and, consequently to transplant these grafts safely.

Clinical immunosuppression II

RO-252 IMP-DEHYDROGENASE IN ERYTHROCYTES – A MAKER OF LONG TERM MPA EXPOSURE?

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Introduction: Mycophenolic acid (MPA) inhibits inosine monophosphate dehydrogenase (IMPDH), resulting in decreased GTP concentrations and thereby inhibition of lymphocyte proliferation. Ongoing MPA therapy has been associ-

ated with increased IMPDH activity in whole blood and erythrocytes but not in lymphocytes. Elevated IMPDH activity described in erythrocytes does not translate into reduced efficacy of MPA but the consequences of the observed higher IMPDH activity in erythrocytes are unclear.
Methods: In the present study, we investigated IMPDH activity in erythrocytes (eryIMPDH) in a large cohort of patients (n=160) during the first year after renal transplantation. Results were compared with patients, who experienced significant dose reductions, cessation of MPA therapy, or who did not receive MPA after transplantation.
Results: IMPDH activity in erythrocytes is significantly lower than in MNC before initiation of MPA treatment (n=77:12,99±10.8 vs. 102,45±32,3 XMP/μmolAMP*s). Beginning with the first week after initiation of MPA therapy we observed a gradual increase of eryIMPDH over the first three months after transplantation resulting in a more than 20-fold higher eryIMPDH at month 3 (n=44: 305,5±230,0 XMP/μmolAMP*s). In contrast we did not observe any differences in eryIMPDH activity between pretransplant and 3 months posttransplant in 18 patients treated without MPA. In patients with significant MPA dose reductions early after transplantation (< 3months after Tx) no further increase of eryIMPDH was observed after dose reduction (35.5±22.2 vs. 34.6±13.9). Interestingly late (>3 months after Tx) dose reductions resulted in a significant decrease of eryIMPDH (240.5±98.2 vs. 122.3±97.2, p=0.03).
Conclusions: The role of eryIMPDH as surrogate maker for long-term MPA exposure and assoction with outcome should be further investigated.

RO-253 INDUCTION THERAPY WITH BASILIXIMAB AND DELAYED INTRODUCTION OF TACROLIMUS IS ASSOCIATED WITH A REDUCED REQUIREMENT FOR POST-OPERATIVE RENAL REPLACEMENT THERAPY IN HIGH-RISK PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION (OLT)

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Introduction: Early renal impairment following OLT is a frequent occurrence often aggravated by the use of calcineurin inhibitors (CNI).
Induction therapy consisting of basiliximab with delayed introduction of CNIs has the potential to protect renal function.
Aims: Determine the need for renal replacement therapy (RRT) in the immediate post-transplant period in patients with pre-operative renal impairment. Compare RRT rates in patients receiving induction therapy with basiliximab/ delayed introduction of tacrolimus to those receiving tacrolimus from the outset.
Methods: Retrospective review of patients undergoing OLT at the Scottish Liver Transplant Unit between Dec 2005 and October 2009 with creatinine levels of >120mmol/l at the time of transplantation.
Patients were treated with standard immunosuppression of steroids, azathioprine and tacrolimus (control group) or basiliximab on day 0 & 4 with steroids and azathioprine from day 0 and tacrolimus introduction delayed until day 7 (study group).
Appropriate statistical tests were used.
Results: 35 patients underwent OLT with a preoperative creatinine >120mmol/l (18 patients basiliximab induction: 17 patients standard immunosuppression). MELD score was higher in the study group (27 vs. 23).
The study group had higher preoperative creatinine levels compared with the control group (mean 213 vs 154mmol/l). Despite this the study groups had lower rates of post transplant RRT (18% vs. 47% p=0.035). At day 30 and 60 post transplant there was no significant difference in renal function between the two groups.
Discussion: In a high risk group of patients, in spite of higher serum creatinine levels and higher MELD scores, those receiving basiliximab and delayed introduction of tacrolimus had a significantly reduced incidence of post-operative renal dysfunction requiring RRT when compared to those receiving standard immunosuppression.

RO-254 ONCE DAILY PROLONGED RELEASED (ADVAGRAF) VERSUS TWICE DAILY TACROLIMUS (PROGRAF) AS PRIMARY IMMUNOSUPPRESSION IN LIVER TRANSPLANTATION

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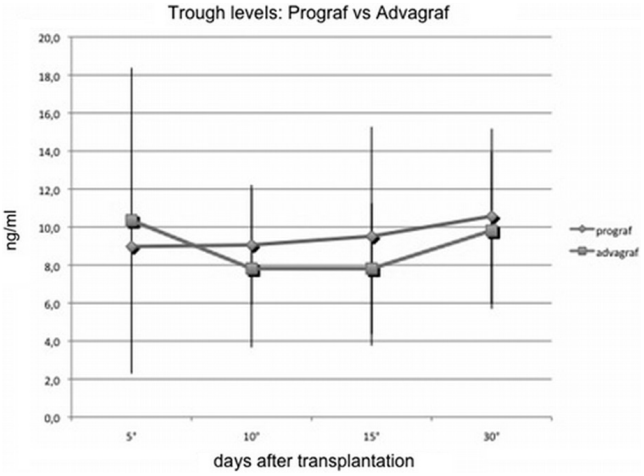
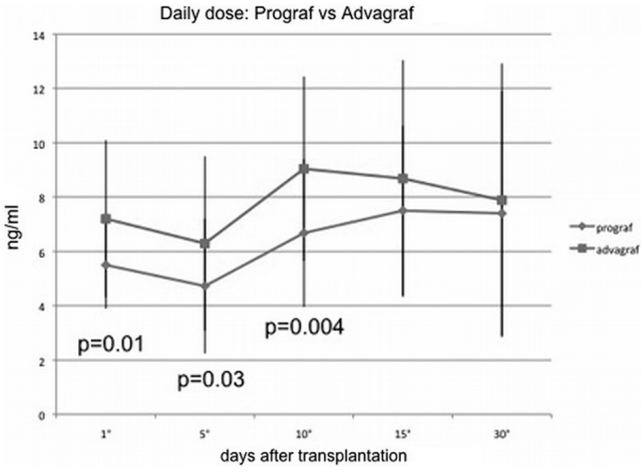
The use of once daily prolonged release tacrolimus (Advagraf) as primary immunosuppression after liver transplantation (LT) is a matter of debate due to delayed absorbance and longer time to achievement of target levels compared to twice daily tacrolimus (Prograf). Aim of this study is to retrospectively compare Advagraf vs Prograf as primary immunosuppression after LT for through levels, daily dosage, renal function and acute rejection within 30 days from LT. 80 LT received Prograf (group 1 #42) or Advagraf (group 2 #38) as primary immunosuppression plus steroids (no induction). Gender was male in 71% vs 68% (p=0.76). Age was 50 (25-67) vs 56 (33-70) (p=0.02) and MELD score at transplantation was 13 (6-46) vs 15 (6-30) (p=0.74) respectively in group 1 and 2. Pre-transplant creatinine was 1 0.3 vs 1.2 0.4 mg/dl (p=0.002). Trough levels were analyzed at +5, +10, +15 and +30 days after LT and did not differ between Prograf and Advagraf.



The tacrolimus daily-dose was recorded at +1, +5, +10, +15 and +30 days and showed a higher dosage of Advagraf at +1 (p=0.01), +5 (p=0.03), +10 (p=0.004), while no differences were noted at +15 and +30. Post-LT creatinine did not show any differences between the two groups.



The incidence of acute rejection was 21% vs 16% (p=0.51) in group 1 and 2. Five patients in the Prograf (12%) and 3 in the Advagraf group (8%) were switched to cyclosporine due to neurotoxicity or new-onset diabetes (p=0.55). In conclusion based on this retrospective analysis de novo Advagraf immunosuppression is comparable to Prograf except for an higher daily dosage at days +1, +5, +10 to maintain the same trough levels, this difference is no more evident at days +15 and +30.

RO-255 THE ROLE OF m-TOR INHIBITORS IN NEUROLOGICAL COMPLICATIONS (NC) DEVELOPMENT AFTER LIVER TRANSPLANTATION (LT)

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Background: NC can frequently and significantly affect morbidity and mortality of LT recipients. We retrospectively analyzed incidence, risk factors and outcome of NC following LT.
Methods/Materials: From 11-2000 to 6-2010 we performed 465 LT in 427 patients, 75 cases (16.1%) showed 78 NC. We considered as "minor" complications that usually are self-limiting and required only a symptomatic treat-

ment; as "major": seizures, central pontine myelinolysis, flaccid paralysis, restless leg syndrome, consciousness alterations and toxic and metabolic encephalopathies.
Results: The NC occurred in a median time of 0.53 months after LT (range 0-60.36), 50% of them were classified as minor NC. In the 40.0% of cases the NC have not been treated, in the 28% has been adopted a pharmacological symptomatic therapy, in the 9.3% an immunosuppressant's adjustment of the daily dose was performed and in the 22.7% an immunosuppressive switch from calcineurin inhibitors (CNI) to m-Tor inhibitors was performed. In 62 cases (82.7%) the patient recovered from the NC. Both the average length of stay in ICU and hospitalization resulted statistically longer in patients who experienced NC. The 1-, 3- and 5-year graft and patient survival resulted similar in patients with or without NC. Multivariate analysis showed as independent risk factors of NC: a MELD-score≥20, (p=0.029, OR:1.855, CI:1.066-3.229) a serum-bilirubin level ≥4mg/dl (p=0.007, OR:2.157, CI: 1.238-3.758) and an immunosuppressive regimen not including the use of m-Tor inhibitors (p=0.002, OR: 3.252, CI: 1.547-6.835).
Conclusions: NC significantly affect the length of ICU and hospital stay but not survival after LT. Considering that the only modifiable risk factor of NC development resulted the use of m-Tor inhibitors, the administration of such immunosuppressants in patients with non-modifiable risk factors (MELD-score≥20, serum-bilirubin level ≥4mg/dl) may contribute to reduce the incidence of NC.

RO-256 SUPERIOR MEDICATION ADHERENCE TO TACROLIMUS MODIFIED RELEASE ONCE-DAILY (QD) COMPARED TO TACROLIMUS TWICE-DAILY (BID) IN STABLE RENAL TRANSPLANT PATIENTS

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Background: With effective agents available for prevention of post-transplant organ rejection, medication adherence becomes a key factor for successful treatment-outcomes. A QD, modified-release oral dosage form of tacrolimus was developed to simplify dosing and improve medication adherence in ambulatory post-transplant patients.
Methods: The ADMIRAD study is a randomized (2:1), controlled, open-label, multi-centre trial, conducted in Belgium to compare medication adherence between modified-release tacrolimus QD (Advagraf®) and tacrolimus BID (Prograft®). Patients included were stable renal transplant patients treated with tacrolimus BID for at least 3 months before inclusion. After enrolment, all patients continued the BID regimen for a further 3 months, then were randomized between the two forms of tacrolimus and followed for 6 months. During the entire study, medication adherence was electronically measured. A longitudinal logistic model was used to compare medication adherence and its sub-components (execution-persistence).
Results: 219 patients (45% male; 3±2 years since transplantation) were analyzed (145 QD, 74 BID). Medication adherence was significantly higher in the QD- compared to the BID-group (p=0.0026). The difference was mainly driven by superior execution of the QD regimen: 88.2% vs 78.8% (p=0.0009) of the patients took the prescribed number of daily doses and 83.7% vs 73.4% (p=0.0015) of the patients dosed consistently within 2 hours of their respective average intake time. Persistence with the regimen was marginally higher in QD than in BID group (p=0.0824).
Conclusions: Patient adherence to the modified-release QD tacrolimus regimen was significantly superior to the BID regimen. There was, however, a residual prevalence of sub-optimal adherence that will have to be countered by means other than reformulation and regimen simplification. Electronically compiled dosing histories provide detailed data on patient adherence that can be used for efficient medication management.

RO-257 STEROID WITHDRAWAL IN RENAL TRANSPLANT RECIPIENTS AFTER CONVERSION FROM A CYCLOSPORINE BASED IMMUNOSUPPRESSIVE REGIMEN TO TACROLIMUS MONOTHERAPY; A PROSPECTIVE MULTICENTER TRIAL

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Body: In spite of the introduction of new immunosuppressive (IS) agents and regimens, steroids (st) are still used widely. St are associated with an increased incidence of diabetes, hypertension and hyperlipidemia, aggravated by the use of Cyclosporine (CsA). Aim: to evaluate whether conversion from a CsA based IS to Tacrolimus (Tac) monotherapy resulted in improvement of these side-effects.
Methods: 79 renal transplant recipients (58M/21F) from 9 centers, with mean age of 59 (range 25 -80) years with CsA and st associated side-effects were included. The patients were converted to a Tacrolimus based regimen with the subsequent withdrawal of st with a f-u of 24 months. Baseline results were compared to 24-month results with paired t-test. Levels are expressed as mean ± SD.
Results: 62 of the 79 patients (78%) completed the study and 43 (69%) were completely off st after 24 months (nopred), whereas 16 were still treated with prednisolone (pred), 2.5-7.5 mg/day. 2 patients died (lymphoma and heart failure) and 3 grafts were lost. 10 additional patients were withdrawn. None experienced acute rejection or developed diab during follow-up.

	s-crea	s-chol	s-trig	BP
Pred BL(n=19)	140±32	5.18±1.50	1.99±0.85	140/75
Pred 24 months	167±69	4.96±1.04	1.89±0.95	135/77
P value	0.05	ns	ns	ns
Nopred BL(n=43)	127±37	5.33±1.54	1.76±0.86	137/80
Nopred 24 months	134±45	4.48±1.28	1.53±0.85	135/80
P value	0.044	0.011	0.042	ns

Conclusion: Conversion from Cyclosporine based IS was safe and well tolerated. No patient had acute rejection or developed diabetes. The conversion from Cyclosporine resulted in a significant decrease in s-chol. Discontinuation of pred and Tacrolimus monotherapy resulted in a significant decrease in both chol and trig levels with a lower, but increase in crea levels over 24-months. Conversion from Cyclosporine based IS in renal transplant recipients with the subsequent withdrawal of steroids was possible in 73% of the patients and may result in a more favourable cardiovascular risk profile after renal transplantation.

RO-258 MINIMAL DOSE OF CALCINEURIN INHIBITOR COMBINED WITH EVEROLIMUS IS AN EFFECTIVE IMMUNOSUPPRESSIVE REGIMEN FOR KIDNEY TRANSPLANTATION RECIPIENT

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Although the application of mTOR inhibitor is beneficial for the preservation of kidney graft function, for a mechanism not completely elucidated, acute rejection rate and proteinuria increase in patients receiving calcineurin free regimen. This observation implies that minimal dose of calcineurin inhibitor may be helpful for the control of acute rejection and proteinuria. To test this hypothesis, we designed a regimen composed of Everolimus and minimal dose of calcineurin inhibitor to see if we can tackle these problems. Patients currently received calcineurin inhibitor base regimen with a stable eGFR, which is higher than 40ml/min, are recruited into this study while patients receiving multiple organ transplantation and patients with active infection are excluded. Once recruited, we reduce calcineurin inhibitor dose by 50% and progressively taper it to either cyclosporine 25mg/day or tacrolimus 0.5mg/day. Everolimus are started from 1.5mg/day and adjusted accordingly to have through level 3-8ng/ml. Mycophenolic acid dose are reduced by 50% and the dose of prednisolone is unchanged. Haemogram, biochemistry tests, 24 hour collected CCr, and urine total protein were assessed regularly. From August 2010 to February 2011, ten patients are included into this study. Their mean age is 51.7±1.8 years old and their mean duration of transplantation is 211.7±31.5days. After switch, their mean collected CCr increased from 75.6±6.1 to 87.6±11.6ml/min. As we expected, there is no increment of proteinuria with this regimen (600.7±419.4 vs 697.1±387.0 mg/day), and no acute rejection was observed. In conclusion, in this trial, minimal dose of calcineurin inhibitor combined with Everolimus is an effective regimen for kidney transplant recipients and more importantly with this regimen, we are able to avoid the most worrying side effects of calcineurin free regimen, i.e. acute rejection and proteinuria.

RO-259 PROGRESSION OF RENAL DISEASE IN RENAL TRANSPLANT RECIPIENTS

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Background: Modern immunosuppressive agents have dramatically decreased the incidence of rejection but the long-term graft survival did not have a parallel improvement. This has been attributed to increased mortality by cardiovascular diseases and graft losses by chronic allograft nephropathy. The purpose of this study was to assess the rate of decline of graft function and the risk factors associated with this change in the new immunosuppressive era.
Patients and methods: From a prospective database of 2600 kidney transplants performed from January-2000 to December-2002 in 14 Spanish hospitals, patients with at least 3 measurements of graft function (eGFR calculated by the abreviated MDRD equation) and more than 12 months follow-up, were included in the study. The following parameters; serum creatinine, fasting glucose, serum cholesterol, tryglicerides, plasma levels of cyclosporine (CsA) or tacrolimus (TAC), and concomitant medications were collected at six moths and yearly. All patients were followed until death, graft loss or 5 years. The rate of decline of eGFR was performed using joint modeling of longitudinal end-time-to-event data.
Results: 2153 recipients were included. The eGFR at 6 months (intercept) was 51.1±18.8 ml/min/1.73m2. The patient slope was -0.28±0.08 ml/min/1.73m2 per year (mean±standard error). Variables associated with intercept were: recipient gender, donor age and gender, delayed graft function, acute rejection in the first 6 months, proteinuria at 6 months and hepatitis C virus status. Longer time on dialysis, older donor age, immunosuppression with CsA and serum glucose at 6 months have a negative effect on graft function. During the follow-up, graft losses were 10% and about 50% of these were due to chronic allograft nephropathy.
Conclusions: Our results show a quite stable graft function during 5 years follow-up. Changes in immunosuppression and glycaemic control could help to slow the decline in graft function even more.

RO-260 HIGHER SELF-REPORTED NON-ADHERENCE WITH CO-MEDICATION COMPARED TO IMMUNOSUPPRESSIVE DRUGS IN HEART, LIVER AND LUNG TRANSPLANT PATIENTS

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Background: Transplant patient's drug regimen includes immunosuppressants (IS) as well as co-medication to prevent or treat co-morbidities. Medication non-adherence (NA) is a major limiting factor in the effectiveness of drug regimens. Little is known about non-adherence with co-medication after solid organ transplantation. We hypothesized that NA to co-medications is higher compared to NA to IS in heart, liver and lung transplant patients.
Methods: Using a descriptive, comparative cross-sectional design, we included a convenience sample 238 adult transplant patients (heart: 33%; liver: 23%; lung: 44%). NA with IS and co-medication was measured using the Basel Assessment of Adherence with Immunosuppressive medication Scale (BAASIS), administered as a patient interview, combining a Visual Analogue Scale (VAS) (0-120) and a 4-item scale (taking, timing, drug holidays and dose reductions). NA is defined as any deviation in one of the 4 dimensions.
Results: *Immunosuppressants:* Using the VAS scale, heart transplant patients (M: 90.0; IQR: 80.0-100) were significantly more NA than liver (M: 92.5; IQR: 85.0-100) and lung transplant patients (M: 95.0; IQR: 90.0-100) (p=0.011). NA was 40.4% in lung, 36.7% in heart, 23.6% in liver transplant patients using the 4 item-scale (p=0.200). *Co-medication:* Using the VAS, no significant difference between organ groups was found. NA based on 4-item scale showed significantly higher NA rate in lung (53.4%) compared to heart (39.2%) and liver (21.4%) transplant recipients (p=0.008). Comparison between IS and co-medication showed higher NA with co-medication (*VAS*: co-medication: M: 91.0; IQR: 80.0-100.0, IS: M: 95.0; IQR:8 5.0-100.0 (p=0.013); *4 item scale*: 42.3% co-medication; 35.3% IS (p=0.001)).
Conclusion: A higher rate of NA to co-medication compared to NA to IS was found. This difference might be explained by a higher priority that patients give to correct intake of IS. However, the importance of taking co-medication cannot be neglected in an effort to prevent or treat co-morbidities. Intervention need to target both NA with IS and co-medication.

RO-261 RENAL TRANSPLANTATION IN DONOR SPECIFIC ANTIBODY POSITIVE RECIPIENTS: SINGLE CENTER EXPERIENCE

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Lymphocyte Cross Match (LCM) is one of the tests which is used to screen for donor specific antibodies (DSA) agaist HLA antigens in renal transplant (RTx) recipients. However there is an controversial sensitized patient population who are DSA positive and LCM negative. The renal transplant protocol is still not well established in those patients.
Aim of this study is to present our clinical experience and renal transplant protocol in LCM (-), DSA (+) patients.
Material and Methods: Four patients with LCM (-) DSA (+) were included into the study. Demographics of the patients is presented in Table 1.

Table 1. Demographics and clinical history of patients

	Patient 1	Patient 2	Patient 3	Patient 4
Age	50	36	25	27
Sex	F	F	F	F
Time of Diaysis (month)	145	25	28	6
Previous Blood Transfusion	(+)	(+)	(+)	(-)
Pregnancies	2	1	0	0
Nomber of RTx	1st	2nd	1st	2nd
HD/CAPD	HD	CAPD	CAPD	CAPD

HD: Hemodialysis; CAPD: Continous Ambulatory Dialysis.

LCM test was performed with AHG-CDC. DSA screening and identification was performed with Luminex (GEN-PROBE).
Desensitization protocol: Mycophenolic Acid (MMF) 2 gr/day, tacrolimus 0.01 mg/kg, prednol 0.5 mg/day was started at day -6 before RTx. Double filtration plasmapheresis was performed at day -5 and -4. A dose of 5 g IVIG was administered at day -3 and -2. Rituximab 200 mg was administered at day -1. Induction therapy was done with IL-2 RB (basiliximab). Serum samples were collected at day -6, 0 and 30.
Immunological findings were explained at Table 2.

Table 2. Immunological data and results

	Patient 1	Patient 2	Patient 3	Patient 4
Number of Mismatch	6	3	6	3
PRA class I	10%	64%	(–)	(–)
PRA class II	26%	(–)	50%	76%
DSA type	DR10-DQ7	B35	DQ2-DQ7	DR16-DQ7
Baseline MFI level	1750–1750	5719	4210–4448	3600–2358
MFI level at day 30	696–0	6496	403–522	2744–1713
Acute Rejection (Treatment)	Acute Humoral Rejection (pp+ATG+IVIG) Rejection (+)	(–)	Acute Cellular Rejection (unresponsive to steroid therapy, ATG 300 mg)	(–)

PRA: Panel Reactive Antibody; PP: Plasmapheresis; ATG: Antithymocytelymphoglobulin.

Conclusion: Renal transplantation in LCM(–) and DSA(+) patients can be successfully performed with current desensitization protocol. However increased acute rejection risk should be considered. Further research is needed to determine the level of antibody titer for successful transplantation. Also number of plasmapheresis sessions and the dose of IVIG is stilll controversial.

Liver VI

RO-261A ABO-INCOMPATIBLE ADULT LIVING DONOR LIVER TRANSPLANTATION WITH NEW PROTOCOL: NO SPLENECTOMY, NO LOCAL INFUSION THERAPY AND USUAL IMMUNOSUPPRESSION UNDER RITUXIMAB PROPHYLAXIS

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Background: Among strategies to overcome ABO-blood barrier, local infusion therapy (LIT) accompanies substantial risk of morbidities such as bleeding, vascular injury or thrombosis. Since the introduction of rituximab (Rit), the incidence of acute humoral rejecyion (AHR) become nadir and LIT lacks intrinsic capacity for the prevention of AHR.
Methods and Materials: December 2008 to March 2011, we have performed 53 cases of adult ABOi LDLTs. Each patient received a single dose of rit-

uximab 2 weeks prior to LT. The frequency and timing of plasma exchange, depended on hemagglutinin titer, aiming at an antibody titer of 1:8 or less before LT. Spleen was preserved in all cases. LIT was employed in first 20 cases (Group A) and no LIT in the rest (Group B).
Results: There was no difference in demographic and clinical data of donor and recipient. The only 1 in-hospital mortality caused by pneumonia occurred in group A. And the additional mortality occurred on post-transplantation 4 month in Group A and the cause of death was biliary sepsis. The 3-month patient's survival rate was 95.0% (Group A) and 100% (Group B), respectively. There was no significant difference in the incidence of biliary complication, acute cellular rejection but infectious complication was more frequent group A. Total 7 episode of LIT-related complication occurred in 5 patients. Two groups showed the similar pattern in the trend of post-LT anti-donor antibody titer and CD19 cell population. One case of AHR occurred in Group B which was successfully rescued by steroid pulse and PE.
Conclusion: In our result, the protocol without LIT can abolish the LIT-related complication and can be successfully applied to overcome ABO-blood barrier without any increase of immunologic risk.

RO-261B DELTA STUDY: DUTCH EVALUATION IN LIVER TRANSPLANTATION TO ASSESS THE EFFICACY OF CYCLOSPORIN A MICROEMULSION WITH C_2 MONITORING VERSUS TACROLIMUS WITH TROUGH MONITORING IN *DE NOVO* TRANSPLANT RECIPIENTS

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The DELTA Study was a triple-centre, open-label, 6 months study with 12 months follow-up aiming to demonstrate superior efficacy, tolerability and safety of cyclosporin (Neoral BID) with two-hour postdose monitoring (C2) or tacrolimus (Prograft BID) with trough level monitoring (T0) in de novo liver transplantation, using a two drug regimen of T0 or C2 plus steroids. 171 patients were randomized 1:1 to receive C2 (N=85) or T0 (N=86).
The primary endpoint, treated biopsy proven acute rejection (BPAR) occurred within 3 months in 17% of patients with C2 and 8% with T0 (P=0.076), and within 6 and 12 months in 20% versus 9% of patients respectively (P=0.038). Graft failure occurred in 11% on C2 versus 5% on T0 (P=0.161). Chronic rejection led to graft failure in 3 patients on C2 and none on T0. After 1 year 84% of C2-treated patients survived, compared to 94% of T0-treated patients (P=0.049). At end of study incidence of hypertension (17% C2 vs. 8% T0), levels of fasting blood glucose and lipid spectrum were similar in both groups. Mean serum creatinin ($107\pm30.3\mu$mol/l vs. $105\pm35.1\mu$mol/l) and creatinin clearance (83 ± 31.3ml/min vs. 87 ± 35.7ml/min) were also comparable. Except for diarrhoea (31% C2 vs. 64% T0, P=<0.001), adverse and serious adverse events were comparable between groups. The incidence of patients who had one or more infections was similar (83% C2 vs. 93% T0, P=0.06).
Conclusion: Cyclosporin with 2-hour monitoring was associated with more acute rejection, lower patient survival but less diarrhoea than tacrolimus with trough level monitoring. Renal function, blood pressure, glucose and lipids were similar.

RO-261C POSTINTERVENTIONAL TUMOR NECROSIS PREDICTS RECURRENCE-FREE LONG-TERM SURVIVAL IN LIVER TRANSPLANT PATIENTS WITH HCC

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Background: The aim of this trial was to analyze the effect of pretransplant interventional bridging therapy (IBT) on long-term survival after liver transplantation (LT) in patients with HCC.
Patients and methods: 91 liver transplant candidates with HCC were included. If being eligible, patients underwent pretransplant interventional tumor treatment by transarterial chemoembolisation (TACE) or radiofrequency ablation (RFA). The impact of this treatment on tumor recurrence rate and long-term survival was investigated by uni- and multivariate analysis.
Results: 57 patients underwent interventional bridging therapy (IBT; 64%; TACE n=49; RFA n=8) pre-LT. Twenty-one patients developed tumor recurrence (23%), 10 patients in the non-treatment group (29%) and 11 patients in the IBT group (19,3%, P = 0,27). Recurrence-free survival rates were 67% in the non-treatment population and 76% in the IBT group after 5 years (P = 0,3). Response to IBT resulted in a significantly better 5-year recurrence-free survival rate (93%) than non-response to interventional therapy (50%; P = 0,001). Patients revealing partial/complete tumor necrosis at explant pathology, HCC recurrence rate was significantly lower (2,3%) than in patients without tumor necrosis (66,6%; P < 0,001). Tumor necrosis was identified as most important independent predictor of recurrence-free survival (odds ratio 52; P < 0,001) in patients undergoing IBT. Milan Out patients with tumor necrosis at explant pathology achieved an excellent recurrence-free survival at 5 years (80% versus 0%; P < 0,001). AFP-level < 100 U/ml (P = 0,01) and absence of 18F-FDG tumor uptake on PET (P < 0,001) were predictable for postinterventional tumor necrosis.
Conclusion: Patients with advanced HCC revealing postinterventional tumor necrosis may achieve an excellent long-term survival. Low AFP levels and PET – status identify HCCs that are eligible for IBT-induced tumor necrosis and thereby improved survival.

RO-261D THE CHANGING MANAGEMENT AND OUTCOMES OF PATIENTS WITH ACUTE HEPATIC FAILURE BEING ASSESSED FOR LIVER TRANSPLANTATION OVER TWO DECADES

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Introduction: The aim was to evaluate the underlying etiologies, management and survival of patients with acute hepatic failure (fulminant and subfulminant), presenting to a liver transplant service.
Methods: Retrospective chart review plus of data within unit database of all adult patients with acute liver failure assessed for liver transplantation and managed from 1987-2009. Sub-group analysis was also performed for 3 era's 1987-1994 (era 1), 1995-2002 (era 2) and 2003-2009 (era 3). Statistics were by SPSS.
Results: A total of 114 patients with fulminant and subfulminant hepatic failure were identified. The most common overall underlying causes of hepatic failure were hepatitis (44%), paracetamol overdosage (17%) and other drugs (16%). Furthermore the incidence of acute hepatic failure due to paracetamol usage increased significantly over time (p=0.0011-era's 1 versus 3; p=0.0142-eras 2 versus 3).
The management of acute hepatic failure has altered over time, with an increase in patient intensive care unit (ICU) stays between the first and the last era's (p=0.0134) and a significant increase in the use of dialysis between the first era and the last two era's (p=0.0125 and p=0.0049). The use of n-acetylcysteine has also increased with time [p=0.0003]. An increasing proportion of patients were managed without liver transplantation as evidenced between eras 1 and 3 [p=0.0018] and era's 2 and 3 [p=0.0219]. The overall survival rates of adult patients have improved over time including the survival following transplantation (p=0.027).
Conclusions: Paracetamol is an increasing underlying cause of acute hepatic failure in Australia in adults presenting for consideration for liver transplantation. Patients with acute hepatic failure are also increasingly requiring ICU management including undergoing more intensive dialysis. The survival rates for acute hepatic failure are increasing both with and without liver transplantation.

RO-261E RESULTS OF LIVER TRANSPLANTATION IN A LARGE COHORT OF MORE THAN 100 HIV INFECTED PATIENTS – A MONOCENTRIC EXPERIENCE

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Liver disease progression to cirrhosis is faster in HIV infected patients and liver transplantation (LT) is an accepted therapeutic option for patients with end stage liver disease.
We have analyzed the outcome of more than 100 patients in term of survival according to the indication of LT and the response to anti HCV therapy.
105 HIV infected patients (mean age: 45 yrs ±5.9; male: n=88 (83%) have been transplanted in our center between December 1999 and July 2010. Indications of LT were as follows: HCV cirrhosis: n=59 (56%); hepatocellu-

lar carcinoma: n=20 (19%); HBV cirrhosis: n=8 (7.6%); HBV/HCV cirrhosis: n=5 (4.7%), HBV/HDV cirrhosis: n=1 (0.9%), fulminant hepatitis: n=2 (1.9%), nodular regenerative hyperplasia: n=4 (3.8%), hemochromatosis: n=1 (0.9%), hepato-pulmonary syndrom: n=3 (2.8%) and secondary biliary cirrhosis: n=2 (1.9%). The mean MELD score at the time of LT was 18.9±8.73 [7-49]. Mean CD4 cell count at LT was 291.3±194.37 cells/mm3 [10-1020]. The mean delay of follow-up was 3 years ±2.3 [0-10.2]. The overall cumulative survival was 55% at 5 years. The survival of patients transplanted for HCV cirrhosis, HCC and HBV cirrhosis were 45%, 49% and 100% at 5 yrs, respectively. Anti-HCV therapy (PegIFN + Ribavirin) was given in 36/58 (62%) patients; the response rates were as follows: no response: n= 24 (66.6%); partial response: n=2 (5.5%); sustained virological response: n=4 (11%) and complete response: n= 2 (5.5%).

Conclusions: survival at 5 yrs after LT in a cohort of 105 HIV infected patients is 55%. Because of a low rate of sustained virological response after LT with PegIFN and Ribavirin, new drugs against HCV viral infection must be tested in a very near future.

RO-261F A NOVEL MICROSURGICAL MODEL OF HETEROTOPIC SMALL BOWEL TRANSPLANTATION IN MICE

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Background: Clinical outcomes after small bowel transplantation are still challenging compared to other solid organs. Therefore, animal models are critical to better understand the immunology and physiology of these grafts. In particular with regards to transplant immunology the mouse is the "gold standard" but the microsurgical techniques involved are extremely technically challenging. Here we report a simplified, reproducible and reliable mouse model for small bowel transplantation using a non-suture cuff technique.

Materials and Methods: Syngeneic transplants were performed using C57BL6 mice (n=20). A 5-cm segment of the jejunum based on the superior mesenteric artery and portal vein was harvested. The donor artery and vein were mounted with polyimide cuffs (artery cuff: inner diameter: 0.404mm, wall thickness: 0.025mm; vein cuff: inner diameter: 0.455mm, wall thickness: 0.025mm), and subsequently anastomosed to the recipient's common carotid artery and external jugular vein. Following reperfusion of the graft, the proximal and distal ends of the graft were brought out as stomata.

Results: Success rate of this model was high (90%) with 2/20 graft losses resulting from postoperative bleeding. No vascular thrombosis occurred. Donor operation lasted 60±12min and recipient operation 45±7min. Warm ischemia time could be limited within 20±2min. Graft biopsies were performed at serial time points and long-term graft survival (>100 days) was confirmed by gross and histological appearances without evidence for chronic pathologic changes.

Conclusion: This represents the first cervical heterotopic small bowel transplantation model using a non-suture cuff technique for revascularization. Advantages are that the high-flow common carotid artery keeps anastomosis patent, and diastolic suction of the heart minimizes the risk of venous stasis and thrombosis resulting in high success rates. This novel technique will be best suited to investigate basic immunology and ischemia-reperfusion-injury in intestinal transplantation.

RO-261G REDUCTION OF HEPATIC ARTERIAL PERFUSION BY INHIBITION OF NITRIC OXIDE PRODUCTION IMPAIRS THE RECOVERY FROM FOCAL HEPATIC VENOUS OUTFLOW OBSTRUCTION IN LIVER RESECTED RATS

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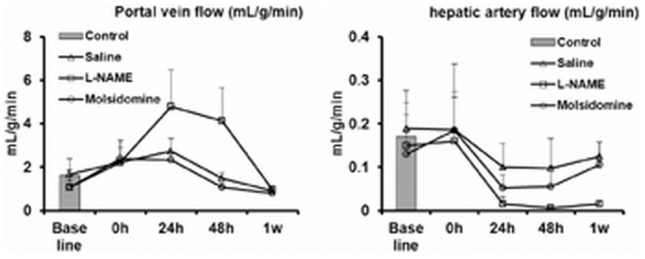
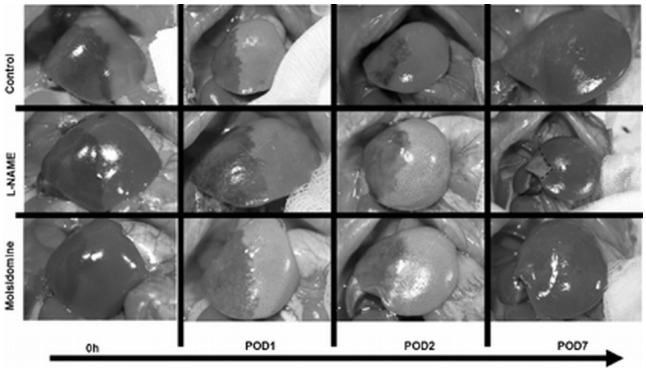
Background: Extended partial hepatectomy (PH) is leading to portal hyperperfusion but reduced hepatic arterial inflow (HAI) (1) and is invariably causing focal hepatic outflow obstruction (FHOO). We observed, that FHOO caused confluent parenchymal necrosis interspersed with viable portal tracts in the obstructed territory and large sinusoidal vascular canals in the border zone after rat PH and right-median-hepatic-vein-ligation (RMHV-L) (2). Lack of hepatic arterial perfusion impaired spontaneous course of recovery in terms of enlarged parenchymal necrosis, delayed regeneration and the absence of draining vascular canals. We hypothesized that restoration of the reduced HAI in PH-rats via application of the NO-donor Molsidomine would reverse the impairment of the spontaneous course.

Methods: Lewis rats were subjected to 70% PH with RMHV-L. Either Molsidomine (10 mg/kg) or of L-Name (NO-synthase inhibitor, 100 mg/kg) applied daily (POD1_to_POD7) was used to increase respectively decrease hepatic arterial inflow. Hepatic damage, microcirculation, regeneration and vascular remodeling were evaluated at POD1, 2 and 7.

Results: As expected, significant increase of portal venous inflow with a concomitant decrease in HAI was observed in all groups after PH.



Molsidomine-treatment did neither affect hepatic hemodynamics nor the spontaneous course. In contrast, L-NAME-treatment further decreased HAI which impaired hepatic microcirculation (reduced mean sinusoidal diameter and a reduced functional capillary density), aggravated parenchymal damage, decelerated recovery (figure 2), and impaired the formation of sinusoidal canals.



Conclusion: Reduction of HAI via inhibition of nitric oxide production worsened the recovery from FHOO. Drugs increasing HAI need to be evaluated to reverse the hyperperfusion induced impairment of the spontaneous course after FHOO.

Reference List:

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RO-261H TREATMENT OF SMALL HEPATOCELLULAR CARCINOMAS (HCC), LIVER (LT) TRANSPLANTATION, LIVER RESECTION (LR) AND RADIOFREQUENCY ABLATION (RFA)

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Background: LT for chronic liver disease and HCC presents better long term survival but it can be offered only to a limited number of patients because of donors shortage. Alternative treatments for HCC are LR and RFA.

Methods: review of patients from January 2004 to March 2010 treated for a single lesion of HCC <3 cm, with LT, LR or RFA. Patient selection, and overall and disease-free survival were analyzed.

Results: 162 LT, 75 LR and 65 RFA were performed for HCC; of these 54 (33%), 11 (15%) and 27 (41.5%) respectively had a single lesion with a diameter <3cm. Patients characteristics are showed in Table 1.

Table 1

	Gender (n)	Age, years (median)	Presence of Cirrhosis (n)	Aetiology (n)	α-Fetoprotein, ng/ml (median)	MELD & Ukeld (median)
LT (n=54)	F 14 (26%) M 40 (74%)	54 (36–71)†	51 (94%)	HBV 10 (18.5%) HCV 18 (33%) ALD 9 (17%)	20 (1–3430)†	11 (4–36)† 52 (44–67)†
LR (n=11)	F 3 (27%) M 8 (73%)	71 (53–80)†	5 (45.5%)	HBV 2 (18%) HCV 1 (9%) ALD 1 (9%)	90 (2–1685)†	7 (6–13)† 47 (43–52)†
RFA (n=27)	F 7 (26%) M 20 (74%)	61 (43–78)†	25 (93%)	HCV 9 (33%) ALD 8 (30%)	13 (1–632)†	9 (6–13)† 50 (44–55)†

†Range.

On histology 19 (35%) patients in the LT group and 5 (45%) in the LR one presented vascular invasion. Median follow-up was 36, 20 and 22 months for LT, LR and RFA respectively, 3-year survival was 78%, 54.5 and 74% respectively (p=0.108) and 3-year disease-free survival was 98%, 64% and 59% respectively (p<0.001).
Conclusion: LT for small HCC presents the best survival (78%), with a low rate of recurrence. However RFA can also provide good results with a survival of 74%, a longer follow-up will be needed to support this results.

RO-261I THE ASSESSMENT OF GFR AFTER ORTHOTOPIC LIVER TRANSPLANTATION USING CYSTATIN C AND CREATININE-BASED EQUATIONS

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Background: Rising survival rates after orthotopic liver transplantation (OLT) increased the incidence of chronic kidney disease (CKD) in this population. The measurement of kidney function after OLT is still a clinical challenge. Equations using serum Creatinine (sCr) are often inaccurate. Serum Cystatin C (CystC) has been proposed as a marker for renal function that might overcome the limitations of sCr-based equations. The aim of this study was to define the accuracy of sCr- and CystC-based equations in the assessment of CKD after OLT.
Methods: In this cross sectional study CystC and sCr were measured in 98 patients undergoing OLT. The glomerular filtration rate (GFR) was calculated using the Modification of diet in renal disease (MDRD 4), Cockroft Gault (CG), Hoek, Larsson, chronic kidney disease epidemiology (CKD-EPI), CKD-EPI-CystC, and CKD-EPI-CystC-Crea equations. The Inulin clearance (IC) was measured and used as a standard. The prognostic capacity to assess CKD after OLT of these equations was compared with respect to IC.
Results: Median age was 52 years (23-70), median time after OLT was 6 (1-15) years. Two years after OLT, 45% of the recipients had a GFR < 60mL/min/1.73 m2 according to the IC. The IC correlated significantly with the CKD-EPI, the CG and the CKD-EPI-CystC equation (p=0.001). The Larsson and the Hoek equation and the CKD-EPI-CystC formula identified the highest percentage of patients with CKD correctly (100%, 94%, 94% respectively). The CKD-EPI-CystC-sCr and the Hoek equation showed the smallest degrees of bias (0.5 and 7.9 mL/min/1.73 m2 respectively) with 11% each of their estimates being within 10% of the IC measurement (see figure).
Conclusion: CystC based equations were superior as compared to sCr based equations in the assessment of renal function in patients after OLT in the presented study.

Tuesday, 6 September 2011

Kidney VII

RO-262 POST KIDNEY TRANSPLANT RE-HOSPITALIZATONS IN THE FIRST YEAR POST TRANSPLANT-A PRACTICE MONITORING AND IMPROVEMENT PROJECT

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Introduction: Re-hospitalizations early post kidney transplant are in important metric of morbidity and increased health care costs. A task force was set up to continually monitor, study and provide feedback to the practice on causes and trends in re-hospitalizations.
Methods: A nephrologist, physician assistant and a senior RN formed a team to review cases. A dictionary was developed. After each hospitalization, the medical chart was reviewed and the proximate and final cause of the admission was determined. The circumstances of the admission were reviewed and if alternate outpatient management could have been. The team met frequently.The first 6 months cohort with one year of follow-up was reviewed. Presentations will be made to the practice twice yearly. Here we present the first cohort.
Results: 81 adults received kidney transplants between 1/1/2009 and 6/30/2009. Mean age 53±14 year, males 63%, Caucasians 92%, and deceased donor recipients 24.7%. 79 readmissions occurred in the first year in 32 patients. 20 patients had a single admission and one patient had 15 admissions during the first year. Eight patients had more than two admissions and accounted for 53/79 admissions. 21 patients were admitted within the first month post transplant. Three more than once totalling 24 admissions within 30 days. Admission within 30 days were mainly surgical/electrolyte/volume problems (16/23). Admissions from 30-365 days were more varied but the largest grouping was infections (15/55) with Urinary tract infections and urosepsis being the commonest.
Conclusion: Re-hospitalizations in the first year post kidney transplant are common. A small number of patients have frequent re-admissions. Infections are a common cause. This has been a learning experience that revealed potential avenues for practice improvement.

RO-263 IMPLANTATION OF THE RENAL ALLOGRAFT ARTERY ON AN ILIAC VASCULAR GRAFT: EARLY COMPLICATIONS AND LONG-TERM RESULTS

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Background: Patients undergoing kidney transplantation often present diffuse macroangiopathy needing for surgical aorto-iliac or aorto-femoral by-pass using prosthetic material.
Aim of the study: To evaluate the safety and long term results of the implantation of the kidney allograft artery on a vascular prosthetic graft.
Materials and methods: Retrospective review of the clinical records of the recipients of a kidney transplantation from January 1995 to December 2010.
Results: Over a 15 years period, renal artery was implanted on a prosthetic graft during 27 kidney transplantations in 26 patients (1.89% of patient transplanted in the same period). Median follow-up was 53 months. Two patients received a living donor allograft. The vascular graft was implanted during or after the transplant operation in two and three patients, respectively. In all the remaining patients renal artery was implanted on a pre-existing vascular graft. The main indications to aortic carrefour or iliac arteries replacement were abdominal artery aneurysm and iliac arteries stenosis. Arterial thrombosis occurred in two patients (7.4%). No other arterial thrombosis or vascular problem was observed during the entire follow-up. Local infectious complications occurred in two patients (7.4%). No graft was lost due to local infection. Furthermore, the cases of arterial thrombosis and local infection were not directly imputable to the presence of a prosthetic graft at the surgical site.
Conclusions: In our experience the implantation of the kidney allograft artery on a prosthetic vascular graft seems safe. Long-term results are excellent: except the two graft lost for arterial thrombosis, all patients presented with a patent kidney allograft artery at the end of follow-up, with no evidence of stenosis.

RO-264 EXTENSIVE CORONAR CALCIFICATION IN YOUNG SLE RENAL TRANSPLANTED PATIENTS

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Background: Coronary Vascular calcification is a frequent finding in SLE and in Renal disease. The aim of the study was to investigate risk factors for Coronary calcification in SLE transplanted patients without coronary symptoms.
Methods/Materials: In a cross sectional study thirty-nine renal transplanted SLE patients with a functioning transplanted kidney were offered a clinical examination, laboratory tests and SLE disease activity indexes. Each patient underwent an ECG-gated multislice spiral CT scan of the heart for quantification of coronary calcification (Agatston score). Arterial and aortic stiffness was assessed by means of pulse wave velocity (PWV).
Statistical analysis: Comparisons between groups were performed using Mann Whitney t-test or Fisher's exact test. Univariate and multivariate logistic regression were used to assess odds ratios for severe coronary calcification.
Results: Coronary artery calcification (CAC) was present in 82% of the patients (32 out of 39). The mean CAC score was 894 (1679) with a median of 135. Subjects with an Agatston less than 400 were considered to have mild to moderate risk of coronary disease, while subjects over 400 were considered to have a high risk coronary disease. There were no significant differences in

Multiple linear regression for outcome of Coronary artery calcification, n=39

Risk factor	Age, years	P-value	Multivariate	P-value
Pulse wave velocity, meter/second	0.38 (0.07, 0.69)	0,018	0.41 (0.17, 0.66)	0,001
Time since diagnosis of lupus	0.52 (0.24, 0.80)	0,001	0.66 (0.43, 0.71)	0,000
Body mass index , kg/m2	0.19 (–0.14, 0.51)	0.257	0.39 (0.15, 0.63)	0,002
Age, years	0.19 (–0.14, 0.51)	0.259	0.02 (–0.22, 0.27)	0.857

age, time on dialysis, blood pressure, dyslipidemia, bone metabolism, renal function, smoking or diabetes, serological SLE markers or SLEDAI between subjects with low or high calcification score. One third (36%) of the patients had evidence of high level of arterial calcification with an Agatston score above 400. CAC score was associated with pulse wave velocity, body mass index and time since diagnosis of lupus nephritis.
Conclusions: Coronary artery calcification is prevalent in SLE transplanted patients. Early detection of vascular wall alterations and subclinical atherosclerosis is important to identify in this high-risk SLE population for early therapeutic intervention preventing cardiovascular complications.

RO-265 PRESERVATION SOLUTIONS FOR STATIC COLD STORAGE OF KIDNEY ALLOGRAFTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Static cold storage is the most prevalent method for renal allograft preservation worldwide. Numerous preservation solutions have been designed to counteract the detrimental effects of the retrieval process, graft cooling and reperfusion injury. We aimed to appraise the evidence for the efficacy of the currently available preservation solutions.
Methods: We performed a systematic literature search using Ovid MEDLINE, EMBASE, the Cochrane Library and the Transplant Library. Searches combined MeSH and EMTREE keywords with free-text aliases. No date or language limits were applied. Inclusion criteria specified any comparative, prospective study of preservation solutions for cadaveric renal allografts. Studies were assessed for methodological quality. Our primary outcome was delayed graft function (DGF).
Results: Seventeen studies were included: 10 Randomised Controlled Trials (RCTs) and 7 Non-Randomised Controlled Trials. This represents a limited amount of prospective data. Random effects meta-analysis suggests that the Relative Risk (RR) of DGF is higher with Eurocollins solution compared to both HTK (RR=1.85, CI= 1.21-2.83, $p<0.01$) and UW (RR=1.27, CI= 0.98-1.64, p=0.07). UW is associated with a comparable rate of DGF compared to Celsior (RR=0.97, CI= 0.76-1.23, p=0.79), and HTK (RR=1.04, CI= 0.85-1.27, p=0.72). Acute rejection and patient survival were unaffected by preservation solution. There is some evidence that Eurocollins is associated with worse graft survival than UW or HTK. There is no RCT of Marshalls solution, although registry data suggests that it is as satisfactory as UW or HTK.
Conclusions: Current practice is largely based on 2 RCTs which are supported by retrospective studies, registry and experimental data. As there are significant cost implications in the selection of preservation solutions there is a need for more robust evidence for the efficacy of the different preservation solutions.

RO-266 RENAL TRANSPLANTATION IN PATIENTS WITH AA AMYLOIDOSIS NEPHROPATHY: RESULTS FROM A FRENCH MULTICENTER STUDY

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Background: Although end stage renal disease (ESRD) related to AA amyloidosis nephropathy is well characterized, there are limited data concerning patient and graft outcome after renal transplantation.
Method: We performed a large multicentric retrospective survey to assess both graft and patient outcome among 59 transplanted patients for renal disease caused by secondary amyloidosis. The origins of the AA amyloidosis included: recurrent hereditary periodic fever syndromes, chronic infectious disease, inflammatory rheumatic disease, and undetermined causes.
Results: The overall 5 and 10 year patient survival was significantly lower in the AA amyloidosis patients compared with a control group (p =0.0001, 0.028 and 0.013 respectively). In contrast, we did not observe any statistical differences in the 5- and 10- year graft survival censored for death between our study group and the control group. AA amyloidosis transplanted patients exhibited a high incidence of infectious complications after renal transplantation (73.2%). Causes of death included both acute cardiovascular events and fatal septic complications. Multivariate analysis demonstrated that the recurrence of AA amyloidosis on the graft (adjusted OR = 14.4, p= .01) and older recipient age (adjusted OR for one year increase = 1.06, p=0.03) were significantly associated with risk of death. The recurrence rate of AA amyloidosis nephropathy was estimated at 14%. Univariate analysis did not reveal significant factor associated with recurrence including the presence of inflammatory syndrome at the day of transplantation (p=0.64) and origin of AA amyloidosis (p=0.43).
Conclusion: Finally, patients with ESRD associated with AA amyloidosis nephropathy are eligible for renal transplantation but require careful management of both cardiovascular and infectious complications to reduce the high risk of mortality.

RO-267 A RELATIVE SURVIVAL MODEL TO ASSESS THE SPECIFIC MORTALITY RELATED TO RENAL TRANSPLANTATION

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Background: Cox models do not discriminate whether deaths are linked to or independent of transplant status.
Patients and method: The additive relative survival method allows the estimation of the specific mortality rate for a disease in comparison with the non-specific mortality rate from a matched general population and the assessment of the effect of the covariates on this specific mortality. We applied this method to 3843 adult kidney transplant recipients between 1996 and 2009 from the validated DIVAT bank, and we compared the results to a Cox analysis.
Results: Overall DIVAT cohort recipient mortality is 11% at 10 years. Compared with French mortality tables, the excess risk of death related to transplantation is 5%. Males have a risk of overall mortality (HR = 1.52, P = 0.008), but in fact this has no impact on specific transplant-related mortality (HR= 1.2, p=0.427). A more accurate estimation of the risks related to recipient age (HR = 1.63, p = 0.049) is made using the relative survival model rather than the Cox model that over-estimates this relationship for overall mortality (HR = 2.12, $p<0.001$). Interestingly, diabetic recipients are subject to twice the risk of mortality in relation to transplantation (HR= 2.32, p=0.001) meaning that this mortality risk is significantly under-estimated by studying overall mortality (HR = 1.81, p = 0.002). This is also the case for patients with a delayed graft function who have a 22% higher probability of dying from transplant-related causes (HR = 2.12, p=0.001) than the estimated risk for total mortality (HR = 1.73, $p<0.001$).
Conclusion: Relative survival models assess the risk of transplantation status related death more accurately.

RO-268 FIRST WEEK TACROLIMUS LEVEL BUT NOT DELAYED GRAFT FUNCTION PREDICTS 1-YEAR ALLOGRAFT FUNCTION IN RECIPIENTS OF KIDNEYS FROM DONORS AFTER CARDIAC DEATH (DCD)

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Objective: To report our unit's experience of DCD kidney transplantation over the last 5 years and identify factors that may influence outcome.
Methods: Over 5 years, 514 adult renal transplants were performed, of which 80 (15.5%) were DCD. All DCD recipients patients received ATG induction, and low-dose tacrolimus (Tac), MMF and prednisolone maintenance therapy. Data for DCD recipients was collected on allograft function, delayed graft function (DGF) rate and patient and graft survival. Kaplan-Meier estimates were used

to assess survival and binary logistic regression to identify factors associated with DGF.

Results: Median follow-up time for DCD recipients was 29.8 [2-73.8] months. Donor and recipient ages were 47 [17-68] and 51.5 [19-72] years respectively. Median cold and warm ischemic times (CIT, WIT) were 13 [5-27] hours and 17 [8-24] minutes respectively. Median eGFR at 1, 2, 3 and 4 years was 51.5, 53, 49 and 51 ml/min respectively. There were no instances of primary non-function but 55 (73%) patients experienced DGF. Female gender was protective against DGF (OR 0.181, p=0.002), whilst elevated 1st week Tac levels, recipient diabetes, CIT and WIT were not significant predictors of DGF. Patients with lower 1st week Tac levels (average <6 μg/l) had better 1-year graft function compared to those who had levels >6 μg/l (eGFR 59 [31-84] vs 47 [14-95]; p=0.03), but the lower Tac levels did not increase acute rejection (p=0.5). One year (100% vs. 96%) and 3-year (93% vs. 93%) cumulative graft survivals were independent of the occurrence of DGF (Log Rank p=0.85) (Figure 1)

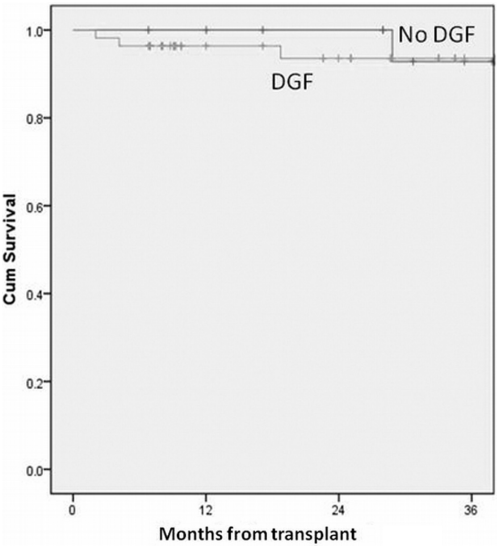

Figure 1

Conclusions: DGF did not affect medium-term graft outcomes in DCD kidney recipients. Initial Tac levels, but not DGF had an adverse effect on 1-year graft function.

RO-269 TRANSPLANT URETERIC STENT TRIAL (TrUST): EARLY VERSUS STANDARD REMOVAL. A RANDOMISED CONTROLLED TRIAL – PILOT DATA

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Introduction: The introduction of transplant ureteric stents (TUS) has significantly reduced the incidence of major urological complications post renal transplant from 9% to 1.5%. However TUS themselves cause complications and optimal time for stent removal has not been established, with no systematic comparison between early (<7 days) and standard removal (1-3 months) yet made.

Methods: A randomised control trial to compare the current standard of cystoscopic TUS removal at 6 weeks to early removal on day 5 (achieved by attaching the stent to the catheter). Primary objective to determine the effect of early TUS removal on stent related complication rates. Adult and paediatric patients ($\geq$2 yrs) listed for either living or deceased donor renal transplant at our centre were screened. Randomisation performed via an online system. Multi-centre ethics approval gained 2009.

Results: From May 2010 - Jan 2011, 36 patients screened for eligibility. 24 met the inclusion criteria, consented and were randomised into trial (early arm n=9, standard arm n=12). No serious adverse events or major urological complications in either arm. Stent complications, n=1 (UTI) in standard arm. Of those allocated to the early arm, 4 did not receive the allocated intervention due to technical difficulties in attaching the stent to the catheter.

Conclusion: It appears feasible to remove TUS on day 5 after transplant without cystoscopy through a non invasive technique with the potential benefits of better patient acceptability, reduced stent complications, reduced costs and resources associated with cystoscopy. This study now has a NIHR Research for Patient Benefit grant and multi-centre recruitment will permit required sample size of 88 patients per group (*80% power, 5% type 1 error with aim of 15% reduction in complications*) to determine safety and benefits of early TUS removal.

RO-270 EFFECTIVENESS OF RENAL TRANSPLANT PRE-ASSESSMENT CLINICS- GLASGOW EXPERIENCE

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Background: Most patients in our unit are listed following a consultation of around 30 minutes with the transplant surgery team which aims to build on prior counselling by specialist nurses, nephrologists and patient self education using sources such as the internet and departmental literature. The study was designed to assess what value was added to patient understanding of kidney transplantation at the surgical transplant assessment clinics.

Methods: A 20 items survey questionnaire in a multiple choice single best answer format was developed and tested for validity. The questions sought to highlight 20 key facts relating to renal transplantation as designed by the clinical team. It included questions (Table 1) covering different aspects of renal transplantation which are discussed with renal patients before including them on transplant waiting list. 31 patients filled the questionnaire before and after pre-transplant assessment clinic and results were analysed to assess the difference in the answers. SPSS 15.0 was used for statistical analysis.

Results: The validation of questionnaire showed an Intraclass Corelation Coefficient 0.79 to 0.98 with 95% confidence interval (CI 0.75-0.99). The transplant clinic created significant difference in understanding 9 topics as shown by the improvement in the result [Table 1]. There ware only 2 questions which were answered correctly by all patients after the clinic.

Table 1 Outcome of pretransplant assessment clinics on the understanding of renal patients waiting for a transplant

Question	Correct answer before clinic, N (%)	Correct answer after clinic, N (%)	P value
What is a kidney transplant?	31 (100%)	31 (100%)	NS
What does the doctor mean by a "clinical trial"?	16 (52%)	13 (42%)	NS
What are the alternative treatments for kidney failure?	28 (90%)	29 (94%)	NS
Is there a risk of death from a kidney transplant?	31 (100%)	30 (97%)	NS
How successful is kidney transplantation?	30 (97%)	29 (94%)	NS
What is a negative cross match test?	9 (29%)	15 (48%)	0.02
How are organs from people who have died allocated for transplantation?	30 (97%)	31 (100%)	NS
How long do you usually have to wait to get a kidney from a donor who has died?	12 (39%)	16 (52%)	0.04
What are the possibilities for having a living donor transplant?	27 (87%)	28 (90%)	NS
Do all kidney transplants work straight away?	19 (61%)	23 (74%)	0.04
Does the patient need to take special tablets after transplant?	28 (90%)	29 (94%)	NS
Will there be side effects after the transplant?	24 (77%)	26 (84%)	NS
What would happen if the patient stopped taking their tablets after transplant?	29 (94%)	28 (90%)	NS
How will the hospital contact the patients once there is a kidney available for them?	24 (77%)	26 (84%)	NS
Does having a kidney transplant affect a patient's chance of getting cancer?	17 (55%)	22 (71%)	0.03
Does having a kidney transplant affect a patient's chance of getting diabetes	18 (58%)	23 (74%)	0.03
How often will the transplant doctors see a patient after kidney transplant?	13 (42%)	21 (68%)	0.001
What does the doctor mean when he talks about a "clinical trial"?	18 (58%)	25 (81%)	0.001
How long will the transplant work for?	22 (71%)	27 (87%)	0.03
What does the doctor mean by "clinical trial" of my kidney transplant?	20 (65%)	24 (77%)	0.04

NS, non significant; student t-test.

Conclusion: The pre-assessment transplant clinics significantly improved the level of understanding of the process of transplantation in patients as regards 9 of the key issues. Some patients still remain confused on certain topics indicating the need for additional reliable information sources. Further studies/analysis will be applied to assess understanding of the same patients at the actual time of transplant. The data will allow the effectiveness of other additional information sources such as DVDs or Transplant Websites to be assessed.

RO-271 TRANSPLANT KIDNEY'S STIFFNESS MEASUREMENT BY ELASTOGRAPHY: A PILOT STUDY

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Background: Interstitial fibrosis and tubular atrophy (IF/TA) development is the major determinant of renal allograft failure but non invasive techniques are still lacking to measure its progression. Transient elastography is a non invasive,

quick and reproducible technique to measure stiffness in liver diseases but it has not been thoroughly evaluated until now in kidney transplantation.
Methods: The goal of this study was to analyze the feasibility and the reproducibility of this technique and its correlation with the histological data of kidney biopsies analyzed according to the Banff 09 updated-classification. Forty nine kidney transplant recipient (KTR) were included in this study.
Results: 43 KTR had both a transplant biopsy and elastography measurement by two radiologists. The median age was 51 years-old (22 female/21 male). The median time between the transplantation and the biopsy was 27 months. The main diagnosis was IF/TA (n=31). The cortical median stiffness value was 24 kPa. The intra-observer and inter-observer variability coefficients were 20% and 12% respectively. We did not observe any correlations between the renal cortical stiffness and any clinical parameters nor any single semi-quantitative Banff score parameters taken separately. However, the sum of the chronic lesions (ct+ci+cv+cg) and the sum of all lesions (i+t+v+g+cpt+ct+ci+cv+cg+mm+ah) were significantly correlated with the renal cortical stiffness (R=0.34, p=0.05 and R=0.41, p=0.03, respectively).
Conclusion: Renal cortical stiffness measurement by elastography is a promising non invasive tool evaluating global histological deterioration. However, it needs to be improved and tested in larger cohorts.

Kidney VIII

RO-272 LIVING DONOR KIDNEY TRANSPLANTATION IN A SINGLE CENTER: 45 YEARS EXPERIENCE

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Background: Living Donors Kidney transplantation is on the increase in an attempt to overcome the discrepancy between available organs and the number of patients awaiting transplantation. Aim was to report long-term results from our center and analyze factors affecting outcomes.
Methods/Materials: 461 consecutive patients operated on between 1963 and 2008; 386 received from related donor. 145/461 transplantations were performed before the advent of calcineurine inibitors (CNIs)-based immunosuppression, 167/461 were preemptive. Data were analyzed using Kaplan-Meier survival plots and Cox proportional hazards regression analysis.
Results: At 1, 5, 10 and 20 years after grafting, overall patient survival was 96%, 91%, 84% and 69%, graft survival 92%, 78%, 65% and 44%, respectively.
The relative risk of rejection was smaller in the group of patients treated with CNIs compared to patients without CNIs (HR: 0.46, 95% CI=[0.3,0.6]). It was not influenced by whether donors were related or unrelated, even when CNI treatment was considered. One and two class I HLA antigen missmatches (HLA-mms) were associated with increased risk of acute rejection of respectively 1.8 (95% CI=[1.1,3.1]) and 2.1 (95% CI=[1.3,3.4]) compared to no class I HLA-mm.
Graft survival was affected by the occurrence of at least one acute rejection episode (HR=2.5, 95% CI=[1.8-3.4]), at least one class I HLA-mm (HR=2.3, 95% CI=1.3,3.9) and, in patients transplanted without CNI treatment (before 1986), by donor abnormal BMI (HR=2.0, 95% CI=1.1-3.9).Patient survival was negatively impacted by at least two class I HLA-mms (HR=2.9, 95% CI=[1.4,6.3]), grafts from unrelated donors (HR=2.3, 95% CI=[1.4,3.8]), and pre-transplant dialysis in patients grafted after 1986 and receiving CNI-based immunosuppression.
Conclusions: Living Donor Kidney transplantation offers markedly extended graft survival over time. CNI treatment has been shown to be a major factor in prevention of acute rejection. Acute rejection and HLA-mm negatively affect graft survival.

RO-273 RENAL DYSFUNCTION IN SPANISH KIDNEY RECIPIENTS UNDER MAINTENANCE

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Background: Renal dysfunction (RD) in renal transplant (RT) patients is a common complication with difficult management. We aim to evaluate clinical approaches to RD in RT patients.
Methods: Observational, prospective, and multicenter study. Adult simple RT recipients under maintenance with RD and ≥24-m post-transplant evolution were enrolled.
Results: 368 patients were included (mean age 55.6±12.9 y, 38.3% women). Mean time since transplantation was 8.2±5.4 y. Baseline mean serum creatinine and glomerular filtration rate (GFR) were 1.63±0.31 mg/dl and 43.6±7.5 ml/min. At inclusion, 41.3% of patients presented 24h-proteinuria >300 mg, 37.0% anemia, 88.9% hypertension and 26.1% diabetes. Despite antiproteinuric, antianemic and antihypertensive baseline therapies in 34.2%, 34.2% and 86.6% of patients, and intensification of them in 66-79% non-controlled patients, 34.7%, 7.6% and 68.6% of individuals don't reach treatment objectives at 6-m. 86.5% of patients remained unchanged for immunosuppressive treatment (IT) during follow-up: CNI (83.4% baseline vs. 79.1% 6-m visit), antimetabolites (79.6% vs. 82.1%) and mTOR-inhibitors (16.9% vs. 17.2%). 28% of patients had ≥10% GFR-worsening. Biopsy was performed on 28 patients (7.6%) with chronic rejection as the most frequent result, and conditioning intervention in 20,9% (mainly IT-change). Multivariate logistic regression model showed that independent predictors of GFR worsening were higher 24h-proteinuria (OR for each mg 1.001, 95%CI 1.000-1.001, p=0.020), and longer time since transplantation (OR for each month 1.009, 95%CI 1.002-1.016, p=0.017). A trend towards negative effect of donor age was detected (OR for each year 1.021, 95%CI 0.996-1.047, p=0.106).
Conclusions: Secondary markers of RD that remain uncontrolled are frequent in RT patients. Differences between clinician perceptions and objective parameters exist in patients' management leading to clinical inertia.

RO-274 MAINTENANCE IMMUNOSUPPRESSION AND LONG-TERM RESULTS OF RENAL TRANSPLANTATION: THE DIVAT DATABASE

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One-year graft survival after renal transplantation has improved as well the rate of acute rejection (AR) has decreased significantly, but improvement in long-term outcomes is controversial. We undertook an analysis of the maintenance immunosuppression with mycophenolate mofetil (MMF, CellCept®) and long-term outcomes after renal transplantation at six French centers. We examined data from the DIVAT database for transplant recipients from January 1996 to September 2010. The DIVAT is the Western Europe cohort of kidney transplanted recipients.
Analyses were conducted on adult (≥18 years), kidney or double kidney as well kidney-pancreas recipients. A total of 7407 evaluable recipients were analyzed. Of these, the immunosuppressive regimen including MPA was initiated in 5988 recipients. MMF was introduced into clinical use in France in 1996. 29% of transplants initiated MMF regimen in 1996, 75% in 2000, and 85% in 2003. In 2010, 87% of patients initiated MPA regimen received MMF. Among recipients started MPA regimen 5344 (90%) were deceased-donor transplants, median recipient age (years) was 49.0 (18.0-84.0), 2296 (38%) patients were female, mean length of follow-up was 4.2±3.3 years; mean ischemic time was 19.2±9.7hrs. DGF defined as the requirement for dialysis during the first week post-transplant was 31%, estimated GFR (ml/min/1.73m^2) was at 3 months 55.8±17.9, at 1 year 56.1±17.2, at 5 years 55.9±16.8, at 10 years 55.6±16.7. Overall AR episode incidence was 27%; patient and graft survival were 88% and 78% respectively at 10 years. The rates of *de novo* malignancy, cardiovascular event, diabetes in this cohort were 8%, 12% and 13%, respectively.
Conclusion: This is the first descriptive analysis of the French large cohort of renal recipients from DIVAT database in regards to immunosuppressive regimen. Further analysis is ongoing to describe the long term outcomes according to the type of immunosuppression.

RO-275 ACTIVATED TUBULAR EPITHELIAL CELLS PRODUCE CHEMOKINES THAT ATTRACT T_H1, BUT NOT T_H17 CELLS

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Introduction: Renal tubular epithelial cells (TECs) play a central role in inflammatory processes during ischemia-reperfusion injury and allograft rejection. Tubulitis is the hallmark of cellular rejection leading to structural graft damage. We hypothesize that TECs modulate the outcome of the inflammatory process by the production of distinct chemokines that determine the attraction and activation of different T-cell subsets. Here, we studied whether TECs af-

ter stimulation by IFN-γ and TNF-α have the potential to attract T_h1 and T_h17 T-cell subsets.
Materials and Methods: TEC cell lines (N=10) were cultured from cortex tissue of human donor kidneys obtained at the time of transplantation and stimulated by IFN-γ (50ng/ml) and TNF-α (20ng/ml) *in vitro* in time dependent manner. Cell surface expression of CD40 and HLA-II were analyzed by 8 colour flow cytometry. Cytokine and chemokines produced by activated TECs were measured using Luminex and/or ELISA.
Results: The combined stimulation with IFN-γ and TNF-α resulted in increased expression levels of the costimulatory molecule CD40 (3 fold increase) and HLA-II (2 fold increase) as compared to non-stimulated state. CD80/CD86 molecules were not detectable on TECs in resting or in activated state. This was observed after 24h stimulation and remained present for at least 72h. The cytokine activated TECs abundantly secreted the pro-inflammatory cytokines IL-6 and IL-8 (5-7 fold increase), while IL-1β and IL-12p70 were not detectable. Moreover, IFN-γ and TNF-α stimulation significantly upregulated the production of the T_h1 ligands RANTES, IP-10 and MIG after 72 hours ($p<0.001$) and not the T_h17 ligand MIP-3α. In addition the T_h17 associated cytokine IL-23 was not measurable.
Conclusion: Our data show that the proinflammatory cytokines IFN-γ and TNF-α stimulate TECs to produce the chemokines necessary to specifically attract T_h1-, but not T_h17 cells.

RO-276 EARLY SURGICAL COMPLICATIONS AFTER 348 SINGLE KIDNEY TRANSPLANTATIONS (KT) FROM HEART-BEATING DECEASED DONORS

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Aims: we evaluated the role of prompt diagnosis, and treatment of all the complications which required re-operation or radiological treatment in the first year after KT, and their impact on one-year patient/graft survival.
Materials and Methods: On a cohort of 504 single KT, we evidenced 145 symptomatic complications (28.77%). 348 patients were male (68%), 156 female (32%), and age was 55±11 years-old. Median time between diagnosis, and treatment has been 4 days (range 1-12).
Results: Vascular complications were 25 (4.96%): 3 cases of arterial thrombosis (0.6%), 11 of vein thrombosis (2.18%), and 2 of concomitant arterial/venous thrombosis (0.4%). Graft nephrectomy was performed in 11 cases. 1/6 cases (1.2%) lost the graft for arterial rupture; in 5 cases, re-operation permitted restoring of the graft function. 3 patients (0.6%) with fungal arteritis, lost the graft. Renal rupture occurred in 3 patients (0.6%) with 2 graft loss. In 31 patients (6.15%) urinary collection required surgical operation (3 graft loss). Conservative approach (pyelostomy, and vesical catheter for a month) was obtained in 2 cases (0.45%). 2 bladder perforations (0.4%) were treated by surgical suture. 10 patients (1.98%) developed symptomatic stenosis/reflux, treated by new ureteral-vesical anastomosis. Since 2004 the position of the ureteral stent in all cases permitted a reduction of urinary tract complications (6.6% vs 3.9% respectively, P 0.001). Stenosis of the ureteral-vesical-anastomosis after stent removal occurred in 1.3% of patients; resolution was always obtained by pyelostomy, and anastomosis dilatations. Symptomatic lymphoceles occurred in 61 patients (12.10%). Intestinal complications occurred in 13 cases (2.6%), with 3 acute pancreatitis (0.6%).
Conclusions: Regardless of the type of complication urological or vascular in nature, one year patient and graft survival was 95.7%, and 85.3% respectively, similar to non-complicated patients, 96.8%, and 87.9% respectively (P 0.04).

RO-277 ASSOCIATION BETWEEN EARLY CHANGES IN CHRONIC KIDNEY DISEASE STAGE FOLLOWING KIDNEY TRANSPLANTATION AND GRAFT SURVIVAL

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Introduction: Renal function (RF) one year after kidney transplant has been shown to be a strong predictor of graft survival (GS). This study characterizes the relationship between early changes in post-transplant RF and GS.
Methods: Adult Medicare beneficiaries in the United States Renal Data System who received a kidney-only transplant 01 January 2001-31 December 2008 were eligible for inclusion. RF, by estimated glomerular filtration rate (eGFR), was calculated by the MDRD equation at hospital discharge and 6 months. CKD stage was defined by the National Kidney Foundation. GS was estimated using the life-table method. Hazard ratios (HRs) for graft failure (GF) and 95% CIs were estimated using Cox hazards model.
Results: Study patients (n=84,819) were 61% male, 29% Black, with mean age 50 years. Median follow-up was 4 years. At discharge, 82,277 patients were alive with a functioning graft. Of these, 4.5%, 18.0%, 38.1%, 18.5%, and 20.9% were at CKD stages 1 through 5, respectively. Change in CKD stage from discharge to 6 months post-transplant and 4-year GS is shown in Table 1. Patients in CKD stage 2 through 4 at discharge who had a one stage worsening in CKD stage by month 6 were at greater risk of GF at 4 years. Patients who moved from CKD stage 3 to 4 were at increased risk of GF (HR=2.95 [2.66 - 3.26]) with 29% lower GS (83% vs. 54%) at 4 years.

Table 1. Association between Change in CKD Stage (Discharge to Month 6) and Graft Survival

CKD Stage at Discharge	CKD Stage at Month 6	Graft Survival at 4 Years (%)	Hazard Ratio	95% CI for Hazard Ratio
Stage 1 (n=3,745)	Stage 1	87	1.000	
	Stage 2	88	0.893	0.734–1.088
	Stage 3	79	1.472	1.175–1.845
	Stage 4	47	4.966	2.761–8.932
	Stage 5	44	5.124	2.103–12.480
Stage 2 (n=14,775)	Stage 2	87	1.000	
	Stage 3	83	1.311	1.034–1.662
	Stage 4	46	5.387	3.918–7.406
	Stage 5	23	16.244	9.323–28.301
Stage 3 (n=31,350)	Stage 3	83	1.000	
	Stage 4	54	2.946	2.311–3.754
	Stage 5	24	8.156	5.901–11.271
Stage 4 (n=15,251)	Stage 4	54	1.000	
	Stage 5	26	2.826	2.008–3.979

Stage 1: eGFR $\geq$90; Stage 2: 60 $\leq$ eGFR $\leq$ 90; Stage 3: 30 $\leq$ eGFR $\leq$ 60; Stage 4: 15 $\leq$ eGFR $<$ 30; Stage 5: eGFR $<$15.

Conclusion: A one-stage worsening in CKD stage by month 6 is associated with increased risk of GF at 4 years; a transition from stage 3 to 4 is associated with a 3-fold increase in GF and 54% GS. These results have important implications for management strategies targeted at preserving RF in the early post-transplant period.

RO-278 VITAMIN B6 AND IMMUNITY IN ELDERLY KIDNEY TRANSPLANT RECIPIENTS

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Vitamin B6 belongs to micronutrients involved in regulation of the immune response. The elderly, as well as patients with impaired renal function are especially susceptible to vitamin B6 deficiency. However, vitamin B6 status, and its influence on immunity markers have not previously been investigated in the elderly kidney recipients.
The study aimed to determine vitamin B6 status in elderly (age $\geq$ 60 years) and younger recipients of allogeneic kidney graft and to investigate associations between vitamin B6 status and immunity markers.
We recruited 34 kidney allograft recipients (17M/17F) and allocated them into two groups; patients with age over 60 years (18 patients) and younger patients (16 patients).Plasma levels of pyridoxal 5'-phosphate (PLP), pyridoxal (PL), pyridoxine (PN), pyridoxamine (PM), pyridoxamine 5'-phosphate (PMP) and 4 pyridoxic acid (4-PA) were determined by HPLC method. Measured immunity markers were: serum cytokines (IL6, IL10 and TGFβ), levels of T lymphocyte subsets and the proliferative ability of peripheral blood mononuclear cells (PBMC).
Concentrations of all vitamin B6 vitamers in plasma (PLP, PL, PMP, PM, PN, 4PA) were comparable in the two studied groups. There were no cases of PLP deficiency in the study population, but 29% of patients had PLP concentrations above the upper reference limit. There was no difference in immunity markers according to age. However, the plasma concentrations of vitamin B6 vitamers were inversely associated with levels of CD28+ lymphocyte subsets, as well as with the proliferative response of PBMC in both groups.
Whereas we - unexpectedly - did not find any case of vitamin B6 deficiency among kidney allograft recipients, not even in recipients aged 60 years and over, the observed inverse links between vitamin B6 vitamers and markers of cellular immunity suggest that vitamin B6 status should be further investigated in kidney allograft recipients.

RO-279 PERIODIC LIMB MOVEMENT IN SLEEP IN WAITLISTED DIALYZED AND KIDNEY TRANSPLANTED PATIENTS

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Background: Periodic Limb Movements in Sleep is prevalent among dialyzed patients and it is associated with increased risk of mortality. Our study aimed to determine the prevalence of this disease in a sample of transplanted and wait-listed hemodialyzed patients.
Methods: 100 transplanted and 50 wait-listed patients underwent polysomnography. Mild and severe disease were defined as Periodic Limb Movements in Sleep Index (PLMSI) higher than 15 and 25 events/hour, respectively. The ten-year coronary heart disease risk was estimated for all patients using the Framingham Score. Moreover, the ten-year estimated risk of stroke was calculated according to the modified version of the Framingham Stroke Risk Profile.
Results: Disease was present in 27% of the transplanted and 42% of the wait-listed group (p=0.094); the proportion of severe disease was twice as high in wait-listed versus transplanted patients (32 vs. 16%, p=0.024). Patients with severe disease had higher ten-year estimated risk of stroke in the transplanted group (10 (7-17) vs. 5 (4-10); p=0.002) and higher ten-year coronary heart disease risk in both the transplanted (18 (8-22) vs. 7 (4-14); p=0.002), and the wait-listed groups (11 (5-18) vs. 4 (1-9); p=0.032). In multivariable linear regression models the PLMSI was independently associated with the Framingham cardiovascular and cerebrovascular scores after adjusting for important co-variables.
Conclusions: Higher Periodic Limb Movements in Sleep Index is an independent predictor of higher cardiovascular and cerebrovascular risk score in patients with chronic kidney disease. Severe Periodic Limb Movements in Sleep is less frequent in kidney transplant recipients compared to waitlisted dialysis patients.

RO-280 LIVE DONOR KIDNEY TRANSPLANTATION IN THE LIMITED RESOURCE SETTING; PREDICTORS OF ALLOGRAFT SURVIVAL

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Introduction: The renal transplant program in Sri Lanka is still in its infancy, consisting of primarily Live Donor Renal Transplants (LDRT). In this study we have looked at our results in the limited-resource setting with emphasis on possible predictors of graft outcome.
Material and methods: A prospective analysis of all LDRT performed between July 2006 and April 2010 was carried out. Recipient age, donor age, degree of HLA mismatch, duration of pre-transplant dialysis, incidence of acute rejection and post-transplant CMV infection were studied in a multivariate logistic regression model.
Results: 248 consecutive LDRT were performed during this period. Follow-up data was complete in 239 (96.4%). Mean follow-up was 18 (5-50) months. The mean recipient and donor ages were 41 (17-68) and 38 (20-60) years respectively. Overall patient survival was 227/248 (92%). The causes of death were sepsis (17), myocardial ischaemia (2), stroke (1) and pulmonary embolism (1). There were 17 (7%) Graft Failures (GF); 12 primary and 5 secondary GF (mean graft survival 9 months). Pre-transplant dialysis beyond 12 months (p=0.02), HLA mismatch over 50% (p=0.03) and biopsy proven acute rejection (p=0.02) were found to be independent predictors of GF on multivariate analysis. Donor age, recipient age and CMV infection failed to show a significant relationship to GF.
Conclusion: In a limited resource setting, we have achieved acceptable results comparable to centers elsewhere. Reduction in waiting times and better HLA match with deceased donor transplants and possible paired donation programs may help to improve the results further.

RO-281 RATES OF DELAYED GRAFT FUNCTION IN KIDNEY ALLOGRAFTS IS SIGNIFICANTLY ASSOCIATED WITH A FALL IN TARGET ARTERIAL BLOOD PRESSURE

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Background: DGF is a major issue in kidney transplantation and is associated with reduced graft and patient survival. Many underlying factors are not modifiable but reducing cold ischaemic time and machine perfusion, have improved the DGF incidence. Peri/post-operative perfusion is also critical to the development of DGF. We investigate the affect of perioperative hypotensive episodes and other key donor and recipient variables on the incidence of DGF.
Methods: DGF was defined as dialysis in the first week post transplant or failure of creatinine to fall by 50% post transplant. Post operative management targeted a CVP of >8cm H20 and MAP of >100mmHg. 189 consecutive renal transplants were performed. Data was prospectively collected for all patients in an electronic database and supplemented by clinical records. Analysis for factors associated with DGF was by univariate and multivariate logistic regression analysis (SPSS).
Results: The occurrence of any recorded sub-target ABP episode was significantly associated with DGF (Odds ratio 2.63 p=0.04). The occurrence of sub target CVP levels was not, as was the use of ACE inhibitors in the recipient prior to implantation amongst other factors. Of the donor variables, only deceased donor kidneys were significantly associated with DGF whilst donor age and cold ischaemic time approached significance.
Conclusions: Most renal transplants are managed post-operatively outside critical care with intermittent CVP and limb blood pressure monitoring but routine continuous blood pressure monitoring is rare post operatively. Since a fall in MAP below target levels was associated with an increased risk of DGF whilst a fall below target CVP was not, invasive ABP monitoring may be more accurate than CVP in assessing renal perfusion and guiding fluid/inotrope management.

Immunobiology / basic science II

RO-282 SOLUBLE INTERLEUKIN-2 RECEPTOR INHIBITS CD4+ T CELL ACTIVATION AND MAY REPRESENT A NOVEL THERAPEUTIC AGENT FOR TRANSPLANTATION

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Introduction: Allospecific T cell expansion is dependent on IL-2 binding to membrane bound IL-2R. Soluble (s)IL-2R may competitively inhibit this process. The aim of this study was to; 1) determine sIL-2R concentration following heart transplantation (HTx), and 2) assess if sIL-2R selectively inhibits IL-2 mediated T cell activation *in vitro*.
Methods: n=70 HTx recipients were recruited into the study. Acute rejection was diagnosed by a consultant histopathologist and graded according to ISHLT guidelines. Using a bead array based assay, IL-2 and sIL-2R were quantified in peripheral blood. A series of *in vitro* cultures were also produced with peripheral blood mononuclear cells exposed to varying doses of sIL-2R. Cultures were performed in triplicate with superantigen, IL-2 or without stimulation. Cytotoxic and naive/memory helper T (Th) cells were quantified via flow cytometry.
Results: sIL-2R negatively correlated with IL-2 concentration (p=0.014, co-ef -0.724) *in vivo*. Stable HTx recipients had significantly higher levels of sIL-2R than patients with acute rejection (p=0.024). *In vitro*, high dose sIL-2R significantly decreased CD3+CD4+ (p=<0.001) and CD4+CD45RO+ memory T cell (p=<0.001) numbers compared with control. This effect was not ameliorated by administration of excess IL-2 (p=<0.001 and p=0.002 for CD4+ and memory T cells respectively). No significant effect was observed on cytotoxic T cell number.
Discussion: IL-2 is required for T cell activation following antigen binding to the TCR. In the transplant setting, this process occurs following allorecognition, and induces immunologic memory and ultimately, graft rejection. We demonstrate that *in vitro*, sIL-2R outcompetes CD4+ T cell membrane bound IL-2R, impeding clonal expansion. *In vivo*, sIL-2R is associated with clinical stability in HTx recipients. Potentially, sIL-2R may represent a CD4+ T cell specific immunomodulatory agent with potential therapeutic benefit in transplantation.

RO-283 INTERSTITIAL C4d, ANTI-HUMAN LEUKOCYTE ANTIBODIES (Anti-HLA) AND DONOR SPECIFIC ANTIBODIES (DSA) IN LIVER TRANSPLANTATION (LT): ROLE OF EARLY AND LATE GRAFT DYSFUNCTION

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Introduction: C4d deposition is implicated in antibody mediated rejection, and recent interest is focused on humoral mechanisms amounting to graft dysfunction following liver LT. Objective of this study was to investigate evidence for these in a cohort of patients receiving LT.
Method: C4d immunostaining of Menghini liver biopsies of 41 (DBD, n=27; DCD, n=14) grafts, obtained during cold storage (t-1) and reperfusion (t0) was semi quantitatively scored. Recipient serum samples obtained prior LT were pre-screened for anti-HLA, and positive sera were tested for HLA specificity by Luminex method and recorded as MFI units. These were compared against donor HLA types to identify DSA and the clinical course was studied.
Results: Significantly increased C4d in peri-portal, peri-venular and peri-lobular hepatocytes were seen in t0 compared t-1 biopsies ($p<0.05$) in 34 liver grafts. None demonstrated peri-sinusoidal or portal capillary microvascular staining. Nine (9/41; 22%) were positive for anti-HLA Class I(CI)/II(CII) confirmed by Luminex, all were positive for C4d., whereas C4d without anti-HLA was seen in 25/34 (73%). Only 03/41 (7%) sera contained DSA at the time of transplant. One patient was positive for both CI (Anti-B60; >6000) and CII (anti-DR4; >4000). Significant graft dysfunction followed and a biopsy on day 8 showed acute cellular rejection with weak C4d staining of portal microvasculature. Graft function stabilised after 3 weeks following standard anti-rejection therapy. At 14 months post-LT graft confirmed late rejection. Other two recipients showed only CI antibodies without significant post operative sequelae.
Conclusion: This limited data suggests subclinial hyperacute rejection is not common in t0 biopsies of patients with preformed DSAs, with C4d staining dead hepatocytes related to preservation-reperfusion injury. Impact of preformed DSA on short and long term graft dysfunction is so far not clearly understood, our data demand for explicit studies.

RO-284 INTRAGRAFT Foxp3+Tregs IN PROTOCOL BIOPSIES IS A PROTECTIVE BIOMARKER FOR KIDNEY ALLOGRAFT OUTCOME

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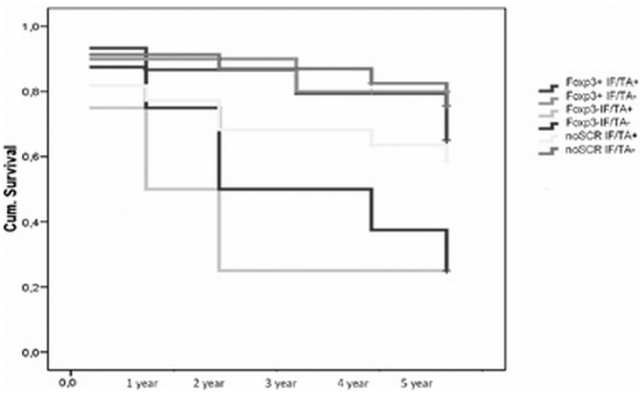
Introduction: Presence of subclinical rejection (SCR) with IF/TA in protocol biopsies of renal transplant recipients has been shown to be an independent predictor factor of graft loss. Also, presence of intragraft Foxp3+Tregs in patients with SCR has been suggested to differentiate harmful from potentially protective cellular infiltrates. Nonetheless, whether presence of Foxp3Tregs in patients with SCR and IF/TA may potentially protect from a deleterious graft outcome has not yet been evaluated.
Methods: This is a case-control study in which 37 patients with the diagnosis of SCR and 68 control patients with absence of any cellular infiltrate at 6-month protocol biopsies matched for age and time of transplantation (1998-2003) were evaluated.



Results: We first confirmed that intragraft Foxp3-expressing T cells in patients with SCR positively correlates with Foxp3 demethylation at the Treg-specific demethylation region. Patients with SCR without Foxp3+Tregs within graft infiltrates showed significantly worse graft function evolution than those with SCR and Foxp3+Tregs and that patients without SCR from 2 until 5 years of follow-up ($p<0,05$ in all time points). When presence of SCR and IF/TA were assessed together, presence of Foxp3+Treg could discriminate a subgroup of patients showing the same graft outcome as patients with a normal biopsy. Logistic-regression curve estimates achieving eGFR< 40 ml/min in patients with neither IF/TA nor SCR, those with SCR and presence or absence of Foxp3+ and presence or absence of IF/TA.
Conclusion: Presence of Foxp3+Tregs in patients with SCR, even with IF/TA, is associated with a favourable longterm allograft outcome.

RO-285 CD26 – INHIBITION RECRUITES REGENERATIVE STEM CELLS VIA SDF-1 – CXCR4 AXIS AND IMPROVES ISCHEMIA-REPERFUSION INJURY IN THE MOUSE MODEL OF LUNG TRANSPLANTATION

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Background: CD26 is a transmembrane glycoprotein that is constitutively expressed on activated lymphocytes and in pulmonary parenchyma. This molecule possesses a catalytic domain (dipeptidyl peptidase IV, DPP4) that cleaves a host of key biologically active peptides. Here, we aimed to identify an important substrate of CD26/DPP 4 – stromal cell-derived factor 1 (SDF-1) – which functions as a key modulator for stem cell homing together with its receptor CXCR4 in response to lung ischemia-reperfusion (I/R) injury.
Methods: Orthotopic single-lung transplantation (Tx) was performed between syngeneic C57BL/6 mice. Inhibition of CD26/DPP 4 in recipients was achieved using vildagliptin sc. 6 hours ischemia time was applied to induce I/R prior to implantation. Histology, ELISA for SDF-1, and fluorescent activated cell sorting for its receptor CXCR4, and for markers of regenerative progenitor cells were assessed in Tx lungs upon CD26/DPP IV-inhibition.
Results: Compared to untreated Tx grafts, systemic CD26/DPP IV-inhibition of Tx-grafts resulted in an increase of protein-concentrations of SDF-1 in plasma (1347 vs. 1176 pg/ml), lung (740 vs. 611 pg/mg), and spleen (1726 vs. 1545 pg/mg). Concordantly, the fluorescence intensity (MFI) of CXCR4 rose in blood (46.9 vs. 24.3) and in lung (74.4 vs. 60.2) when compared to WT. CD34 and the regenerative stem cell marker c-kit showed enhanced MFI in CD26/DPP IV-inhibited blood and transplants compared to WT. Histology and immunohistochemistry of inhibited grafts revealed less recruitment of immune cells compared to Tx-lungs alone.
Conclusion: Less degradation and enhancing of the SDF-1 – CXCR4 axis through CD26/DPP IV-inhibition increased progenitor cells capable for recovering of I/R lung injury. Stabilization of endogenous SDF-1 may be a promising strategy to intensify sequestration of regenerative stem cells, emerging as a novel therapeutic concept.

RO-286 DIRECT CYTIKINE MEASUREMENT IN URINE AND PLASMA IN A RAT MODEL OF CHRONIC KIDNEY REJECTION

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Although there is no guarantee that a more or less of mRNA also leads to increased or reduced expression of a protein, up to now in the Fisher to Lewis rat kidney chronic rejection model (CR) cytokines were mostly indirectly measured as cytokine expression in tissues by RT-PCR. Even if the protein is expressed, its concentration may not correlate with its activity. Reasons include but are not limited to translational modifications, reaction with oxygen radical and allosteric regulation. Recently, a novel "direct" cytokine measurement tool for rat urine and plasma samples based on antibody-beads-Luminex™-technology has become commercially available. We present first results of sequential urine and plasma cytokine analysis during the development of experimental chronic kidney rejection.
Using the well established Fisher to Lewis chronic kidney rejection model, 24-h-urine and plasma samples of 10 rats (250-300g BW at transplantation) were collected pre-transplantation and every two weeks post-transplantation over a 6 months period.
500µl of urine samples were concentrated by centrifugation whereas 25 µL of

plasma samples were diluted five times, as described by the manufacturer recommendations. Luminex™ assays for the following cytokines were performed: IFN-g, IL-10, IL-12, IL-18, IL-1a, IL-2, IL-4, IL-6, MCP-1, RANTES, TNF-a.
Histological analysis revealed clear signs of CR at time of harvest 6 months post-transplantation.
Significant differences in Cytokine excretion over 24 h in urine compared to pre-transplantation were found for IL-18, IL-1a, RANTES and MCP-1. Plasma levels of IL-18, IL-1a, IL-2, RANTES and MCP-1 also showed significant differences vs. pre-transplantation.
Although not every tested cytokine could be satisfyingly detected in urine and plasma, the above-mentioned inflammatory macrophage and T-Lymphocyte cytokines were easily measurable with minimal sample volumes. Direct non-invasive cytokine measurement may lead to an easier and more accurate monitoring of kidney allografts.

RO-287 HISTONE DEACETYLASE INHIBITION REVEALS A POTENT IMMUNOSUPPRESSANT EFFECT IN AN *IN VITRO* MODEL OF TRANSPLANTATION

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Background: Current renal transplant immunosuppression regimens have numerous, well documented limitations. Recent evidence suggests Histone Deacetylase Inhibitors (HDACis) may represent an immunosuppressive class of drugs with potential application toward transplantation. This study compares the non-selective HDACi suberoylanilide hydroxamic acid (SAHA) and a novel HDAC6-specific inhibitor KAR3000 with Cyclosporine (CyA) in an in vitro model of alloreactivity.
Methods: Peripheral blood mononuclear cells (PBMC's) from healthy volunteers were cultured in a mixed lymphocyte reaction (MLR) assay in the presence of immunosuppressive compounds. Alloreactivity was assessed by IFN-γ release.
Results: The effect of experimental compounds on IFN-γ production by alloreactive T cells was assessed in a standardized MLR. As expected CyA displayed a potent inhibitory effect at concentrations used (Figure 1). However, the HDACi compounds displayed the most potent inhibitory effect, reducing IFN-γ release by 82% and 91% (SAHA and KAR3000 respectively at 1μM concentration). Dose response curves were generated for each of the three compounds which reveal IC50 of 567nM, 13nM and 82nM for CyA, SAHA and KAR3000 respectively (Figure 2).
Conclusions: HDACis represent a novel class of potent immunosuppressant therapeutics with application toward transplantation. Those that are currently used clinically are generally safe and well tolerated. These data support the hypothesis that HDACis have a role in transplantation and are likely to mediate their effect by inhibiting the alloreactive $CD4^+$ T cell subset.

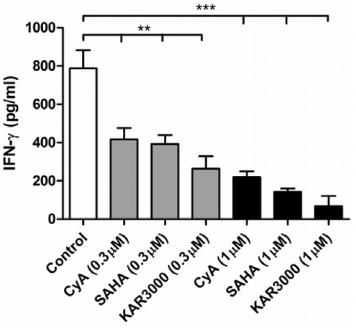

Figure 1

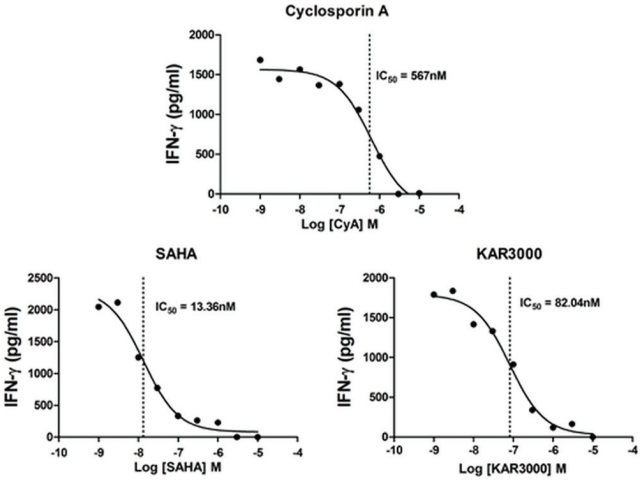

Figure 2

RO-288 CHARACTERIZATION OF CD4+ NKG2D+ T LYMPHOCYTES IN KIDNEY TRANSPLANT PATIENTS. IMPLICATIONS IN THE OUTCOME OF THE TRANSPLANTATION

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The NKG2D activating receptor is expressed on γδ T, αβ CD8+ T, NKT and all NK cells but not on CD4+ T cells. However, under certain circumstances, such as infections, autoimmune diseases or tumors, an anomalous expression of NKG2D on CD4+ T cells can be detected. Flow cytometric analysis of NKG2D expression on CD4+ T lymphocytes from several transplanted patients (kidney, heart, liver) and healthy donors revealed that kidney and liver transplanted patients presented an unusual subset of CD4+ NKG2D+ T lymphocytes (41.0% and 27.6% respectively) whereas only in a negligible number of heart transplanted and control donors this cell type could be detected.
Whole genome microarray expression studies were performed with this CD4+ NKG2D+ T cell population compared to CD4+ NKG2D- T cells in order to determinate its phenotypic and functional characteristics. Furthermore, functional analyses using Gene Ontology annotations were conducted in order to identify molecular pathways that exhibit activation or repression in this cell type.
Functional analysis showed that several pathways associated with immune response, apoptosis, inflammatory response and cellular catabolic processes were significantly affected. Examination of costimulatory molecules and specific cytotoxic cell markers as well as apoptosis-related molecules showed that the CD4+ NKG2D+ T cells in the kidney and liver transplanted patients represented a highly differentiated T cell subset with cytotoxicity ability and apoptosis resistance.
The presence of NKG2D in CD4+ T cells from transplanted patients could be used determine the outcome of the allograft and predict the immune response in these patients.
The identification of biomarkers to predict the allograft outcome and immune response in transplanted patients is decisive to decrease the current transplantation failure.

RO-289 EFFECTS OF ANTIBODY TO HUMAN LEUKOCYTE ANTIGEN (HLA) ON VON WILLEBRAND FACTOR (VWF) SECRETION FROM ENDOTHELIAL CELLS

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Antibody Mediated Rejection (AMR), caused by the presence of alloantibody on microvessels of the graft, is thought to lead to cardiac allograft vasculopathy (CAV). It has been suggested that antibodies to HLA bind to class I molecules on the surface of endothelial cells (EC) and stimulate the release of von Willebrand Factor (VWF) from pre-formed organelles the Weibel Palade Bodies (WPBs) and this may underlie thrombosis and inflammation in the graft.
Here we investigated the effect of antibodies against HLA class I (W6/32) and class II (L2; anti-DQ and L243; anti-DR) molecules on the release of VWF from primary Human Umbilical Vein EC (HUVEC), Human Aortic EC (HAEC) and Human Heart Microvascular EC (HHMEC). The kinetics and extent of WPB exocytosis were analysed directly using high-speed live cell imaging in HAEC expressing the WPB specific marker Proregion-EGFP (VWF-propolypeptide-EGFP). HAEC were Fura-2 loaded allowing simultaneous visualisation of changes in $[Ca^{2+}]_i$ with WPB exocytosis.
Proregion-EGFP expressing HAEC evoked increases in $[Ca^{2+}]_i$ and WPB exocytosis in response to histamine. There was no effect of pre-exposure (5-10 minutes) of HAEC to 10μg/ml W6/32 on the kinetics or extend of histamine-evoked WPB exocytosis. During exposure to vehicle, W6/32 or control antibody alone, irregular Ca^{2+} spiking was detected in about 30% of cells studied however there was no evidence of WPB exocytosis. Similarly, assayed by ELISA, a 1 hour incubation of HUVEC or HHMEC with 10μg/ml W6/32, L2 or L243 did not evoke significant release of VWF.
These data shows that short-term exposure to anti-HLA class I or class II antibodies does not elicit significant WPB exocytosis or VWF secretion from the

ECs studied here and does not modify the time-course of exocytosis evoked by the physiological secretagogue histamine.

RO-290 INTESTINAL BIOLOGICAL SCAFFOLDS FOR TRANSPLANTATION

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Background: Treatment of numerous diseases is limited by the inability to replace diseased tissue. Tissue engineering forms a potential solution by the theoretical production of functional replacement tissue. In transplantation, such treatments could reduce waiting lists and if engineered using recipient cells, negate the need for immunosuppressants.
Gastrointestinal diseases may necessitate surgical removal of parts of the intestine. Patients may develop post- colectomy or short bowel syndromes (SBS). Transplantation is the only curative treatment for SBS but is associated with high morbidity and mortality. This justifies the search for an alternative form of treatment such as use of biological scaffolds for cell seeding and transplantation.
Methods/Materials: A series of pigs underwent heart beating retrieval of colon under general anaesthetic. Grafts were removed with vascular arcades preserved. Thrombolysis and routine organ preparation were performed. Grafts were decellularised via vascular and colonic lumens using peristaltic pump perfusion with a series of enzymes and detergents. The resultant decellularised extra- cellular matrix (ECM) scaffold was analysed by H&E and picrosirius staining to assess cellularity and ECM architecture respectively. Following establishment of a suitable decellularisation protocol, future ECM scaffolds were transplanted to assess properties post- perfusion. Transplanted specimens were explanted within one hour and subjected to analysis as described above.
Results: Grafts were successfully decellularised as demonstrated by H&E staining where intact cells were absent. Successfully decellularised specimens demonstrated a variable amount of preservation of ECM architecture on picrosirius staining. Transplantation of ECM scaffolds was technically feasible and successfully performed with resultant perfusion. Graft survival was limited by thrombosis.
Conclusion: Large animal intestine can be decellularised with intact vasculature allowing successful ECM scaffold transplantation. This work suggests that graft thrombosis may be a limiting factor in graft survival and should be addressed as the model develops further.

RO-291 MELATONIN INDUCES T CELL PROLIFERATION AND IL-10 PRODUCTION IN VITRO

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Introduction: The nocturnal hormone melatonin has defined roles in circadian rhythm regulation. Recent studies suggest melatonin induces the commitment and polarisation of T cells, by an as yet unknown mechanism. The clinical application of this in the transplant setting is certainly relevant, yet research remains limited. This study was designed to assess the effects of melatonin on T cells in culture.
Methods: Peripheral blood was collected from 40 heart and lung transplant recipients. PBMC were isolated and cultured for 4 hours with low dose (10pg/ml), high dose (300pg/ml) or no melatonin. In n=20 samples, T cell subsets were identified via cell surface characterisation of: CD3, CD4, CD8, CD25, CD45RA/RO, CD107a and CD127. In the remaining n=20 samples, IFNγ and IL-10 secretion was quantified via ELISpot. A negative control was included for comparison.
Results: Melatonin co-culture was associated with increases in CD3+CD8+, CD3+CD45RA-/CD45RO+ and CD8+CD45RA-/CD45RO+ populations (p=0.005, p=0.030, p=0.011 respectively). Melatonin induced the upregulation of CD45RO expression on CD4+ memory T cells (p=0.008). However, melatonin did not affect regulatory T cells in this culture model. Melatonin induced mass secretion of IL-10 from PBMCs (p=$<$0.001), which was approximately 30x greater than IFNγ. There were no significant differences between high and low dose melatonin culture and IL-10 or IFNγ secretion (p=0.101 and p=0.410 respectively).
Conclusion: Melatonin induces proliferation of memory and effector cytotoxic T cells, upregulates IL-10 production, yet elicits no effect on regulatory T cells *in vitro*. If these findings are reproducible *in vivo*, melatonin may represent an important molecule involved in the pathogenesis of graft rejection. Furthermore, our data may indicate that administration of immunosuppression during the night may have beneficial effects on clinical outcome.

Composite tissues and xenotransplantation

RO-292 SIMULTANEOUS BONE MARROW TRANSPLANTATION PREVENTS TRACHEAL ALLOGRAFT OBLITERATION IN RATS

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Backround: As composite tissue transplantation, tracheal transplantation is a challenge because of the lack of proper vascularisation and early obliterative airway disease (OAD) developpement. The present study examines whether simultaneous vascularized bone marrow transplantation (VBMTx) allows acceptance of orthotopic tracheal allografts and prevents the formation of OAD.
Materials: Group 1 (n=15) included allogenenic tracheal allografts (ATA) from Brown Norway rats (BN) which were grafted orthotopically to Lewis rats (Lew). In group 2 (n=15) ATA from BN were grafted into Lew with simultaneous heterotopic upper limb transplantation into neck region. Both of these groups were administered 7 mg/kg per os of ciclosporin A for 3 days after transplantation. Grafts were harvested after 2, 7, 14, 30 days post-transplantion for histologic evaluation.
Results: In group 1, airway epithelium was rapidly destroyed and OAD progressed with complete luminal occlusion in 30 days. Group 2 maintained a patent airway with intact epithelium 30 days after transplant with absence of graft versus host disease.
Conclusion: Simultaneous VBMTx in tracheal transplantation can prolong survival graft and prevents OAD. Further investigation may verify this approach to be applicable for the prevention of post-transplantation OAD.

RO-293 VASCULARIZED BONE MARROW TRANSPLANTATION AS AN ALTERNATIVE TO CONVENTIONAL CELLULAR BONE MARROW TRANSPLANTATION

Andra-Elena Petrascu[1], Dragos Zamfirescu[2], Ioan Lascar[2]. *[1]Faculty of Medicine, Carol Davila Medicine and Pharmacy University, Bucharest, Romania; [2]Plastic and Reconstructive Surgery, Floreasca Emergency Hospital, Bucharest, Romania*

Backround: Bone marrow transplantation is routinely used for treatment of hematologic diseases, genetic disorders and autoimmune diseases. Vascularized bone marrow transplantation (VBMT), in comparison with conventional marrow transplants, has the advantage of providing a microenvironment and immediate engraftment of both mature and progenitor hemopoietic cells at the time of transplantation in the absence of immunomodulation or irradiation. We aimed to study the applicability of the vascularized bone marrow transplant as an alternative to conventional bone marrow cells suspension transplantation (BMCT).
Methods: Group 1 (n = 10) included Lewis rats (LEW) which received a heterotopic Brown Norway (BN) hind limb. In group 2 (n = 10), from BN, 5×10^7 bone marrow cells in suspension were given intravenous to LEW rats. Cyclosporine A was given in a dose of 17 mg/kg per os for 60 days. Cellular microchimerism assessed by cytometric analysis was investigated in recipients of VBMT versus BMCT.
Results: Donor-derived cells could be detected in VBMT recipients at 30 and 60 days but not in recipients of intravenous bone marrow cells suspension grafting.
Conclusion: VBMT would function in a superior manner compared with conventional cellular marrow transplantation. It may be possible to develop a new approach for bone marrow transplantation based primarily on a microsurgical procedure (transplantation of vascularized bone marrow flaps).

RO-294 ESTABLISHING A CLINICAL HAND TRANSPLANT PROGRAM

Hatem Amer, Nadine Rynerson, Lynette Fix, Ellen Casey, Mary K. Schwab, Bridget F. Avikanen, Charles B. Rosen, Brooks S. Edwards, Keith A. Bengtson, Mike A. Morrey, Sheila G. Jowsey, Thomas R. Schwab, Brian T. Carlsen, Stephen L. Moran, Stephanie Stewart. *William J von Liebig Transplant Center, Mayo Clinic, Rochester, MN, USA*

Introduction: The outcomes of hand transplantation have been encouraging. The purpose of this report is to describe the development of a clinically approved hand transplant program in the United States.

Methods: Our institution has 9 hand and microvascular surgeons who routinely perform reattachments. We also have an transplant center with 8 organ specific transplant program performing > 600 transplants annually. Expertise was pooled from the various organ systems and across the institution and local organ procurement organization.
Results: Groups met over 24 months, including bioethicists. The first task was to assess the need for hand transplantation in our community. Secondly, was to assess available outcome data of both hand transplants and immunosuppression to allow patients to make an informed decision. Next was to ensure that all the necessary resources were in place and trained including early and continuos discussion and collaboration with the local organ procurement organization. Patient education material including educational brochures, videos and animation clips were created. The evaluation consists of a phone screen, two phase clinical evaluation separated by 3 months as a cooling off period. These include extensive medical and surgical evaluation to attempt to quantify the risk of immunosuppression, the support structure of the patient and whether there are other options other than transplantation that would achieve the patient's goals.
Conclusion: Hand transplantation is a natural extension of clinical practice and should be offered as an option in the spectrum of rehabilitation for severe upper extremity trauma in selected patients if there is the necessary expertise. Important and limiting factors in offering this option is the need for immunosuppression and intense physical therapy. In well selected individuals it may however be the only way of restoring reasonable quality of life.

RO-295 ANTI-CLASS II HUMANIZED ANTIBODY, IMMU-114 ATTENUATES HUMAN TO BOVINE XENOGENEIC IMMUNE RESPONSE

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Background: IMMU-114 is an anti-Class II-DR humanized monoclonal antibody that is of interest for the treatment of GVH disease. In this study, we evaluated the effect of IMMU-114 in a human/bovine xenogeneic mixed lymphocyte reaction (MLR).
Methods: Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy volunteers (n=5), and were prepared for responders of MLR. Bovine PBMCs were isolated from Japanese Black Cattle, were inactivated by irradiation (30 Gy), and were prepared for stimulators of MLR. Responders were co-cultured with stimulators for 7 days, in the presence of control antibody (Control) or IMMU-114 (Immunomedics, Inc., Morris Plains, New Jersey, USA). Control antibody and IMMU-114 were used at the concentration of 10 nM. Phenotypic changes of human PBMCs were analyzed by flow cytemetry, and activated CD4 T cells and CD8 T cells were determined by CFSE-negative and CD25-positive compartments. Also, ^{3}H-thymidine incorporation rate was measured.
Results: Flow cytemetry showed that frequencies of ClassII-DR-positive cells in Control and IMMU-114 were 58.1% and 12.2%, respectively ($P<0.01$). Frequencies of CD3+/CD25+ T cells in Control and IMMU-114, were 7.1% and 3.7%, respectively ($P<0.05$). Frequencies of CFSE-negative, CD4-positive, and CD25-positive T cells were 0.25% in Control and 0.13% in IMMU-114, respectively ($P<0.05$). Frequencies of CFSE-negative, CD8-positive, and CD25-positive T cells were 0.38% in Control and 0.19% in IMMU-114, respectively ($P<0.05$). Thymidine-incorporation rates at 1:1, 1:2, 1:4, and 1:8 responder/stimulator ratios, were 22080.7±602.4, 5022.5±772.8, 2430.0±48.1, and 571.0±216.2 cpm in Control, and 2254.5±118.1, 1031±286.5, 604.7±71.8, and 478.7±80.4 cpm in IMMU-114, respectively ($P<0.01$).
Conclusion: IMMU-114 successfully suppresses human to bovine xenogeneic MLR.

RO-296 PROLONGED CARDIAC XENOGRAFT SURVIVAL BY ELIMINATING NATURAL KILLER CELLS WITH MONOCLONAL ANTIBODY

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Background: This study was designed to investigate the effect of natural killer cells in the model of guinea pig-to-rat cardiac xenotransplantation by eliminating natural killer cells in rat with monoclonal antibody.
Material and methods: Donar (guinea pig) and recipient (SD rat) were divided randomly into three groups. Group A (Contral group): The heart from guinea pig was transplanted into the abdomen of SD rat; Group B (CVF group): The recipient were injected with cobra venom factor (CVF) 20μg/kg in abdomen; Group C (mAb group): The recipient were injected with monoclonal antibody 3.2.3 100μg in abdomen 24 hours prior to transplantation.CVF was injected as group B. The mean survival time (MST)and the pathology of grafted hearts were observed. The quantity of NK cells in peripheral blood was detected by flow cytometry.The expression of IFN-γ,ICAM-1 were assayed by ELISA.
Results: The donor hearts in group A showed hyperacute rejection and delayed xenograft rejection were observed in other groups. The mean survival time of groups was 0.56±0.10h; 45.2±2.42h; 53.4±1.98h separately. The quantity of NK cells was markedly decreased in SD rats injected with monoclonal antibody.The ratio of $CD8^{+}$T cells and $CD4^{+}$T both increased in Group B and Group C after transplantation. The cytokines IFN-γ and ICAM-1 also increased in Group B and Group C.
Conclusions: Monoclonal antibody 3.2.3 can eliminate natural killer cells and prolong the survival time but fail to overcome delayed xenograft rejection thoroughly.

RO-296A BIOLOGICS AND DONOR BONE MARROW CELLS FOR TARGETED IMMUNOMODULATION IN COMPOSITE TISSUE ALLOTRANSPLANTATION – A LARGE ANIMAL TRANSLATIONAL TRIAL

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Background: Bone marrow (BM) infusion is a prerequisite for potential donor-antigen specific tolerance induction. We developed a preclinical swine model to determine the optimal dose of BM cells to achieve microchimerism. Furthermore, induction therapy was optimized by augmenting the BM infusion with biologics in the form of co-stimulatory blockade (CTLA4Ig).
Materials and Methods: Yucatan miniature swine (n=12) underwent total body and thymic irradiation for cytodepletion. Animals received 15, 30 or 60 million cells/kg of whole unmodified BM. The optimal dose of BM cells was then applied to subsequent experiments evaluating the addition of CTLA4Ig. Yucatan miniature swine (n=9) underwent heterotopic hind limb transplantation and received 30 days of FK506 treatment. Group I (control) received irradiation and BM infusion; Group II received irradiation, BM infusion, and CTLA4Ig; Group III received CTLA4Ig only.
Results: Microchimerism was established in all animals after BM cell infusion; at POD 9 it was significantly increased for 60 million cells/kg (p=0.0001). Transplanted animals in Group I rejected the skin portion of the allograft at 50, 52, and 53 days post-transplant. Remaining allograft components (muscle, bone, nerve, vessel) survived indefinitely. Group II animals had complications (unexplained weight loss) leading to sudden death (n=1) or were euthanized at 28 and 35 days post-transplant. Group III animals demonstrated significantly prolonged graft survival beyond 150 days post-transplant. Skin and muscle histology in all long-term surviving animals were normal.
Conclusions: Bone marrow cell infusion with 60 million cells/kg results in stable levels of microchimerism. The addition of CTLA4Ig enabled us to optimize induction therapy, reduce maintenance immunosuppression, and prolong graft survival. Such combined BM cell-based strategies and biologics might facilitate immune tolerance and eliminate the need for multi-drug immunosuppression to maintain graft survival after CTA.

RO-296B CD4-CD8- DOUBLE NEGATIVE REGULATORY T CELL BASED THERAPY INDUCES DONOR-SPECIFIC TOLERANCE IN A MURINE COMPOSITE TISSUE ALLOTRANSPLANTATION MODEL

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Background: In our previous report, ex vivo CD4+ T-cells converted CD4-CD8- double negative regulatory T cells (DN Tregs), which regulate allo- and auto- immune responses, significantly prolong islet allograft survival. In this study, we explore the DN Treg-based therapy in mouse CTA model.
Materials and Methods: We tested the DN Treg-based therapy (5×10^{6} cells) with a short course of low-dosed immunosuppressant, rapamycin (0.6 mg/kg/day for 28 days), in a MHC mismatched mouse heterotopic CTA model (DBA/2 to C57BL/6). Antilymphocyte serum (ALS) and/or IL-2/Fc were also used in the experimental groups in conjunction with DN Tregs and rapamycin.
Results: DN Tregs and rapamycin had a synergistic effect on decreasing both CD4+ and CD8+ T cell proliferation and increasing apoptosis detected by significantly induced Annexin V staining for both CD4+ and CD8+ T cells in vivo. In mouse CTA model, the single transfer of DN Tregs plus 28-day IL-2/Fc and low-

dosed rapamycin treatment significantly prolonged hindlimb allograft survival in comparison with untreated group (MST 46 days vs. 10 days, p=0.0026) and IL-2/Fc plus rapamycin treated group (MST 46 days vs. 32 days, p=0.0064). Moreover, the addition of ALS to DN Tregs, rapamycin and IL-2/Fc treatment could achieve permanent engraftment (>180 days). Macrochimerism was detected 30 days after hindlimb osteomyocutaneous flap transplantation. Significant increase of CD4+Foxp3+ Tregs was found over the period of 3 months post transplantation. Donor specific tolerance was reflected in vivo by survivors accepting donor while rejecting third-party skin grafts.
Conclusion: Using ex vivo CD4+ T-cells converted DN Tregs is a highly potent and antigen specific induction method. DN Tregs prevent acute rejection and induce donor-specific hindlimb osteomyocutaneous flap tolerance hence representing a novel treatment strategy for CTA.

RO-296C NO LONG TERM TRANSMISSION OF PERV IN FIFTY FIVE PATIENTS RECEIVING PORCINE SKIN XENOGRAFTS

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Introduction: Human cadaver skin is not always available and commercially available porcine skin has been shown to be effective in treating patients with severe burns. However, like other xenotransplantation practices, the use of porcine skin has raised issues about the viral safety of this technology. In addition, the long term safety monitoring of these practices is paramount to ensure that there is little or no risk of infection to the recipient.
Methods: This study examines 55 xenograft recipients with a post exposure to porcine skin grafts time up to 408 months (average 116.0 months ±SD74.3). All patients had 2nd and 3rd degree burns and were minimally immunesuppressed due to their condition. All samples were tested for PERV RNA, DNA, pig cell microchimerism and antibodies to PERV. Animals from the donor herd were also tested for the ability to transmit PERV *in vitro*.
Results: No evidence of persistent and/or productive PERV infection or antibody to PERV was seen in any of the patients examined when compared with controls (n=34). In addition, this is the first instance where the donor animals PERV transmission status has been documented.
Conclusion: It is clear that there is a risk for the transfer of pathogens via porcine skin xenografts, however, the evidence *in vivo* to date would suggest that the risk of PERV transmission is extremely low even in severely burned recipients.

Donation / retrieval II

RO-297 DECEASED ORGAN DONATION AND TRANSPLANTATION ACTIVITY IN SAUDI ARABIA: 2000-2004 VS. 2005-2009

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Objective: Organ transplantation is the best available method for the treatment of end-stage failure of most essential organs. However, the need for viable organ supply limits its progress; thus, we studied the algorithm of process for deceased heart beating donors with the rate of conversion of the critical pathways of organ donation from possible to potential to eligible to consent and to actual deceased donors (DD) in the country.
Methods: A retrospective study comparing the figures and composition of the cases possible DD reported nationally during the first and last phase of the decade from 2000-2009 to Saudi Center for Organ Transplantation (SCOT).
Results: The Study shows a remarkable increase in the Possible Deceased Donor cases from 1781 of 2000-2004 to 2446 of 2005-2009. A slight increase in the Potential Deceased Donor can be seen from 1104 (62%) to 1550 (63%) of the total cases. Eligible Donors increase in number from 920 to 1242 of which 238 (26%) and 464 (37%) respectively were classified as Actual DD. The number of Utilized DD also increased from 218 to a remarkable 417 cases.
Conclusion: There is a remarkable increase in the number of Possible DD reported in the second half of the decade to SCOT. In relation to this, the strategies including the establishment of mobile team in every region of the kingdom formulated by the center are quite effective in looking for possible organ donors.

RO-298 A ONE YEAR RETROSPECTIVE AUDIT OF REFERRALS COMPARED TO PROCEEDING DONORS AFTER CIRCULATORY DEATH (DCD)

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Background: As DCD programmes have developed, patients that were previously not considered potential donors due to age or other factors are now being considered. This has caused concern amongst some clinicians and specialist nurses for organ donation (SN-OD) as there was limited evidence to suggest that organs from such patient groups are being successfully transplanted.
We wished to see if we could identify patterns of patient referral that led to proceeding or non proceeding DCD, or if patient groups were being declined by recipient centres at the point of referral.
Method: A one year (2009-2010) retrospective audit of all patients in our region referred to the SN-OD team was conducted. We initially looked at relevant referral information such as age, diagnosis, past medical history, blood results, and then compared this to those patients who were subsequently accepted by transplant centres.
The second part of the audit compared the information available at referral to eventual proceeding or non proceeding donors
Results: 239 patients were referred, 78 (33%) were declined by transplant centres at the point of referral as they were considered not medically suitable. 23 (9.6%) patients proceeded to DCD, however 55 (23%) patients were consented for DCD. The oldest patient that proceeded to DCD was 63, and the youngest proceeding was 11. 22 (96%) patients that proceeded with DCD had a neurological diagnosis.
Conclusion: The findings of this retrospective audit has proven of interest to clinicians, other SN-ODs and the local retrieval teams.
During this time period SN-OD's referred to the local transplant centre only for potential DCD. We anticipate when we analyse the data for 2010-2011; this will show significant differences when consulting with transplant centres nationally for potential suitability for DCD.

RO-299 FEASIBILITY OF LIVE KIDNEY TRANSPLANTATION FROM MORBIDLY OBESE DONORS

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Introduction: The number of living kidney donors is increasing to meet the demand of an expanding renal transplant list for patients with end stage renal disease. Living donation demonstrates superior long-term outcomes compared with deceased donor transplantation. However selection guidelines for potential live donors may limit this scarce organ pool. Whilst one such exclusion criterion is obesity, our small series demonstrates that morbidly obese donors can safely provide kidneys.
Methods: We describe seven live kidney donors who according to the World Health Organisation's definition, fell into the category of "morbidly obese" with a body mass index of over 40 kg/m^2.
Results: All seven pairs of donor-recipient transplants had successful outcomes with a mean donor follow-up period of 20 months (range 4-48).
Discussion: Due to a year-on-year static number of available deceased donor kidneys, encouraging live donation is crucial to meet the demand for organs. We feel that in a centre undertaking large numbers of live donor nephrectomies and a sensible pragmatic approach is applied, obese patients can donate their kidneys with minimum risk. Our series therefore may demonstrate that it is safe and feasible to re-evaluate previous exclusion criteria such as obesity to expand the organ pool.

RO-300 REGIONAL PARTNERSHIP FOR TRANSPLANTATION. THE WAY TO INCREASE DONATION RATE FROM DECEASED DONORS

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Organ donation rate in our country has never been satisfactory, but over the

years kidney transplantation from deceased donors has reached the level of 26 kidneys pmp In 2007 40% decrease of identified donors and recovered organs due to a number of reasons has occurred. Since that time the number of kidney transplantations has never come back to its level in 2006.
In order to increase the donation rate, a special program - Regional Partnership for Transplantation was initiated one year ago by the Polish Union of Transplantation Medicine and Poltransplant in 12 Districts of Poland and the letter of intention signed by the local government officials, the Governor, the President of the local Medical University, President of the physicians Chamber, and the local transplant centers The plan of action included:

- training of coordinators from 80 hospitals,
- visits to these hospitals and discussion with the managers concerning the need of participation in the donation program,
- communication skill training workshops for ICU physicians (with the participation of two actors, experienced anesthesiologist and the psychologist)
- contacts with the local media (press, tv and radio)
- various educational activities for the high school students
- contacts with Regional Catholic Church Authorities

The preliminary results (after the first year) show raised activity of the local hospitals in the donation process. Donation rate rose in the last year from 11 to 13.5/pmp.
Conclusions: Improvement in logistics and necessary educational measures are important for an increase of donation rate.

RO-301 STANDARDIZATION OF ORGAN PROCUREMENT AND E-LEARNING AS A TOOL TO IMPROVE QUALITY OF EDUCATION IN DONOR SURGERY: FIRST RESULTS OF A NEW CERTIFICATION SYSTEM IN THE NETHERLANDS

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Background: Considering a persistent donor shortage in The Netherlands, it is mandatory to optimise training of surgeons in organ procurement and reduce discard or injury. In 2010 a new curriculum for donor surgery training was launched. This curriculum comprises three training and certification modules including an E-learning module, training-on-the-job and a Masterclass. This abstract focuses on the E-learning module as a key component of the curriculum which has been developed in cooperation between the University Medical Centers of Leiden and Groningen and the Dutch Transplant Foundation.
Methods/Materials: The objectives of the E-learning module are to support training-on-the job and to prepare the candidates for the highly complex multi-organ donor operation as well as to test acquired knowledge of the procedure. After completion of the module a questionnaire is filled out. An online system allows assessment of trainee by himself and his supervisor to evaluate progress in performing clinical procedures.
Results: Since the launch of the programme, twelve surgeons of three university medical centres have been participating in the training of retrieval surgery abdominal organs. Per January 2011 six surgeons started and/or completed the E-learning module. Data will continuously be collected until July 2011. These data will be discussed with the supervisors of the procurement teams to define the value and challenges for the E-learning module.
Conclusion: We would like to present this curriculum as well as the unique E-learning training module as a valuable tool to enhance and document the learning curve of skills and knowledge of surgical trainees acquiring certification for donor surgery. The actual results of the evaluation after one and a half year experience will be presented and discussed.

RO-302 CURRICULUM THORACIC TRANSPLANTATION (CTTx): TRAINING ON HEART AND LUNG EXPLANTATION AND IMPLANTATION

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Background: Survival of organ transplantation depends to a major part on successful organ explantation and implantation, especially in light of the increasing number of marginal donor organs. Thus, we initiated the CTTx as hand-on training for surgeons to learn the specifics of heart and lung transplantation (HLTx).
Methods: On two weekends (14hours/weekend), a maximum of 6 participants with advanced experience in heart and lung surgery, work in teams of two. Each team is supervised by an experienced physician in HLTx.
CTTx Part-I is performed in the Institute for Legal Medicine of the University Hospital Hamburg-Eppendorf, Germany, to practice of in non-preserved corpses. CTTx Part-II takes place in the animal laboratory of the Heart Center Leipzig, Germany, to mimic the live situation by using pigs supported by cardiopulmonary bypass (CPB) for implantation of the heart and lung. The training consists of 3 rounds with 3 donor animals to perform 3 HTx and 3 LTx in 6 recipient animals. In both parts of the CTTx the teams rotate in order to allow each participant practicing the HLTx techniques.
Results: The success of the operation is measured by weaning-off the transplanted heart and lung from CPB. Single left transplant lung functional assessment is achieved through isolated left lung ventilation following clamping of the right lung hilus. CME and certificates are awarded following the participation in both parts of the CTTX.
Conclusion: The CTTx is unique as it combines an initial training on human corpses and the subsequent training in an animal live setting. Until today two CTTxs have successfully been completed in 2010 with an overall satisfaction of the participants. As a consequence a biannual CTTx is planned for young heart and lung surgeons.

RO-303 A COMPUTER ASSISTED LEARNING PACKAGE ON ORGAN DONATION: A TOOL FOR WIDESPREAD EDUCATION OF PROFESSIONALS

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Background: The 2008 Organ Donor Taskforce Report called for training of all clinical staff likely to be involved in the treatment of potential organ donors. To provide this, and to ensure continual professional development for large numbers of clinical staff, additional learning resources are required. Computer Assisted Learning (CAL) benefits from increasing accessibility, breadth of content, the ability to update information, and interactive control over time, place and pace of learning (Greenhalgh (2001) BMJ [online] 322 (40)).
Method: A learning needs analysis was undertaken in order to determine the target population's prior knowledge of organ donation. The CAL package was produced in a web editor so that it could be displayed in Internet Explorer – a widely accepted browser with which most users would be familiar. A true/false test was used to assess effectiveness of the package and feedback was collected through use of an online survey.
Results: Results of the evaluation tool showed that this CAL package was an effective learning resource for the topic of organ donation. All participants reported a positive experience of using the package and said that they would recommend others use this CAL package.
Conclusions: This CAL package is successful in fulfilling the aim of producing a useful resource for teaching about organ donation. Staff were impressed by the opportunities CAL offers for learning. Evaluation of the CAL package was limited by time constraints but results do suggest it will be an effective and lasting resource. Further use and evaluation of the package over a longer period of time would give the opportunity for future development and assessment of the effectiveness of this CAL package within clinical practice itself.

RO-304 TPM: AN EFFECTIVE MODEL IN TRAINING DONATION PROFESSIONALS

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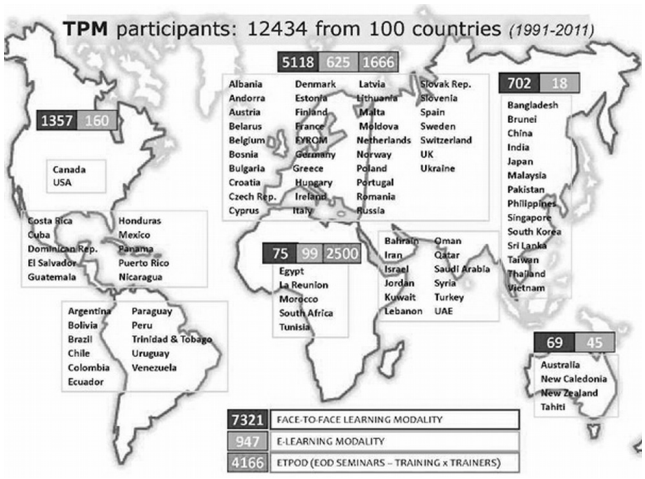
Background: Transplant Procurement Management (TPM) is an international educational program that aims at increasing the quantity, quality and effectiveness of organ and tissue donation by training healthcare professionals at different involvement levels. TPM was launched in 1991 under the auspice of the Universitat de Barcelona (UB) with the technical support of the Organización Nacional de Trasplantes (ONT). In 1994 it gained the recognition of the Transplant Committee of the Council of Europe. In 2008 it was awarded for Education and Training in Transplantation by The Transplantation Society (TTS).
Methods: The training process is structured in modules using *Face-to-Face*, *On-Line* and *Blended learning* methodologies. Theoretical sessions are followed by simulations to enhance proactive learning, covering all phases of organ donation. Advanced courses are yearly implemented in Spanish, English, Italian, French and Portuguese. Whenever required, educational materials are translated into other languages and adapted to the needs of each country.
Results: TPM represents the formal Transplant Coordination Training Program in Italy (CNT), France (ABM) and Portugal (ASST). It counts with a worldwide network of qualified professionals (12434 from 100 countries) that sustains the undertaken training impact in their area. It developed along with its project partners The European Training Program on Organ Donation (ETPOD), co-financed by DG–SANCO 2005205, and distinguished in the EC Action Plan on Organ Donation and Transplantation, 2009-2015. The Training for Trainers pro-



gram developed within ETPOD has already been disseminated in 6 countries, covering the training of 4166 participants.
Conclusions: Whereas the donation rate is subjected to several factors such as religious, economic, cultural and legal, the existence of well-trained professionals considerably contributes to enhance it. TPM answers the growing demand in specialized training in the field of organ donation by promoting and implementing effective training programmes for transplant coordinators worldwide.

RO-305 ACUTE KIDNEY INJURY (AKI) BEFORE ORGAN PROCUREMENT IS ASSOCIATED WITH THE WORSE LONG-TERM KIDNEY GRAFT OUTCOME

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Background: As the disparity between the numbers of available organ donors and patients awaiting for transplantation increases, different strategies to extend the donor pool are proposed. Patients with acute kidney injury (AKI) developing during the stay in intensive care unit (ICU) are often considered as donors, but the long-term outcome of such high-risk kidney transplants is unknown. We analysed the renal function of donors and the kidney graft outcomes in 5-year follow-up period.
Material and methods: We collected data from all 61 deceased kidney donors, identified in one ICU, and 120 kidney graft recipients (transplanted between Jan 1999 and Dec 2006). Donors were stratified according to RIFLE classification, based on their creatinine and urine output change since the admission to ICU to the organ procurement. Recipients' kidney graft function (eGFR) calculated according to MDRD equation was estimated every 6 months after KTx.
Results: Out of 61 donors, 10 (16.4%) developed AKI, including seven classified in "risk", two in "injury" and one in "failure" cathegories. The mean follow-up of kidney graft recipients was 49±18 months. Long-term graft loss was significantly higher in the group of kidneys, harvested from the donor with AKI (27.8% *vs.* 7.1%, p=0.02, log rank 0.07), and their excretory function was worse in the whole follow-up period, with the statistical significance between 18-month and 48-month time-points.
Conclusion: The patients with kidney graft harvested from the donor with AKI have higher chance for graft loss and the worse excretory function in the long-term follow-up period.

RO-306 EDUCATION FOR HEALTH IN SCHOOLS, INTRODUCING TRANSPLANTATION – THE OPORTO MODEL

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The North Histocompatibility Centre (CHN) is one of 3 Centres that compose Lusotransplante since 1983 and the Portuguese Registry of Bone Marrow Donors -CEDACE. Actually CHN is also the location of LUSOCORD, the Portuguese Public

Cord Blood Bank: The activity to create the Registry started in July 2003 with 2 media campaigns promoted by 2 children' families. Families' demands for external collections are ferequent. Families involve media, religious, arts and sport groups, associations and opinion makers from regional and national influence, politics, fashion, music, football players etc. Portuguese society has been highly motivated to Bone marrow donation and children are a special group to inform and prepare.
To project to the future the effects of these specific actions and convert them in a culture of solidarity to unknown patients, some organized actions must be taken. Children, schools and universities have been some targets in our model. We privilege external public relations with external collections organization, group's dynamics, opinion makers' recruitment, cross-generations actions, cause ambassadors and early health education in schools. As Educational material we produced 2 CDs, 1 Book, a school concourse and an itinerant exhibition of tile panels paintings. Steps involved: 1- Schools and Universities visits and conferences, 2- Involvement of children and teachers, 3-Local, Regional and National media involvement. Other circumstances as: 4-Patients Associations Protocols, 5 -Identification of motivations, 6-Relatives initiative and family campaigns, can be part of each local program to create a dynamic of donation. With this model we collected in the North of Portugal (3.75 million inhabitants) 110 000 BMD in 7 years. With LusoCord we are now preparing similar educational material and scholar actions.

Allocation

RO-307 DONOR RISK FACTORS AND CORRELATION WITH MELD SCORE IN LIVER TRANSPLANT RECIPIENTS

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Background: We evaluated the effect of donor risk factors and model for end-stage liver disease (MELD) score on liver transplant (LT) recipients.
Methods: Prospectively, data of patients transplanted at University of Bologna between January 2003 and December 2010 were included (n=628). Outcomes included the impact on graft survival of the following variables: recipient liver disease (HCC 43.9%, HCV+ 20.4%, cholestatic 8.4%, alchool 6.7%, HBV+ 5.7%), donor cause of death (Stroke 65.3%, Trauma 25%, Anoxia 9.6%), donor age > 60 yrs (n=305), HBcAb positive donor (n=130), HCV positive (n=38), HBsAg positive (n=20), organ sharing (Region 76.8%, extra-Region 20.6%, extra Nation 2.6%), split liver graft (n=23). The recipients characteristics were: sex (M/F) 73.2%/26.8%, mean age 51.07±0.42 (11-67), MELD at the time of LT 20.86±0.36 (6-51). Outcomes of LT on patients categorized into low (<15), intermediate (15–25), and high (>25) MELD categories were analyzed.
Results: Post-operative mortality was 3.7%, follow-up 1090.55±35.46 days. Five-year graft survival were 80.6% for MELD< 15, 74.8% for MELD 15-25, and 62.3% for MELD> 25 (p<0.0001). HBV+ recipient and HCC determined a poor 5-year graft survival in MELD> 25: 57% (p=0.03) and 46.5% (p=0.001), respectively. MELD 15-25 at transplant and donor death due to anoxia determined a poorer 5-year graft survival: 48.8% (*P*=0.04). No graft function at 5-year from LT in MELD> 25 with HBsAg positive grafts (p=0.002). For split liver, 5-year graft survival is poor in MELD > 25: 20% vs. 71% for MELD 15-25, vs. 91.7% for MELD < 15 (p=0.002). However, in all MELD category, there were a similar graft survival for recipient HCV+, donor age> 60 yrs, HBcAb positive donor, HCV positive donor, organ sharing.
Conclusion: Patients with HCC or HBV+ and MELD> 25 are not good candidate by receiving a split liver or donor HBsAg positive.

RO-308 GRAFT-RELATED TRANSPLANT BENEFIT BASED ON MELD SCORE OF THE RECIPIENT IN LIVER TRANSPLANTATION

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Background-Aim: There are no studies evaluating the 5-year "graft survival benefit" in liver transplantation (LT). The aim of this study is to create a model able to calculate the life months gained for each organ based on the particular value of recipient's MELD score.
Methods: Period: 2003-2010. Study groups: a) pre - LT = 732 consecutive adult patients with chronic end stage liver disease enlisted for first LT; b) post –LT = 400 consecutive adult patients undergone to first LT for ESLD. Two independent Cox's regressions adjusted for age, sex, etiology, and presence of

hepatocellular carcinoma were used for the 2 groups, both aimed to measure the MELD predictive value (pre and post LT respectively). In the post-LT model the selected end-point was the patient survival with the first graft. The MELD related coefficients were then used to create a global predictive model able to calculate the life months gained for each used graft according to MELD score.
Results: In the pre-LT group the initial MELD score (at the moment of listing) showed a significant ability to predict patient survival: hazard ratio = 1.21; 95% confidence interval = 1.14-1.28 (p=0.0000). In the post – LT group, conversely, MELD score at transplant did not show a significant prognostic value: hazard ratio = 0.99; 95% confidence interval = 0.94-1.03 (p=0.5428).
The global model showed that the 5-year graft survival benefit increased as MELD score increased (MELD 6= - 5,4 months; MELD 40= + 51.2 months). MELD 13 was selected as the threshold value below which there is not graft survival benefit after LT.
Conclusion: A MELD score below 13 represents the minimal cut-off justifying LT in terms of gain in life months at 5-year for each used graft.

RO-309 PRIORITIZATION TOOLS TO PREDICT SHORT AND LONG TERM MORTALITY FOLLOWING LIVER TRANSPLANTATION

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Donor and recipient variables may affect survival after liver transplantation (LT). The ideal donor-recipient matching is still an open issue. The aim of this study was to assess the effect of donor and recipient features on patient survival following LT.
Records of adult recipients of LT (2000-06.2009) were reviewed. INR, bilirubin, creatinine, sodium, etiology of liver disease, donor age and gender, cold and total ischemia time, graft type were recorded. Each patient was assessed by 4 scoring systems: Child-Pugh (CTP), MELD, MELD-Na, D-MELD. Outcome was assessed at 3,12, and 36 months after LT. Unadjusted mortality estimates were calculated using the Kaplan-Meier and to compare different patient categories we used log-rank. Unadjusted overall mortality estimates were calculated using proportional hazards regression.
484 patients underwent LT; 318 were included in the study. Mean donor age was 51 yrs, mean MELD, MELD-Na, D-MELD and CTP were 16, 16, 787 and 9. Donor age (p=0.02) and all scores were significantly lower in HCC vs non-HCC patients. HCV+ had a significantly lower MELD (p=.01) and MELD-Na (p=.01) vs HCV- at LT. Patient survival was similar in HCV+ vs HCV- and in HCC vs non-HCC recipients at all time intervals. Donor age $>$ or $<$ 60 yrs did not influence survival in HCV+ or HCV- recipients. Bilirubin (p=.02) significantly predicted 3-month mortality, donor age (p=.02) and recipient age (p=.02) 12-month mortality, D-MELD predicted 3, 12, 36-month mortality (p=.01, p=.02, p=.02 respectively). The 3-year patient survival was lower in D-MELD$>$1600 than in D-MELD$<$1600 (log-rank p=.03) whereas no other variable showed significance. The overall risk of unadjusted patient mortality was proportional to D-MELD (HR 1.00;p=.01) and donor age (HR 1.02;p=.003).
The potential application of various donor and recipient matching scores is aimed at optimizing the outcome of LT.

RO-310 WHAT ARE THE PATIENTS' VIEWS ON THE CURRENT KIDNEY ALLOCATION SYSTEM IN UK?

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Introduction: The aim of this study was to assess patients' understanding and views on how kidneys are allocated on the waiting list in UK.
Methods: A two-part questionnaire was sent to all patients awaiting kidney transplantation at two transplant centres in London after ethics approval. Part-1 assessed patients' knowledge and priorities. Part-2 assessed patients' understanding and agreement after reading the UK kidney allocation guidelines.
Results: The response rate so far was 105/394 (27%). Five did not want to participate and one returned questionnaire was blank. The remaining group included 62F with a mean age 55 (min 27, max 74).
The key issues patients think should be taken into consideration are the degree of tissue matching between recipient and kidney (81%), the time spent on the waiting list (74%), the likelihood the patient will die soon (75%) and whether the patient will take their medication after transplantation (75%).
Ability to pay (74%), contribution to society (50%) ethnic origin (61%) and whether the recipient smokes (38%) were issues that most did not think should be part of the guidelines. 10% thought the ability to pay for a kidney is part of the allocation system.
After reading the enclosed guidelines, there was an increase in understanding of the system from 36% to 77% saying that they mostly or completely understand the guidelines now. Finally, 75% said they mostly or completely agree with the current guidelines.
Discussion: Patients seemed incompletely informed regarding the current guidelines but when they are provided with the appropriate information the majority agree with the prioritization criteria. We conclude from the responses so far that provision of more information and greater patient involvement may increase understanding of the system and help with management of expectations for patients on the transplant waiting list. This is an ongoing study.

RO-311 VALIDATION OF CURRENT INTERNATIONAL LEGISLATION ON ORGAN ALLOCATION WITH ACTUAL PRACTICE IN PERSONS WITH DISABILITY

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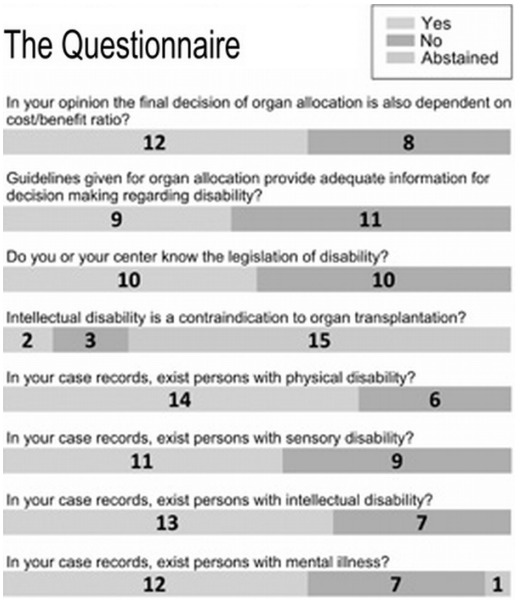
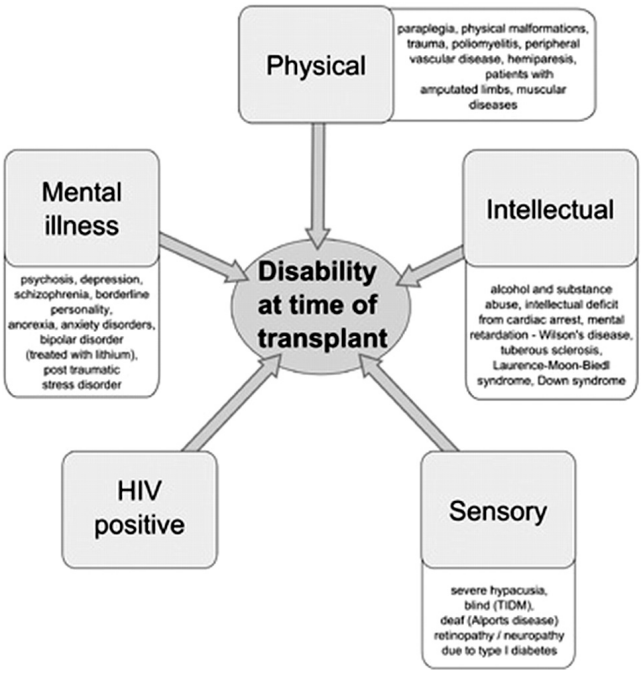
Background: There is increasing concern that persons with disability are being marginalized and discriminated against for their disability status in the organ allocation process despite legislation which guarantees transparency and equity. This is due to perceived infeasibility of organ allocation in this subset of patients with end-stage organ failure.
Methods: A review of current legislation on organ allocation was carried out and validated with actual clinical practice and patient narratives. A questionnaire on organ allocation, and related disability at time of transplant was sent to transplant clinicians, randomly selected both in Italy and internationally. The patient selection criterion for the semi-structured interview was disability at the time of organ allocation, sensory; physical; intellectual; HIV-positive. The respondents answered questions relating to access to organ transplantation, personal perception and understanding of disability and health related quality of life in the post-transplant setting.
Results: The results were not randomized for organ transplant type. They were analyzed for content agreement and disparity regarding international legislation on organ allocation, and actual practices. Twenty physicians completed and returned the questionnaire. Eleven patients shared their narrative, using a semi-structured interview. This allowed for a patient-centered approach, and the questionnaire validated actual clinical experience. There was a significant positive correlation between legislation related to equity in allocation, the completed questionnaire and patient narratives.



Conclusion: Results suggest that organ allocation in persons with disability is feasible, with good results related to health related quality of life. The questionnaire evidences actual clinical practices, which corresponds with the current legislation on organ allocation. It was seen that the level of expertise, and the maturity of the transplant center is the main determinant for organ allocation in persons with disability, and related outcomes.



Abstract RO-311 – Figure

RO-312 ACCESS TO RENAL TRANSPLANTATION AT NOTTINGHAM UNIVERSITY HOSPITALS

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Introduction: Early referral and transplant listing confers distinct advantages in terms of life expectancy, quality of life, graft survival and time accrued on the waiting list. Equity of access and activation appears largely centre specific rather than case mix dependent. The NSF framework recommends patients are listed within 2 years of starting RRT and, if pre-dialysis, listed when eGFR <15.
Aims: To determine the timeline for referral and listing in our prevalent transplant waiting list population.
Methods: We performed a retrospective analysis of all adult prevalent pre-dialysis (eGFR <15), dialysis (HD, PD) and failing transplant recipient patients. In those listed for transplantation we analysed demographics, time from first doctor meeting (FDM) and start of RRT to referral, assessment and list activation.
Results: Of 691 prevalent patients, (193 pre-dialysis (eGFR<15), 390 HD, 108 PD), 159 are listed for transplantation (84 HD, 51 PD and 25 pre-dialysis). 14 pre-dialysis patients were accepted for listing but awaiting activation once eGFR <15. 15 patients have diabetes mellitus, 57% are male and 42% aged ≥50. The table illustrates the median times in the referral process. Despite 74% HD and 88% PD patients with a FDM >90 days, only 8% and 24% patients respectively were listed pre-dialysis. 13% pre-dialysis patients are listed. Delays were identified in 21 patients, mainly relating to investigations.

	Listed n (%)	Referral to surgeon (wks)	Surgeon to list (wks)	Referral to list (wks)	Referred pre-dialysis n (%)	Listed pre-dialysis n (%)	FDM >90 days to RRT n (%)
Pre-dialysis	25 (13%)	11	22	NA	NA	NA	NA
HD	84 (22%)	10.8	9	21.8	20 (24%)	7 (8%)	62 (74%)
PD	51 (47%)	13	4	17.3	23 (45%)	12 (24%)	45 (88%)

Conclusions: Timeline for referral and listing is suboptimal in the dialysis population. Data is retrospective and median times may be skewed due to historic long waits. Delays were mainly related to cardiology investigations, and many of the pre-dialysis patients were seen in advance of the need for listing. Pre-dialysis listing has improved from 9 to 13% in 2 years and work continues with prospective audit showing improvements in the 18 week pathway over the last 12 months.

Kidney IX

RO-313 NEW CONCEPT TOWARD CYCLOSPORINE BLOOD LEVEL EFFICACY IN KIDNEY TRANSPLANT PATIENT

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Background and Aims: In clinical practice, the dosage of cyclosporine (CsA) given to renal transplant recipients is mostly based on its blood levels. We made a retrospective study to evaluate the correlation between CsA blood levels, through (C0) and 2-hour post-dose (C2), and renal allograft function in a large population of renal transplant patients.
Methods and Materials: CsA blood levels were assessed in 1270 kidney transplant recipients, between 2008 and 2010. The patients were divided into three groups according to lab data time since kidney transplantation (<3 months, 4-12 months and more than 1 year after transplantation). Both univariate and multivariate analyses were performed to determine the correlation between CsA levels and serum Creatinine.
Results: A significant relationship, but not strong, was seen between serum creatinine with C0 and C2 (r=0.100, p=0.00 and r=0.104, p=0.00, respectively) in univariate analysis. However, the significant relationship was only seen in groups II and III. Older age of recipients (p=0.00), male gender (p=0.00) and history of CMV infection (p=0.02) were also associated with higher serum creatinine concentrations. In linear regression model, a significant correlation was only seen between serum creatinine and CsA levels beyond one year following kidney transplantation (group III) after adjusting for other confounding factors.
Conclusion: The current study shows that C0 and C2 levels are not reliable indexes within the first year of transplantation. However, they are significantly correlated with late renal allograft function and these indexes have only clinical benefits in monitoring of drug after first year of transplantation.

RO-314 SURGICAL COMPLICATIONS INFLUENCE EARLY AND LATE KIDNEY GRAFT FUNCTION

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Although surgical techniques for transplantation have markedly improved the reported incidence of surgical complication after kidney transplantation varies between 0.5 and 12%. How particular surgical complications influence kidney transplantation outcome is not fully understood.
The aim of our study was to analyze the impact of surgical complications on kidney graft function and 1 year graft survival at our center.
Records from 566 consecutive adult cadaveric kidney transplantations performed at our center between 01/2006-04/2009 were retrospectively analyzed. Surgical complications were defined as ureteral stenosis, urinary leak, renal artery or vein thrombosis and stenosis, lymphocela, wound infection, perirenal hematoma. The onset of graft function was classified as an immediate graft function, delayed graft function (DGF), primary and secondary nonfunction. Kidney graft function at 3rd and 12st month and 1 year graft survival was recorded.
The overall incidence of surgical complications after kidney transplantation was 21.9%. In detail, we observed 3.9% wound infection, 9% perirenal hematoma, 5.1% urinary leak, 1.9% ureteral stenosis, 9.9% lymphocela, 0.7% renal artery thrombosis and 1.1% stenosis, 1.4% renal vein thrombosis. No impact of particular surgical complications on graft function development was observed. Graftectomy due to surgical complication was performed in 18 patients.
Worse graft function at month 3 was observed in patients with urinary leak ($p<0.05$) and at month 12 in patients with lymphocela ($p<0.05$) compared to group with no surgical complications. One year graft survival was determined by wound infection ($p<0.05$), renal artery stenosis ($p<0.05$) a renal vein thrombosis ($p<0.01$).
Surgical complications influence 1 year graft survival and graft function not only in early but also in late time period after kidney transplantation.

RO-315 EX-VIVO RECONSTRUCTION TECHNIQUES OF MULTIPLE RENAL ARTERIES IN LIVING DONOR KIDNEY TRANSPLANTATION

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Aim: The shortage of allografts in living kidney transplantation has forced the use of grafts with multiple renal arteries (MRA) that were previously considered to be unsuitable for transplantation. Several surgical techniques have been

Abstract RO-315 – Table 1. Results

Variable Total number (n)	Ex-vivo internal iliac artery (14)	Ex-vivo Pantaloon (15)	MRA with ligation of polar artery (4)	MRA in situ reconstruction (5)	RA end to side reconstruction (4)
Donor Age	49 (32–69)	48 (28–64)	49 (37–65)	46 (42–53)	62 (57–68)
Recipient age	41 (17–62)	41 (20–69)	50 (39–64	32 (20–46)	50 (44–56)
No. of renal arteries (Avg)	2	2	2	2	3
Cold Ischaemic Time (min)	187	140	104	162	69
Vascular anastomosis time (min)	58	59	53	67	60
Thrombosis of polar artery	0	0	0	1	0
Urological complications	0	0	0	1	0

described for the reconstruction of MRA. We compared different reconstruction techniques of living donor kidney grafts with MRA.
Methods: We retrospectively analysed 169 living donor kidney transplants during the period from May 2005 to July 2010. There were 42 (24.8%) allografts with MRA. We used reconstruction techniques such as ex-vivo reconstruction on recipient internal iliac artery (14), ex-vivo pantaloon (15), ex-vivo anastomosis of polar artery to main renal artery (4) and insitu anastomosis of MRA to recipient arteries/ligation of polar artery (9).
Results: See the Table 1.
Conclusion: The ex-vivo reconstruction of multiple renal arteries minimizes the risk of stenosis or thrombosis. Ex-vivo reconstruction decreases the secondary warm ischaemic time.

RO-316 DECREASE OF BLOOD-TYPE ANTIGENICITY OVER THE LONG-TERM AFTER ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION. CHIMERISM OF BLOOD TYPE ANTIGENS ON THE VESSEL ENDOTHELIUM IN A RECIPIENT WITH GRAFT LOSS

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Background;: Few studies have investigated the changes in the antigenicities of the transplanted organs after transplantation.
Methods;: We examined, by immunohistochemical assay, the changes in expression of the blood-type antigens on the transplanted kidneys over the long-term after ABO-incompatible kidney transplantation with A- or B-antigen incompatibility (blood type A to B and B to A). The subjects were six patients, including one case with graft loss, who had received ABO-incompatible kidney allografts more than ten years previously.
Results;: Expression of the blood-type A or B antigens decreased gradually to 91.8% during the first three months after transplantation, 85.8% during the first five years, 64.1% during the first ten years, and 57.6% over ten years after transplantation on average. In the patient with graft loss due to severe antibody-mediated rejection, the donor's type B blood-type antigens on the transplanted graft had changed but partially to the recipient's blood-type A antigen by 2582 days after the transplantation, suggestive of the occurrence of blood-type chimerism on the endothelium.
Conclusion;: Decrease in the expression of the recipient's blood-type antigen on the endothelium of the graft has been considered as one of the mechanisms underlying the accommodation occurring over the long-term after ABO-incompatible kidney transplantation. On the other hand, establishment of antigenic chimerism on the graft endothelium could be one of the hallmarks of the immunological reaction associated with antibody- mediated rejection.

RO-317 PSA MONITORING IN MALE RENAL TRANSPLANT RECIPIENTS

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Introduction: Solid organ transplant recipients are more likely to die from malignancy than the general population and European Best Practice Guidelines suggest screening for certain malignancies in these patients. In particular, they recommend PSA screening annually in men aged 50+ as data suggests early diagnosis is associated with improved survival.
Aims: To review all eligible male renal transplant recipients aged 50+, ensuring they have had a PSA performed in the last 12 months. To analyse how many of those patients tested had elevated levels and whether they were associated with confirmed malignancy.
Methods: All male patients with a functioning renal transplant aged 50-74 were retrospectively analysed. Renal transplant vintage, treatment outcomes and survival were analysed.
Results: 132 patients transplanted between 1977-2009 fulfilled the criteria. The mean age was 59.2 years, and they had an average transplant vintage of 9 years 4 months (range 11-390 months). 11% had not had a PSA checked and 36% of these patients were less than 12 months post transplant. Of those with a PSA check (n=118), 83% had had one in the last 12 months, and in just 9% was it elevated. Those patients with elevated PSA levels had been transplanted for longer than the cohort mean. Most patients had been seen by urology and were under a "watch and wait" policy. The mean elevated PSA reading was 6.7. Two patients had biopsies and were benign. All had survived to date.
Conclusion: This methodology potentially failed to pick up those men who may have prostate cancer and a normal PSA, but only a minority of men had elevated levels on screening. Our unit had much lower then expected levels of prostate cancer and results raise the question of the economic benefit of screening these men annually.

RO-318 NGAL AS A MARKER OF RENAL DAMAGE IN KIDNEY TRANSPLANTATION

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Background: Neutrophil Gelatinase-Associated Lipocalin (NGAL) belongs to the family of lipocalins and it is produced by several cell types. NGAL production in the kidney increases during acute damage, resulting in a rise in NGAL serum and urine levels. In animal and clinical studies, NGAL was found to be a sensitive and specific indicator of acute kidney injury (AKI). The aim of this work was to investigate prospectively whether serum and urine NGAL can be used as reliable markers of renal transplant outcome in a 3-months follow-up after transplantation.
Methods: Blood and urine samples from 33 kidney transplant recipients were collected before transplantation and after 1, 7, 14 days, 1 and 3 months. NGAL ELISAs were performed using a commercially available assay.
Results: We observed a significant and gradual decrease in serum NGAL levels within 3 months post-transplant (p=0.0001). Analysis of data collected revealed a positive correlation between the trends of serum NGAL and creatinine. Serum NGAL showed significant differences at 1, 3, 7, 14 days after transplantation (p=0.013; p=0.002; p=0.001; p=0.003 respectively). We found that patients whose NGAL serum levels exceeded 200 ng/ml at day 7, had higher creatinine levels at all times examined than those patients with NGAL serum levels $<$200 ng/ml at day 7 (p=0.001). Our results also proved a significant increase in NGAL urine and serum levels in the patients with DGF, compared to patient with immediate recovery. Urine NGAL was increased in DGF patient at day 3 and 7 (p=0.002; p=0.006).
Conclusion: Our results showed a correlation between NGAL and creatinine serum level in patients after kidney transplantation, in patients with improvement of renal function and patients with DGF.

RO-319 DONATION AFTER CARDIAC DEATH (DCD): A SOURCE FOR KIDNEY TRANSPLANTATION

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Introduction: The use of DCD for expanding kidney transplantation programs offers an answer to the problem of donors shortage. Despite a renewed interest in DCD kidney transplantation, there are few clinical programms utilizing this type of donors. We analyzed the function and outcome of kidneys grafts from DCD performed in our hospital.
Methods: From 1999, 32 patients were grafted with kidneys from DCD. This group was compared with recipients of heart beating donors (HBD) matched for age, sex, number of transplant and HLA. Immunosuppression was performed with Basiliximab, Prednisone, Micophenolate Mophetil and Tacrolimus. Acute rejection episodes were treated with Metilprednisolone boluses, and ATG-FRESENIUS when necesary.
Results: The delayed graft function rate was higher in DCD transplants than HBD grafts. Serum creatinine was significantly better in the DCD (1.6 mg/dl

vs 1.9 mg/dl) compared with HBD group. Graft survival at 5 years was 83% in DCD and 84% in HBD. Patient survival was 100% in both groups. Hospitalization was significantly longer in patients grafted with DCD and need more dialysis. Acute rejection episodes were more frequent in DCD grafted patients.
Conclusion: The DCD kidney transplantation has evidence of equivalent graft funciton and survival compared with HBD grafted patients and may contribute to expand the donor pool.

RO-320 SYSTEMATIC REVIEW ON VITAMIN D PREVENTING AND TREATING BONE LOSS IN RENAL TRANSPLANT PATIENTS

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Objective: To assess the effectiveness and safety of vitamin D in preventing and treating bone loss in renal transplant patients.
Methods: Methods recommended by the Cochrane Collaboration were used. MEDLINE, EMBase, Cochrane Library and CNKI were searched to locate all the randomized controlled trials (RCTs) concerning preventing and treating bone loss by vitamin D in renal transplant patients. The qualities of included RCTs were evaluated by two independent reviewers. RCTs consistent with criteria were analysed by RevMan 4.2 software.
Results: Nine RCTs involving 658 post-tansplant patients were included. The qualities of included RCTs were graded as Grade A in four, Grade B in two and Grade C in three. Meta-analysis showed that after being treated with vitamin D for one year,the difference of BMD, Z-score and T-score between the two groups was statistically significant ($P<0.05$); the difference of PTH concentration was also statistically significant ($P<0.01$), but there was no significant difference in concentrations of serum calcium, and phosphorus, and the incidence of hypercalcemia (($P>0.05$).
Conclusion: Current available evidence demonstrates that vitamin D is effective and safe in preventing and treating bone loss in renal transplant patients.

RO-321 THE RISK OF CMV RECURRENCE AFTER KIDNEY TRANSPLANTATION

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Background: Recurrent CMV infections commonly occur after kidney transplantation. Not much evidence exist for or against the use of secondary prophylaxis, and the optimal duration of secondary prophylaxis is currently unknown. We studied the impact of secondary prophylaxis and other factors on the risk of CMV recurrence.
Methods/Materials: All kidney transplant recipients between 2004-2009 in our institution were analyzed (N=254). Patients with CMV infection were included (N=62). CMV infections were diagnosed with real-time quantitative plasma PCR. CMV D+/R- recipients received valganciclovir prophylaxis for 6 months, and CMV DNAemia was monitored after prophylaxis. After treatment of infection, secondary prophylaxis with valganciclovir was given at the clinician's discretion for 2-26 weeks, and CMV DNAemia was monitored.
Results: Altogether 43 reactivations and 19 primary infections were detected. Antiviral treatment with valganciclovir or ganciclovir was given to 45 patients; others were treated with reduction of immunosuppression. 34/62 (55%) patients received secondary prophylaxis for mean 62 days (range 14-180 days). CMV recurrence occurred in 14/43 (33%) seropositive patients and in 4/19 (21%) patients after primary infection (altogether 18/62, 29%). Patients with no recurrence received somewhat longer secondary prophylaxis (73 ± 54 days vs. 44 ± 22, mean$\pm$SD, P=NS). In logistic regression, delayed graft function (OR 3.4, P=0.04) and high viral load (>100000 copies/ml) at initial diagnosis (OR 5.9, P=0.03) independently predicted recurrence of CMV infection. The use or length of secondary prophylaxis, CMV serostatus, symptoms at diagnosis, level of immunosuppression, HLA mismatch, antiviral treatment of first infection episode, or time to clearance of viremia during treatment did not predict the risk of recurrent CMV infections.
Conclusions: CMV recurrences occur commonly despite secondary prophylaxis. High viral load at diagnosis predicted the risk of recurrent CMV infection.

RO-322 CLINICAL FEATURES AND OUTCOME OF *KLEBSIELLA PNEUMONIAE* CARBAPENEMASE (KPC)-PRODUCING *K.PNEUMONIAE* INFECTION AMONG KIDNEY TRANSPLANT RECIPIENTS

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Background: KPC–producing *K.pneumoniae* is an emerging pathogen with serious clinical and infection control implications. The clinical presentation, therapeutic response and outcome of KPC infection in solid organ transplant recipients are still unknown.
Methods/Materials: We describe epidemiological and clinical characteristics, treatment and outcome of KPC-producing *K.pneumoniae* infection among kidney transplant recipients during the monoclonal outbreak of infection in 2009 until February 2011.Data was retrospectively collected from medical records. Carbapenemase production was demonstrated by modified Hodge test. PCR screening for bla_{KPC} and pulsed-field gel electrophoresis analysis was performed to characterize the molecular typing.
Results: Between November 2009 and February 2011, from 1165 new transplants and 5194 transplant recipients under follow up at outpatient clinic, 91 were colonized with KPC-producing *K.pneumoniae* detected by rectal swab surveillance and 21 developed infection. The mean age was 49 years,67% were male and the mean time on dialysis before transplantation was 68 months. Five patients were recipients of second renal allograft, 18 (86%) received deceased donors transplants and one of these was a simultaneous pancreas-kidney transplant recipient. Five patients (24%) had panel reactive antibodies greater than 30% and 6 (29%) received thymoglobuline induction. The most common immunosuppressive regimen was tacrolimus, mycophenolate and prednisone. Thirteen patients (62%) acquired the infection in the transplant hospital stay, 14 (67%) had a urinary device or central venous catheter and 15 (71%) had used antibiotics recently. The most common treatment was polymyxin B associated with tigecycline (38%). Sixteen patients (76%) required intensive care and 13 (62%) died.
Conclusion: KPC-producing *K.pneumoniae* is an emerging pathogen associated with significant morbidity and mortality among transplant recipients, especially those under higher immunosuppression, who recently received antibiotics and those who have invasive devices. These findings highlight the need to strategies for prevention and infection control.

Clinical immunosuppression III

RO-323 IMMUNOLOGICAL CONSEQUENCES AND TRAFFICKING OF HUMAN REGULATORY MACROPHAGES ADMINISTERED TO RENAL TRANSPLANT RECIPIENTS

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The human regulatory macrophage is a novel type of suppressor macrophage which may be a particularly suitable cell type for promoting transplantation tolerance in the clinical setting because of its robust nature, stable phenotype and potent T cell-suppressive activity. Building on evidence from preclinical transplant studies that preoperative treatment with donor-derived M regs promotes allograft acceptance, M regs were administered to two living-donor renal transplant recipients. Both patients were minimised to low-dose tacrolimus monotherapy within 24 weeks of transplantation and subsequently maintained excellent graft function. To assess the fate of M regs following infusion, the cells were labelled with Indium-111-oxine and tracked in serial whole-body SPECT studies. After central venous administration, most M regs remained viable and were seen to traffic from the pulmonary vasculature via the blood to liver, spleen and bone marrow. By one year posttransplantation, both patients displayed patterns of peripheral blood gene expression converging upon the *Indices of Tolerance* (IOT-RISET) tolerance signature (Sagoo, P. *et al.* JCI 2010; 120(6):1848-61). Furthermore, both patients maintained levels of peripheral blood FoxP3, Tolerance-associated gene 1 (Toag-1) and alpha-mannosidase mRNA expression within the range consistent with non-rejection. It is concluded that M regs warrant further study as a potential immune-conditioning therapy for use in solid organ transplantation. The results of this work are being used to inform the design of *The ONE Study*, a multinational clinical trial of immunomodulatory cell therapy in renal transplant recipients funded by the 7th Framework Programme of the European Union.

RO-324 A HIGH GLOMERULAR FILTRATION RATE (GFR) AND THE USE OF AN ENTERIC-COATED FORMULATION OF MYCOPHENOLIC ACID PREDICT LESS GASTROINTESTINAL COMPLAINTS IN RENAL TRANSPLANT PATIENTS

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Background: Gastrointestinal (GI) complaints are very frequent in renal transplant pacients, especially in those treated with mycophenolic acid. The objective of the analysis was to predict the occurrence of GI adverse effects in renal transplant recipients receiving either EC-MPS or mycophenolate mofetil (MMF).
Methods: We performed a multivariate logistic regression model to predict occurrence of GI complications in GI-sensitive kidney transplant recipients (n=134). Data was obtained from a multicenter, randomized, open-label, parallel groups, 12-weeks trial of conversion from MMF to EC-MPS. The following variables were entered into the model: age, gender, weight, proton-pump inhibitors use, cyclosporine use, diabetes, MPA dose at the onset of GI complication, MPA formulation (MMF/EC-MPS), and glomerular filtration rate.
Results: 67 (50%) patients developed GI complications during the study. In the multivariate model, MMF treatment was associated with a three-fold increase in risk of GI complications (adjusted odds ratio [OR] of 3.3, 95% confidence interval [CI] 1.5 to 7.4, p=0.004), whereas higher glomerular filtration rate (GFR) protected against GI events (OR 0.98 for each additional ml/min, 95% CI 0.96 to 0.99, p=0.030). No significant association was observed between the administration of moderate or high MPA doses ($\geq$1000 mg/day in MMF group or $\geq$720 mg/day –equimolar dose- in EC-MPS group) during the study and GI complications of any type (p=0.453). No significant differences between formulations were observed in the oral dose of MPA at the onset of GI complaints (67.2% of patients with MMF were receiving $\geq$1000 mg/day versus 81.4% of $\geq$720 mg/day –equimolar dose- in EC-MPS group, p=0.058).
Conclusion: A high glomerular filtration rate and the use of an enteric-coated mycophenolic acid predict less GI complaints in renal transplant patients.

RO-325 INTRAVENOUS MYCOPHENOLATE MOFETIL WITH CALCINEURIN INHIBITOR FOR RENAL PRESERVATION FOLLOWING LIVER TRANSPLANTATION

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Background: End stage liver disease (ESLD) is frequently associated with renal failure. In these patients, various calcineurin inhibitors (CNI) sparing, reducing, or CNI-free immunosuppressive strategies are being used following liver transplantation (LT). Lately, mycophenolate mofetil (MMF) has shown promising results for these patients; however, its perioperative oral absorption is < 50%.
Aim: To examine the impact of intravenous (IV) MMF with sparing/delayed use of CNI in ESLD patients with renal failure undergoing LT.
Methods: Eight patients with ESLD on renal replacement therapy underwent LT between 3/2009 and 12/2010. Their mean age and MELD score was 48.6±10.7 years and 37.7±3.8, respectively. Immunosuppression protocol consisted of:
Preoperative: Tacrolimus 0.03-0.05 mg/Kg per oral (PO) on call to operating room.
Intraoperative: IV MMF 1 gm over 2 hours at incision and IV Methylprednisone 500 mg anhepatic.
Post transplant: IV MMF 1 gm twice a day for 4-7 days, start tacrolimus after 3-4 days (0.03-0.05 mg/Kg) PO twice a day and maintain trough levels between 6-8 ng/mL, and standard Methylprednisone taper: 600 mg over 5 days. All patients were followed until 12/2010 and mean follow-up was 50.7±22.4 weeks.
Results: All patients came off dialysis with in 0-6 weeks after LT. The mean length of post-LT hospital stay was 15±6.9 days. None of the patient experienced any episode of acute rejection. The mean serum creatinine and BUN at last outpatient follow-up were 1.5±0.5 and 25.8±8.3, respectively.
Conclusions: In study of 8 patients, IV MMF with sparing and delayed use of CNI allows complete recovery from renal failure and freedom from acute rejection without use of antibody preparation. More studies with larger number of patients are required to validate these observations.

RO-326 THYMOGLOBULINE PRE-TREATMENT AND MINIMIZATION OF IMMUNOSUPPRESSION WITH ADVAGRAF IN LIVER TRANSPLANTATION: PRELIMINARY RESULTS OF OUTCOME AFTER 1 YEAR OF A PROSPECTIVE RANDOMIZED TRIAL

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Background: We designed a tolerogenic regimen of recipient pre-treatment with Thymoglobuline and gradual minimization of immunosuppression in a Advagraf-based prospective trial. We investigated the outcome in liver transplant patients in terms of rejection, recurrence of HCV, infections with other viruses (CMV, EBV, HHV6, HHV8) and other clinical complications.
Methods: Thymoglobuline pre-treatment (3 mg/kg) + low-dose Advagraf monotherapy or Advagraf+Certican; thrombocytopenia or leukopenia were exclusion criteria. Levels were reduced by half at 6 and 12 months in clinically stable patients. Data regarding doses and levels of immunosuppressors, protocol serial liver biopsy, CMV Ag, HCV-EBV-HHV6-HHV8 viremias and clinical charts were prospectively collected at various time points.
Results: after 1 year 15 patients have been enrolled, 7 in group A and 8 in group B; 1 patient died of sepsis subsequent to severe biliary ductopenia after 8 months. Freedom from rejection was complete in all 15 patients despite very low levels of immunosuppressors (mean ADV/CERT levels first 6 months: 5,0/4,1 ng/ml; months 6-12: ADV/CERT 2,5/1,87 ng/ml). No histological signs of immune activation was found in all liver biopsies prospectively examined. HCV recurred in 5 of 7 patients, with extremely mild biochemical and histological signs (only 2/7 pts reaching minimal criteria for Ishak grading and staging) of hepatitis. Increase of qHCV viremia was steady over the first 3 months, peaked at around 120 pod, and then always decreased whether spontaneously or because of antiviral treatment (in 2/7 pts). No activation of EBV, HHV6 and HHV8 viremias was experienced.
Conclusions: Induction with Thymoglobuline and minimization of immunosuppression in a Advagraf-based protocol is safe, allows full control of rejection and freedom from viral infections, and permits optimal outcome after HCV recurrence.

RO-327 CONVERSION FROM CNI TO mTOR INHIBITORS IMPROVES RENAL FUNCTION IN KIDNEY ALLOGRAFT RECIPIENTS WITH MALIGNANCIES

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Introduction: Malignancies are a well-known complication of immunosuppressive therapy among renal transplant recipients. Management of posttransplant malignancies should include both control of the neoplasia and preservation of renal function.

Abstract RO-325 – Table 1

Gender/Age (yrs)	MELD at time of LT	Primary Diagnosis	Duration of Dialysis Pre-LT (weeks)	Number of Dialysis Post-LT	Post-LT hospital stay (days)	BUN 1 mth	S Cr 1 mth	BUN 3 mth	S Cr 3 mth	BUN 6 mth	S Cr 6 mth	Follow up (weeks)
M/59	36	HCV, HCC	2	0	20	37	0.7	24	0.8	32	1.2	52.7
F/69	33	HCV, HCC	2	5	11	17	1.2	34	1.0	21	0.8	97.6
M/54	40	HCV, HCC	2	7	28	67	3.4	30	1.6	26	1.7	60.4
M/59	37	EtOH cirrhosis	1	2	12	17	1.7	21	1.1	31	1.5	56
M/59	39	HCV cirrhosis	6	1	8	12	1.4	23	1.2	16	1	44.1
M/45	34	HCV cirrhosis	14	1	11	48	4.1	32	2.3	29	2.4	38.3
F/26	FHF	FHF-HELLP	1	0	10	21	0.7	24	1.4	17	0.8	33.8
M/46	42	EtOH cirrhosis	2	9	20	59	6.6	34	2.7	32	2.1	23.7

*died from HCC recurrence

Methods: 23 renal transplant recipients (mean age 62 years, 65% male) developed malignancies 70.8 months after surgery (range 12 – 150). Malignant neoplasia were as follows: skin (6), PTLD (3), Kaposi's sarcoma (6), renal cell carcinoma (2), breast (1), colon (1) and bladder (1) carcinoma, melanoma (1), seminoma (1), cholangiocarcinoma (1). After diagnosis, patients were switched from CNI-based immunosuppression to mTOR inhibitors (15 on Sirolimus and 8 on Everolimus) as a part of a triple drug therapy with steroids and MMF. All patients underwent the usual treatment including surgery, chemotherapy or radiotherapy. Mean follow up after the conversion was 54 months (range 12-72). Serum creatinine level, MDRD GFR (M-GFR), cholesterol, triglycerides, proteinuria, glycemia and HbA1C before conversion and at the end of the study (last follow up) were analysed.
Results: During follow up, 1 patient died and 3 are still on some antimalignant treatment. All others are cancer free. The M-GFR increased from 43.4 to 46.7 ml/min, while serum creatinine decreased from 168.2 to 161.2 μmol/l ($p<0.05$). Cholesterol and triglyceride levels increased from 4.9 to 5.7 and from 1.6 to 2.1 mmol/l, respectively ($p<0.05$). There were no difference among the glycaemic status and HbA1C values. The 24 h proteinuria remained stable during the treatment (0.7 vs 0.65). Sirolimus and Everolimus trough levels were predominantly in the normal range throughout follow up.
Conclusion: We confirm the mTOR beneficial effect on renal function during a long follow up which enables a successful treatment of post transplant malignancies as well as a long term preservation of renal function.

RO-328 PROLIFERATION SIGNAL INHIBITORS (PSI) CAN BE SAFELY USED AB INITIO AFTER DUAL KIDNEY TRANSPLANTATION (DKT) FROM ELDERLY DONORS (ED)

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The utilization of PSI in the earliest phase after transplantation has been considered unsafe for the risk of lymphocele, impaired wound healing and prolongation of delayed graft function.
On the other hand, PSI carry the advantage of avoiding CNI nephrotoxicity.
Surgical complications and incidence of DGF have been evaluated in a large series of DKT from ED treated with PSI alone or in combination with low-dose CNI.
Methods: From April 2003 to February 2011, 118 patients underwent DKT from ED (mean age 72.7±5.1). Immunosuppressive protocol included Thymoglobulin induction, followed in 40 pts by low-dose cyclosporine or tacrolimus, everolimus and steroids or, in 78 cases, by rapamune, MMF and steroids. The incidence of surgical complications, DGF and the occurrence of conversion to a CNI-based regimen were evaluated.
Results: Lymphocele requiring surgical treatment occurred in 6 cases (5%), mild wound complications were observed in 6 pts (5%). 32 pts experienced DGF (27%) with a mean duration of 5.8±4.7days. The incidence of acute rejection was 20.3%, and actuarial patient and graft survival at 5 yrs was 94% and 89%. Renal function was very satisfactory at 1 and 5 years with S-creatinine of 114±33 vs 138±54 μmol/L respectively.
Conversion to full dose CNI regimen was deemed necessary in 58 pts (49%), mainly for acute rejection (24 pts) and leukopenia (9 pts).
Conclusions: PSI allows to obtain optimal results in DKT, with optimal renal function and low risk of acute rejection. The introduction of PSI early after transplantation does not seem to increase the risk of surgical complications and DGF, even in the challenging setting of DKT from ED.

RO-329 INTERSTITIAL PNEUMONITIS CAUSED BY EVEROLIMUS; A CASE CONTROL STUDY

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Inhibitors of the mammalian target of rapamycin (mTORi), sirolimus and everolimus (EVL), are potent immunosuppressive drugs and have been introduced in renal transplantation because of their supposed lack of nephrotoxicity. Unfortunately, the use of mTORi is associated with many side effects amongst others interstitial pneumonitis. With this case-control study in renal transplant recipients (RTR), we aimed to identify risk factors for the development of an everolimus induced interstitial pneumonitis (EIP).
This study was conducted as a substudy of a multi-center randomized controlled trial (MECANO). All patients treated with prednisolone/EVL were included. RTR, who developed a probable EIP, were identified as cases. We used the following criteria for EIP: (1) exposure to EVL before the onset of pulmonary symptoms, (2) exclusion of infection, (3) radiographic findings on computed tomography (CT) of the chest not compatible with another diagnosis. RTR without pulmonary symptoms served as control patients.
13/102 patients (12.7%) developed an EIP. We found no predisposing factors for the development of EIP, especially no correlation with EVL trough levels or AUC (target 12 μg/l and 150 μg*hr/ml respectively), prior pulmonary condition or smoking. On pulmonary CT, EIP presented as a cryptogenic organizing pneumonia, a non-specific interstitial pneumonitis or a combination of both. Median time (range) to development of EIP after start of EVL was 109 (14-385) days. Pulmonary function tests were performed just after the onset of symptoms in 6/13 cases, showing normal spirometric values. All patients recovered clinically within one year after cessation of EVL.
EIP is a common side-effect of EVL in RTR No clear predisposing factors could be identified in this case-control study. Pulmonary CT showed cryptogenic organizing pneumonia and/or non-specific interstitial pneumonia. The course of EIP is usually benign with disappearance of symptoms within one year after discontinuation of EVL.

RO-330 PHARMACOKINETICS AND PHARMACODYNAMICS OF TACROLIMUS AND ITS METABOLITES IN KIDNEY TRANSPLANTED PATIENTS; THE RELATIONSHIP WITH THE CYP3A4, CYP3A5, MDR-1 GENOTYPES

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Background: Our objective was to determine the relationship between the genetic polymorphisms in CYP3A4, CYP3A5 and MDR1 and the pharmacokinetics and pharmacodynamics of tacrolimus and its metabolites (M-I, M-III).
Methods/Materials: The twelve kidney transplant recipients receiving tacrolimus were genotyped for CYP3A4*18, CYP3A5*3 and MDR1 C 3435T, 1236T, 2677T. Dose-adjusted trough levels, pharmacokinetics (AUC_{0-12}, Cmax, Tmax, Clast/dose, Vd, Cl) and pharmacodynamics (QTc prolongation, expression of cell surface marker) were determined and correlated with the corresponding genotype.
Results: Does-adjusted concentration (Co) of tacrolimus and its metabolites and AUC_{0-12}, C_{max} were significantly higher in CYP3A5*3/*3 patients (n =7) than in *1/*3 plus *1/*1 patients (n=5) ($p < 0.0001$, <0.0001, <0.0001, 0.03, respectively). Despite of only one patient with CYP3A4*1/*18, Co of tacrolimus and metabolites and AUC_{0-12} of the patients with CYP3A4*1/*18 were significantly lower than those without CYP3A4*1/*1 ($p = 0.038$, 0.001, <0.001, respectively). The patients having MDR1 1236 genotypes with T allele (n=11) showed significantly lower level in Co of metabolites and AUC_{0-12} without T allele (p=0.018, 0.029, respectively). Co of tacrolimus in patients having MDR1 2677 with T allele (n=6) was significantly lower compared with recipients without T allele (p= 0.033). In multivariate regression analysis only CYP3A5*3/*3 showed significant relationship with Co of tacrolimus, metabolites and AUC_{0-12} (p= 0.003, 0.033, 0.011, respectively) Among various leukocyte markers HLA/DR+ monocyte was mostly correlated with Co and pharmacokinetics.
Conclusions: This study shows that the CYP3A5*3 genetic polymorphisms associated with the individual differences in pharmacokinetics as well as in Co of tacrolimus and metabolites (M-I, M-III). But the effect of the genetic polymorphisms in MDR-1 was still controversial in this study.

RO-331 DONOR SUB-TYPE ANALYSIS OF THREE-YEAR OUTCOMES FROM A PHASE III STUDY OF BELATACEPT IN RECIPIENTS OF EXTENDED CRITERIA DONOR KIDNEYS (BENEFIT-EXT TRIAL)

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Background: Belatacept was associated with better renal function and comparable patient/graft survival and rates of acute rejection (AR) versus cyclosporine (CsA) through 3 years in recipients of extended criteria donor (ECD) kidneys (BENEFIT-EXT trial). Here we report outcomes by donor sub-type.

Methods: BENEFIT-EXT was a 3-year, randomized, Phase III study in recipients of de novo ECD kidneys (n=543) who were randomized to a more intensive (MI) or less intensive (LI) belatacept regimen or cyclosporine (CsA). In this study, ECD was defined as those meeting UNOS criteria (UNOS-ECD), CIT≥24hr, or donation after cardiac death (DCD). The current analysis compared patient/graft survival, calculated GFR (cGFR; MDRD), and AR through 3 years in recipients of UNOS-ECD (n=384) and DCD (n=55) kidneys. Because many of those with CIT≥24hr also met UNOS-ECD, this group was not analyzed independently.
Results: In UNOS-ECD and DCD recipients, the proportion of patients surviving with a functioning graft was comparable between belatacept and CsA groups, and was consistent with outcomes in the overall ITT population (Table). Recipients of DCD kidneys in the belatacept LI group had numerically higher cGFR and patient/graft survival, while those in the belatacept MI group had lower AR rates; however, these outcomes need to be interpreted with caution due to small numbers. One patient in each treatment group had an AR after year 2. The differential benefit in cGFR of >10 mL/min/1.73m^2 observed with belatacept in the ITT population was at least preserved across donor types.

Table. Three-year Outcomes by Donor Sub-type

	Belatacept MI n = 184	Belatacept LI n = 175	Cyclosporine n = 184
Patients surviving with a functioning graft, % (overall)	80	82	80
UNOS ECD[1]	80	80	77
DCD[1]	78	100	72
Mean cGFR, mL/min/1.73m^2 (overall)	43	42	32
UNOS ECD[2]	40	39	27
DCD[2]	41	56	27
Acute rejection through year 3, % (overall)	18	19	16
UNOS ECD[1]	20	21	15
DCD[1]	11	21	22

[1]UNOS-ECD: n=129 (MI), n=122 (LI), n=133 (CsA); DCD: n=18 (MI), n=19 (LI), n=18 (CsA) for patients surviving with a functioning graft and acute rejection
[2]UNOS-ECD: n=107 (MI), n=108 (LI), n=100 (CsA); in DCD: n=13 (MI), n=17 (LI), n=14 (CsA) for mean cGFR

Conclusions: In recipients of UNOS-ECD and DCD kidneys, treatment with belatacept resulted in better renal function and at least comparable rates of patient/graft survival and AR at 3 years post-transplantation compared with CsA.

RO-332 METASTASIS OR DOUBLE DE NOVO? MOLECULAR AND PATHOLOGIC ANALYSIS OF SIMULTANEOUS RENAL CELL CARCINOMAS IN BOTH NATIVE AND TRANSPLANT KIDNEYS

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Introduction: We report a rare case of two renal cell carcinomas (RCCs) detected simultaneously in native and transplant kidneys. No similar cases have been reported to the Israel Penn International Transplant Tumor Registry (IPITTR, consult #1003077). We investigated whether both tumors are de novo RCCs or one of them metastatic.
Methods: After 14 years of stable graft function under immunosuppresssion with cyclosporine, MMF and steroid, a 51 y/o African American gentleman was found incidentally to have a renal tumor in his right native kidney and another in his transplant kidney. Radical right native nephrectomy and partial transplant nephrectomy were done uneventfully. Microscopically identified cancerous tissues from both tumors were tested for genetic identity by short tandem repeats (STR). The identified STR alleles of each of the tumors were compared to the recipient and the donor STR alleles.
Results: Microscopically, both tumors are pT1a classical clear-cell type RCCs, with the same nuclear grading (Fuhrman grade 3). There were no microscopic cancer satellites beyond the tumoral capsule. The greatest dimension of the tumor in the native kidney measured 6.5 cm, and that in the transplanted kidney measured 2.8 cm. There were many intra-tumoral vascular channels into which tumor cells can get dislodged, but there are no classical intravenous tumor thrombi demonstrated. None of 9 perihilar lymph nodes dissected during radical nephrectomy revealed any metastasis. Alleles identified in tumors from both native and transplanted kidneys with genetic identity studies were identical to the recipient's STR alleles.
Conclusion: Pathologic and genetic identity studies confirmed that both RCC tumors are of recipient origin. This is the first case reported to IPITTR with simultaneous RCCs in the native and transplanted kidneys.

Pancreas

RO-333 PANCREAS-KIDNEY TRANSPLANTATION – ANALYSIS ON 121 CASES FROM ONE CENTRE

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Simultaneous Pancreas-Kidney Transplantation (SPKT) is the first choice treatment for type 1 diabetic (DM1) patients with chronic nephropathy.
In the last 10 years, 121 SPKT were performed at our centre, using enteric diversion and anastomosis to systemic circulation. Their mean age was 34±6 years; 67 females. Mean time of DM1 was 23.3±5.8 years, and time on dialysis = 31±24 months (except 5 preemptive). Immunosuppression used was ATG+ Tacrolimus+ MMF+ steroids.
Acute rejection was diagnosed in 22 patients (18.2%) - in 4 involving both grafts; in 10 only the kidney; in 8 only the pancreas. It was treated with steroids in 13; with ATG in 5; in 4 cases (humoral) with plasmapheresis and immunoglobulin, plus rituximab in 3. The median admission time was 21days.
Kidney loss occurred in 13 patients. The causes were immunologic (6), thrombosis (3), death of patient (3), infection (1). Pancreas loss, in 29, was due to: thrombosis (9); immunologic (6); bleeding (3); infection (6); death (2); and unclear cause (2). Six patients died, from infection (3), cardiovascular disease (2) and unknown cause (2).
Those with functioning grafts, have at present a mean creatinine of 1.15±0.38 mg/dl, creatinine clearance = 77.1±24.8 ml/min, and urinary protein = 0.46±0.28g/day. Their fasting glucose = 81.9±10.7 mg/dl, HbA1c = 5.28±0.42% and C-Peptide = 3.01±1.96 ng/ml. 46% have hypertension, only 28% of these needing >1 anti-hypertensive drug. Hyperlipidemia treated with statins was registered in 25.2%; and a BMI >25kg/m^2 in 14.8%.
Pancreas rejection correlated not only with pancreas loss (P=0.043, HR=2.8) but also with kidney loss (P=0.005, HR=9.7). Kidney rejection also correlated with kidney loss (P=0.021, HR=5.2).
Survival results obtained were at 1-year - for pancreas, kidney, and patient: 84%, 96% and 96%; 5-years: 76%, 91% and 94%; 9-years: 70%, 88% and 94%, respectively.These good global results of our SPKT program are comparable to others from larger centres.

RO-334 INDICATIONS AND OUTCOMES OF AN ILEOSTOMY FOLLOWING PANCREAS TRANSPLANTATION

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Background: There is little data on the incidence and need for an ileostomy post pancreas transplantation. However it is noted anecdotally that this is not an uncommon occurrence. Our study aims to investigate the incidence and indications of ileostomy post pancreas transplantation.
Method: We maintain a prospective data base of patient outcomes following pancreas transplantation in our unit. We looked at the incidence, indication and outcomes of ileostomy post pancreas transplantation.
Results: Between 2001 and January 2010 we performed 210 pancreas transplants. The patient survival and pancreas graft survival at 1 year were 92% and 80% respectively. 69 pancreases were bladder drained and 135 were enteric drained. 15 patients required ileostomy. The indications for ileostomy were bleeding with intraabdominal sepsis (6), enteric leak with peritonitis (3), vascular thrombosis (2), severe pancreatitis (3), severe rejection (1). All patients who had ileostomy except one had enteric drained pancreas.Of these 15 patients, 6 died within 1 year and did not have their ileostomy reversed.The deaths occurred in the early post-operative period and were due to sepsis/ multiple organ failure (5) and unknown (1). The mean length of time between formation and closure of ileostomy was 13 months. There were no reported complications following ileostomy closure.
Conclusions: An ileostomy is a significant consequence of pancreas transplantation and was required in 7% of patients in a large series. It is associated with high morbidity and mortality. Although enteric drainage of a pancreas transplant is metabolically preferable the need for an ileostomy was 11% in this group. Once patients have recovered from the immediate post-operative risk of sepsis, the majority of these ileostomies can be reversed safely with minimal complications. The high incidence of a stoma makes it a prerequisite to inform patients of this possibility pre pancreas transplantation.

RO-335 ENTERIC DRAINAGE OF PANCREATIC TRANSPLANT PSEUDOCYSTS: MANAGEMENT OPTIONS

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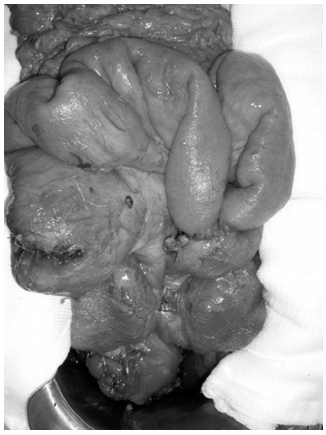
Aims: We present the first recorded case of enteric drainage of a pancreas transplant pseudocyst. Using our experience from the case and through a review of current literature we are proposing guidelines for the approach to pseudocysts related to pancreas transplants.
Methods: Case review - A 41year old lady developed recurrent infected pancreas graft pseudocysts 2 years after a simultaneous kidney pancreas transplant (SPK) for type I diabetes with end stage renal failure. In managing this problem all available options were explored incuding conservative measures, precutaneous drainage, laparotomy washout and necrosectomy before eventually, in September2009, enteric drainage of the pseudocyst was performed using a pseudocysto-ileostomy.



To our knowledge this is the first recorded case of such a procedure being used to treat a pseudocyst arising from a transplanted pancreas. The patient made a good recovery and still shows no evidence of cyst re-accumulation 1year post-operatively.
PubMed search - perfomed using the terms pancreas, transplant and pseudocyst.
Results: The available evidence in this area is limited in scope and quality. However, through extrapolation of evidence for the management of conventional pancreas pseudocysts and, using our experience, combined with that of several case series and case reports regarding transplant pancreas pseudocysts, it is possible to draw some conclusions.
Conclusions: Asymptomatic pseudocysts should be managed conservatively with a low threshold for starting intravenous antibiotics or TPN in this immunosupressed patient group. In symptomatic patients, early intervention is to be recommended due to a high risk of deterioration. With exception of endoscopic procedures, available management modalities for this problem are similar to those for conventional pancreatic pseudocysts i.e. conservative measures, percutaneous drainage, laparotomy and washout. We have demonstrated that enteric drainage is also an option, along with the potential to use transcystic drainage.

RO-336 MANAGEMENT OF RUPTURED MYCOTIC PSEUDO-ANEURYSM FOLLOWING PANCREAS-KIDNEY TRANSPLANTATION

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Background: Mycotic pseudoaneurysms may lead to life threatening complications following transplantation including heamorrhage. Some authors advocate the elective removal of grafts from recipients, who have received a transplant from which Candida sp. has been cultured in the perfusion fluid. Other authors advocate a conservative approach with symptom monitoring, anti-fungal therapy and radiological surveillance.
Methods/Materials: We report the case history of a patient who developed a pseudoaneurysm following simultaneous kidney-pancreas transplantation. We describe the case in detail, highlighting the management steps and review the relevent literature.
Results: We describe the case of a 35 year old patient who 18 days after receiving a simultaneos kidney pancreas transplant developed an iliac-enteric fistula, following mycotic pseudoaneurysm formation. An emergency laparatomy was required to manage a life threatening gastrointestinal hemorrhage, which neccessitated graft pancreatectomy. Resection of the diseased segment of recipient iliac artery onto which the allograft was anastomosed was also required. The patient went on to develop a vascular leak, managed initially by endovascular stenting. With the development of subsequent sepsis and a further leak, operative management was required to remove the infected stent and achieve hemostasis.
Conclusion: Our case report demonstrates the use of stent placement in a transplant recipient with a mycotic aneurysms to allow heamorrhage control. We would not consider covered stent placement as a robust solution to leaking mycotic pseduoaneurysms. However, they may be useful to buy time in a bleeding patient for a more controlled operation. Stent placement carries the risk of erosion through the vascular wall and may also act as a foreign body to attract and harbor infection. We advocate a meticulous open surgical approach in these patients, toilet of the infected tissue and a conservative approach to the immediate revascularisation.

RO-337 ASA PHYSICAL STATUS CLASSIFICATION SYSTEM IN PANCREAS TRANSPLANTATION OUTCOMES; DOES IT ACCURATELY PREDICT RISK?

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Background: The American Society of Anaesthesiologists Physical Status Classification system (ASA) was adopted as a surrogate marker to aid in the assessment of preoperative physiological status. There have been no previous reports of the association between ASA scores and subsequent morbidity and mortality outcomes in pancreas allograft transplantation. We aimed to characterise whether higher ASA scores predicted potential negative sequelae to pancreas transplantation, both in terms of associated morbidity and mortality but also with regard to length of hospital stay.
Methods: A retrospective analysis was carried out of 203 consecutive patients undergoing pancreas transplantation in our unit since the initiation of the programme in 2001 (SPK=155, PAK=36, PTA=12), in 20 cases ASA status was not documented. Primary endpoints included patent mortality and graft loss. Secondary endpoints included associated morbidity and length of hospital stay, morbidity. Statistical analysis was performed using Chi-Square and ANOVA tests.
Results:

	Overall	ASA 2	ASA 3	ASA 4	P value
Median age (years)	42	44.7	41.6	45.1	0.8170
BMI	25.5	27	25.3	25.5	0.1261
1 month graft failure (%)	18	7.7	19.1	0	0.5539
Graft survival (months)	28.6	30.5	27.2	0	0.9634
1 year mortality (%)	13.1	18.5	14.5	0	0.7048
Patient survival (months)	37.6	34.1	38	28.1	0.6282
Median hospital stay (days)	17	20	17	49	0.1703
Median CIT (hours)	14.1	13.6	14.3	16.1	0.3737
Wound infection (%)	14.3	18.5	15.1	25	0.7969
Minor/major fistula (%)	7.9	3.7	8.5	50	0.009 *
Respiratory infection (%)	14.7	18.5	7.9	0	0.5473
Cardiac complications (%)	3.9	7.4	4	0	0.6559
DVT/PE (%)	8	3.7	4.6	0	0.8940
Sample size	183	27	152	4	

Conclusions: ASA has proven to be a reliable indicator of peri-operative anaesthetic morbidity and mortality risk. However, there appears to be no correlation between ASA status classification and outcome data in pancreas transplantation with regards graft outcomes. There was a trend towards longer post-operative stays in patients with ASA 4 and appeared to be a higher rate of intestinal fistulae in high ASA status. Pancreas transplantation, by necessity is performed in patients with poor cardio-respiratory reserve but perceived anaesthetic risk should not be an obstacle to successful transplantation.

RO-337A SIROLIMUS/TACROLIMUS VS MMF/TACROLIMUS IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION (SPKTx): A 3 YEAR FOLLOW-UP IN A SINGLE CENTER

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Introduction: Currently, the tacrolimus/MMF combination reprersents the standard prophylactic immunosuppressive regimen in SPK Tx. The mTOR

pathway inhibitor sirolimus was due its potency and neutral metabolic effect originally considered as a possible alternative for insulin-producing tissue transplants. However, its antiproliferative actions could complicate the postoperative course in both islet and organ pancreas transplantation. We report the 3 year follow-up of an open randomized prospective study comparing tacrolimus/MMF and tacrolimus/sirolimus based immunosuppression in a single center SPK population.
Methods: Type-1 diabetic subjects with chronic renal failure and no age limit were randomly assigned to either tacrolimus/MMF or tacrolimus/sirolimus therapy with ATG induction. Both tacrolimus and sirolimus maintenance target levels were 5-10 ng/ml and the daily MMF dose was 2 g.
Results: Cumulative 1- and 3- year patient survival rates in the MMF group (n=82) were 97% and 97% and in the Rapa group (n=77) 93% and 89%, respectively (p=0.06) with 52 and 40 subjects remaining at risk. Noncensored 3-year pancreas survival rates in the MMF and Rapa groups were 74% and 83%, respectively (p=0.16). Infection was the most frequent cause of death in the Rapa group (4 cases). More pancreases were lost due to technical failure (mainly thrombosis and bleeding) in the MMF group (13 vs 4; p=0.039). Kidney survival did not differ (91% MMF and 86% Rapa, n=0.27). Six patients of the MMF group and 5 of the Rapa group were switched to another immunosuppressive drug.
Conclusion: While the patient survival tended to be better in the MMF group, pancreas survival and especially the technical failure rate tended to be superior in the Rapa group. However, these trends need to be confirmed in a larger multicenter patient series. Grant: MZO 00023001.

Immunobiology / basic science III

RO-338 INTRARENAL IFNγ mRNA EXPRESSION DIFFERENTIATES CLINICAL AND SUBCLINICAL GLOMERULITIS IN RENAL TRANSPLANT RECIPIENTS

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Background: Transplant glomerulitis, characterized by mononuclear-cell infiltration of glomeruli, is likely to occur during clinical or subclinical antibody-mediated rejection.
Mathods: To determine whether T-cell phenotype influences the clinical presentation of this pathological condition, we used reverse transcription quantitative PCR (RTqPCR) to analyse expression of Treg cells (*Foxp3*), cytotoxic CD8 T cells (*Granzyme B*), Th1 cells (*INFγ, T Bet*), Th2 cells (*GATA3, IL-4*) and Th17 pathway (*Il-17*). Our study included 20 renal-transplant recipients exhibiting subclinical isolated glomerulitis (SG) diagnosed after a routine three-month post-transplant biopsy. Results were compared with those observed in 22 patients with normal routine biopsies at three months (N) and 17 patients with clinical glomerulitis (CG) occurring during early acute renal dysfunction within the first year following transplantation in a contexte of acute anti-body mediated rejection.
Results: Our results show that expression of IL-4 mRNA was significantly higher in SG patients than in N patients (p=0.02). Expression of IFNg was significantly higher in CG patients than in SG patients ($p<0.001$). and was predictive of a clinical expression of glomerulitis.
Conclusion: Our results suggest that the balance of Th1/Th2 is likely to differentiate clinical expression of transplant glomerulopathy. They also indicate that therapeutic approaches in cases of subclinical glomerulitis should be defined with caution, and take into account transcriptional criteria.

RO-339 POST-OPERATIVE EXERCISE INDUCED PROLONGED SURVIVAL OF CARDIAC GRAFTS AND REGULATORY CD4$^+$ CELLS

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Background: Exercise therapy has been associated with improvement in functional capacity and quality of life. The role of exercise therapy in heart transplant recipients is of great interest for the transplant society, although concerning the effect of exercise therapy there is little knowledge at present. We analyzed the effect of exercise therapy on alloimmune responses in a murine model of cardiac allograft transplantation.
Methods: CBA mice ($H2^k$) underwent transplantation of C57BL/6 (B6, $H2^b$) hearts and received exercise therapy with treadmill (speed; 12.8m/min, angle of gradient; 5° for 1hour per day) or running wheel. An Adoptive transfer study was performed to determine whether regulatory cells were generated. Immunohistochemical studies, cell proliferation, cytokine assessments and flow cytometry analyses were also performed.
Results: Untreated CBA mice rejected B6 cardiac grafts acutely (median survival time [MST], 7 days). When CBA mice were treated with treadmill and running wheel from the 1 to 7 days and from the 1 to 14 days after transplantation, allograft survivals were prolonged to MST, 35 and 34 days, respectively. However, treadmill-exercise recipients for 1 week before transplantation were not effective to allograft survival (MST, 8 days). Adoptive transfer of whole splenocytes and CD4$^+$ cells from treadmill-exercise recipients resulted in significantly prolonged survival of allografts in naive secondary recipients (MSTs, >30 and >50 days, respectively), compared to that in the recipients with adoptive transfer of naïve splenocytes and naïve CD4$^+$ cells (MSTs, 10 and 8 days, respectively). Moreover, flow cytometry studies showed that the CD4$^+$CD25$^+$Foxp3$^+$ cell population increased in treadmill-exercise recipients.
Conclusion: Exercise therapy with treadmill or running wheel after transplantation could induce prolongation of survival of fully allogeneic cardiac allografts and may generate CD4$^+$CD25$^+$Foxp3$^+$ regulatory cells.

RO-340 OLFACTORY DYSFUNCTION IMPAIRED PROLONGATION EFFECT OF CARDIAC ALLOGRAFT SURVIVAL BY SMELL OF Tokishakuyaku-san IN MICE

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Background: Oral administrarion of Tokishakuyaku-san (TJ-23), a Japanese herbal medicine, could induce prolongation of cardiac allografts survival and generate regulatory cells in mice. Since herbal medicines usually have unique smells and sense of smell was supposed to act as a modulator on the immune system, we examined whether smell of TJ-23 also could induce prolongation of allografts survival and generation of regulatory cells.
Methods: Naïve and olfactory dysfunction CBA mice ($H2^k$) by stereotaxic operation underwent transplantation of C57BL/6 (B6, $H2^b$) hearts and received fumigation of water only or TJ-23 (12.5g/500ml/day; temperature: 30°; humidity: 60%) till rejection. An adoptive transfer study was performed to determine whether regulatory cells were generated.
Results: Untreated CBA mice rejected B6 cardiac grafts acutely (median survival time [MST], 7 days). When CBA mice were treated with fumigation of TJ-23, allografts survival was significantly prolonged with MST of 48 days. Otherwise, grafts were rejected acutely in the water fumigation group with MST of 8.5 days. Moreover, olfactory dysfunction CBA mice treated with fumigation of TJ-23 rejected acutely (MST, 7 days). The proliferation of splenocytes and production of interferon-γ were suppressed. Secondary CBA recipients given whole splenocytes or CD4+ cells from primary TJ-23-treated CBA recipients with B6 cardiac allografts 30 days after grafting had prolonged survival of B6 hearts (MSTs of both groups, >60 days) compared to that in the secondary recipients with adoptive transfer of naïve splenocytes and naïve CD4+ cells (MST, 12 and 8 days).
Conclusion: Naïve but not olfactory dysfunction CBA mice treated with fumigation of TJ-23 induced prolonged survival of fully allogeneic cardiac allograft and generation of regulatory cells.

RO-341 IMPACT OF POLYMORPHISMS OF TLR3 ON ACUTE REJECTION IN LIVER TRANSPLANTATION FOR HEPATITIS C CIRRHOSIS

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Background: Liver transplantation activates the innate immune system by Toll-like receptors (TLRs) potentially leading to allograft rejection and graft failure. The aim of the study was to evaluate the possible association of different single nucleotide polymorphisms (SNP) in several TLR and the incidence of acute graft rejection and the severity of HCV recurrence.
Methods: This is a single center retrospective study of 100 adult liver transplant patients for HCV cirrhosis from 1/1988 to 12/2006 that received calcineurin inhibitors and corticosteroids in addition to mycophenolate mofetil and/or IL-2 receptor antibodies. We examined variants in the TLR1 1805T/G (Ile602Ser), TLR2 2258G/A (Arg753Gln), TLR3 1234G/A (Leu412Phe), TLR4 896A/G (Asp299Gly) and 1196C/T (Thr399Ile), TLR-6 745C/T (Ser249Pro), TLR7 32A/T (Gln11Leu) and TLR9 promoter region polymorphisms at positions -1237C/T and -1486C/T by analyzing the melting curves with the LightCycler 480 system. Recipient genotype frequencies for each SNP were compared among patients with and without acute rejection and with and without severe HCV recurrence (grade 3-4 fibrosis in the Knodell score or established cirrhosis within the first five years since transplantation).

Results: We found the homozygous AA genotype for TLR3 Leu412Phe was associated with protection for acute rejection [Odds ratio (OR)=0.85, 95% confidence interval (95%CI)=0.76-0.94; p=0.01] and a tendency for the homozygous TT genotype for TLR9 -1486C/T with a severe HCV recurrence (OR=2.3, 95%CI=0.98-5.4; p=0.08).
Conclusion: This preliminary study suggests an important role for innate immune system in acute rejection and in the severity of HCV recurrence after liver transplantation. Further studies in other cohorts of patients may provide a more comprehensive involvement of innate immunity in the clinical outcome of HCV positive patients after liver transplantation.

RO-342 SIGNIFICANCE OF CD127 VERSUS FOXP3 TO DEFINE REGULATORY T CELLS IN TOLERANT RECIPIENTS AFTER PEDIATRIC LIVING-DONOR LIVER TRANSPLANTATION

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FOXP3 was reported to be the best marker of $CD4^+CD25^{++}$ regulatory T cells (Tregs). Some researchers, however, have stated that in humans CD127 well represents Tregs within a $CD4^+CD25^{++}$ cell fraction even in the absence of FOXP3.
Method: Frequency of circulating $CD4^+CD25^{++}CD127^{low/-}$ cells was analyzed by FACS in tolerant pediatric recipients after living-donor liver transplantation (LDLTx) (Gr-Tol n=25). FOXP3 staining was added. $CD4^+$ cells were isolated from PBMCs and MLR was performed. In MLR, presence of donor-specific Tregs was examined by depleting $CD4^+CD25^{++}$ $CD127^{low/-}$ cells. The results were compared with those of recipients who failed to stop immunosuppression (IS) (Gr-Intol n=18), recipients in the process of weaning IS (Gr-Weaning n=11), and healthy volunteers (Gr-Vol n=11).
Results: Donor-specific hyporesponsiveness was observed in Gr-Tol, but not in Gr-Intol or -Weaning. Depletion of $CD4^+CD25^{++}CD127^{low/-}$ cells abrogated hyporesponsiveness in a donor-specific manner in Gr-Tol. However, no increase of MLR was observed after depletion of this fraction in Gr-Intol or-Weaning. Frequency of $CD4^+CD25^{++}$ $CD127^{low/-}$ cells within $CD4^+$ cells was significantly lower in Gr-Intol compared to that in Gr-Tol ($p<0.001$), but it did not differ from that in Gr-Weaning (NS) (Gr-Tol, -Intol, -Weaning, and -Vol.;7.8,5.2,6.7 and 8.2%). Adjunction of FOXP3 to CD127 resulted in emergence of a difference between Gr-Intol and -Weaning (Gr-Intol and-Weaning;2.9 and 5.1%, p=0.002), although it did not still distinguish Gr-Tol and -Weaning (Gr-Tol and-Weaning; 5.4 and 5.1%, NS).
Conclusions: Use of CD127 in functional assay efficiently detected donor-specific Tregs in tolerant pediatric recipients after LDLTx. Use of FOXP3 in phenotypical study leaded to a clear difference between IS cessation failure and the weaning process. Thus, a prospective study is required to determine whether adjunction of FOXP3 to CD127 would better predict successful IS withdrawal before starting weaning.

RO-343 ACTIVATED T CELLS AND CYTOKINES PRODUCTIONS CORRELATES WITH CLINICAL OUTCOMES IN CHRONIC RENAL ALLOGRAFT REJECTION

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A cross-sectional analysis of cellular and humoral immunity in human renal allograft recipients with or without deteriorating renal function and biopsy proven chronic rejection (CR) was performed. The prospective study of possible risk factors for CR is based on 6, 7 3, 7 years (form 1-19 years).
Method: Peripheral T cells control immune responses and suppressive capacities were analyzed by limited dilution. In 116 renal recipients' pre and post-transplant serum level of cytokines sCD30, TNF-α, IL-2 and IL-2R and MHC-reactive alloantibodies were detected. Cox regression model was used to assess the significance of PRA, number of precursors of Th lymphocyte (Thp), cytotoxic T lymphocytes (CTLp), cytokines serum concentration and glomerular filtration rate, GFR) with graft survival. All P values are two-sided and considered statistically significant if less than 0.05. Calculations were performed by STATA 7.0
Results: CTL frequencies lymphocytes to donor antigens and the number of patients who responded were statistically higher in CR group ($P< 0.032$). In CR group significant difference is present between measurements r=1.163.66; $P< 0.05$. Serum level of sCD30, IL-2, sIL-2R have no difference while mean level of TNF-α significantly correlated with chronic rejection (P=0,025) and GFR. Development of de novo antibodies in patients with functioning grafts presage subsequent failure with OR=3.92. Thus, there were significantly more failures in those who developed antibodies (P=0, 01).
Conclusions: T cells with alloreactivity against donor antigens are readily detectable in allograft recipients during treatment with full dosage immunosuppression and long term function. Significant difference of TNF-α and renal function are interrelated. Patients with persistently detectable anti-donor immune reactivity and deteriorating kidney function may benefit from alterations in therapy directed by controlling activated T cells or B cells, depending on the type of alloreactivity detected.

RO-344 EX-VIVO LUNG PERFUSION REDUCES GRAFT IMMUNOGENICITY VIA THE REMOVAL OF PASSENGER MONOCYTES – A PORCINE MODEL

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Introduction: Lung transplantation is limited by a shortage of donor organs. One potential solution is ex vivo lung perfusion (EVLP), where marginal lungs are harvested from the sub-optimal donor environment and reconditioned via perfusion/oxygenation, prior to transplantation. EVLP is associated with lower incidence of acute rejection in our small clinical transplant cohort of eight patients, which may be caused by removal of donor monocytes from the graft via mechanical "washing". This porcine study was designed to explore the effects of EVLP on passenger monocyte migration.
Methods: Explanted lungs (n=7) were assessed using standard EVLP (Steen technique). Perfusate samples were collected at 30 minute intervals, and upon completion the leukocyte filter was removed from the circuit. Monocytes were characterised via flow cytometry. Peripheral blood monocytes (n=20) were isolated and differentiation to dendritic cell (DC) or macrophage (mΦ) was determined.
Results: All lungs were reconditioned successfully and would have been suitable for transplantation. Non classical monocytes (NCM, CD14+, CD163–/+) were identified in the perfusate within 30 minutes compared with baseline (mean=20068.14 NCM, P=0.018). Monocyte numbers then declined at each time point until completion of EVLP. Approximately 96% of the cells in the leukocyte filter were of NCM origin. In vitro, NCM readily differentiated to DC phenotypes.
Discussion: This study highlights the importance of the monocyte in lung transplant biology. Our findings are new and clinically relevant; they indicate that passenger NCM migrate rapidly from the graft following transplantation. Monocytes can differentiate into inflammatory DC, and present donor antigen to recipient T cells, a process required to induce graft rejection. The fact the EVLP removes a significant population of this cell type may suggest this procedure should be used constitutively during lung transplantation.

RO-345 FASTING INDUCES RAPID MATURATION AND MOBILIZATION OF T AND B LYMPHOCYTES

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Background: We have previously demonstrated that 72 hours of preoperative fasting offers robust protection against renal ischemia-reperfusion injury (IRI) in mice. However, the mechanism remains to be elucidated. We hypothesize that immunomodulation plays a pivotal role and investigated the impact of fasting on T- and B lymphocytes.
Materials and Methods: Male C57 Bl/6 mice were ad libitum fed or fasted for 72 hours (n=8/group). Lymphoid organs were harvested and blood was taken for flow cytometric analysis.
Results: In the blood, there was a significant increase of B220+ B cells (16.7%) in fasted mice, whereas in the bone marrow (BM), the same cells decreased proportionally. In the spleen, a 27.3% increase in B220+ B cells was noted. In the blood, the percentage of immature T2 (CD23+/B220+) as well as naïve (CD21dim/CD23hi) B cells were increased by 13%. In the spleen, these percentages were 27.3% and 29% respectively. In the BM, immature T1 (CD23–/B220+) and mature (CD21hi/CD23dim) B cells were significantly decreased.
In the thymus, immature single-positive T cells (CD8+CD3-) were decreased by 3.3%, whereas CD3-CD4+CD8+ did not change. However, CD3+CD4+CD8+ cells (4.8%), CD3+CD4+ (5.7%) and CD3+CD8+ (2.2%) cells were all increased. In the BM, CD3+ (8%), CD4+ (4%) and CD8+ (3%) T cells decreased significantly. The spleen demonstrated increased percentages of CD3+, CD4+ and CD8+ T cells (20%, 11% and 21%, respectively). There were no changes in number or composition of B and T cells in the lymph nodes.
Conclusion: Fasting results in major changes in T- and B cell compartments.

Thymopoiesis seems to be accelerated and mature T cells migrate from the BM into the spleen. Both mature and immature B cells are mobilized from the BM into the spleen and peripheral blood. How these changes contribute to protection against IRI remains to be elucidated.

RO-346 MUSIC EXPOSURE INDUCED PROLONGATION OF CARDIAC ALLOGRAFT SURVIVAL AND GENERATED REGULATORY CD4+ CELLS

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Background: In clinical practice, music has been used to decrease stress, heart rate, and blood pressure and to provide a distraction from disease symptoms. This study investigated the effect of music on alloimmune responses in a murine model of cardiac allograft transplantation.
Methods: CBA mice ($H2^k$) underwent transplantation of a C57BL/6 ($H2^b$) heart and were exposed to one of three types of music–opera (*La Traviata*), classical (Mozart), and New Age (Enya)–or one of six different single sound frequencies for 7 days. An adoptive transfer study was performed to determine whether regulatory cells were generated in allograft recipients. Immunohistochemical, cell-proliferation, cytokine, and flow cytometry assessments were also performed.
Results: CBA recipients of a C57BL/6 cardiac graft that were exposed to opera or classical music had significantly prolonged allograft survival (median survival time [MST], 26.5 and 20 days, respectively), whereas those exposed to a single sound frequency (100, 500, 1000, 5000, 10,000, or 20,000 Hz) or New Age music did not (MSTs, 7.5, 9.5, 10, 8, 7.5, 8.5 and 11 days, respectively). Untreated CBA mice rejected B6 cardiac grafts acutely (MST, 7 days). Adoptive transfer of whole splenocytes and $CD4^+$ cells from opera-exposed primary allograft recipients resulted in significantly prolonged survival of allografts in naive secondary recipients (MST, 36 and 68 days, respectively). Proliferation of splenocytes was suppressed in opera-exposed mice, and interleukin-4 production was increased. The immunohistochemical studies showed that cardiac allografts from opera-treated recipients had sparse cell infiltration and only slight myocardial damage. Flow cytometry studies showed an increased $CD4^+CD25^+Foxp3^+$ cell population in splenocytes from those mice.
Conclusion: Exposure to some types of music may induce prolongation of survival of fully allogeneic cardiac allografts and generate $CD4^+CD25^+Foxp3^+$ regulatory cells.

RO-347 CCR7 IS SIGNIFICANTLY UP-REGULATED IN FINE-NEEDLE ASPIRATION BIOPSY SAMPLES FROM ACUTE REJECTION KIDNEY TRANSPLANTS

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Background: CCR7 is a chemokine receptor which is up-regulated during dendritic cell maturation and T and B cell activation. CCR7 expressing cells are poised to migrate to secondary lymphoid tissues where full aloimmune response can be mounted. We studied CCR7 expression in fine-needle aspiration biopsy (FNAB) samples in human kidney transplants (KTx).
Methods: Forty-six KTx were studied, all from cadaver donors treated with CNI, MMF and Pred. They were divided into two groups, I (n=25), rejection-free for the 1st year post-KTx at least and II, acutely rejecting (AR) cases (n=21). AR occurred during the 1st two months post-KTx and was confirmed by an independent pathologist reading a classical biopsy following Banff 97 criteria. Every patient consented in FNAB study, done on day 7 in I and on rejection day in II. After cytocentrifugation each cytoslide was kept at -80°C until further testing. Cytoslides were stained by a mouse IgG_{2A} anti-human CCR7 (R&D) at 25 μg/ml using avidin-biotin enzyme complex. Positive cells were counted as well as kidney parenchymal cells and negative lymphocyte and monocyte-macrophage.
Results: No significant difference was observed concerning demographic characteristics of KTx in I and II. No significant correlation was found between CCR7 and CNI blood levels but CCR7 showed a positive and significant correlation with creatinine ($P=0.047$). CCR7 was significantly up-regulated in II in number of cells ($P<0.000$), in positive/renal cells ratio ($P<0.000$) and in positive/negative mononuclear cells ratio ($P<0.000$).
Conclusions: CCR7 seems to play a significant role in the immune reaction in human KTx. Of interest, its expression does not seem to be highly modulated by CNI. Also, as we were studying allograft infiltrating cells our results surmise that a significant part of dendritic and lymphoid cell maturation is done at the graft site.

Clinical immunosuppression IV

RO-348 THE P450 OXIDOREDUCTASE (*POR*)*28C>T SINGLE NUCLEOTIDE POLYMORPHISM (SNP) IS ASSOCIATED WITH EARLY TACROLIMUS UNDEREXPOSURE AND HIGHER DOSE REQUIREMENTS IN CYP3A5-EXPRESSING RENAL RECIPIENTS

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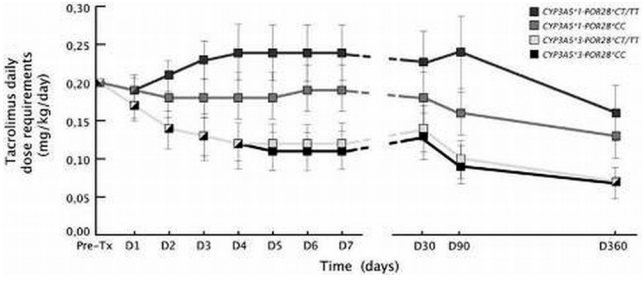
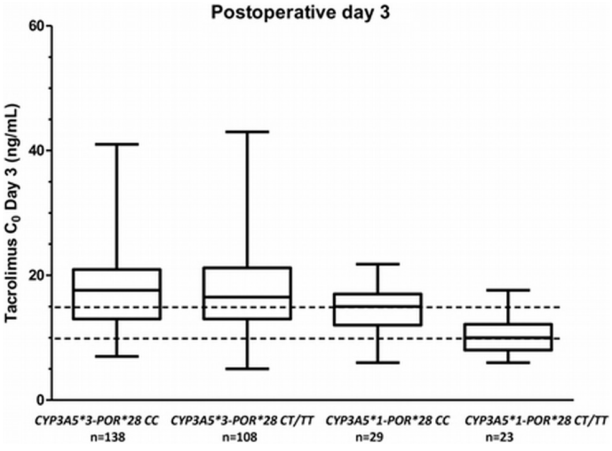
Background: The P450 oxidoreductases (POR) transfer electrons to cytochromes P450 enabling their catalytic activity. The SNP *POR *28* (*rs1057868C>T*) has been associated with loss of function of CYP1A2 and gain of function of CYP2C19/CYP3A.
Methods: In a cohort of 298 renal recipients the effects of the *POR*28C>T* SNP on early tacrolimus (Tac) exposure and dose requirements (TDReq) were examined, taking into account the *CYP3A5*1* carrier state. A Tac loading dose of 0.2mg/kg was used aiming at target 12h-trough concentrations (C_0) between 10-15ng/mL.
Results: Baseline characteristics did not differ between genotype groups. Initial Tac C_0 were significantly lower in recipients with the *CYP3A5*1/POR*28CT/TT* genotype compared to carriers of the *CYP3A5*1/POR*28CC* genotype during the first 3 postoperative days (despite equal loading doses). Consequently, TDReq (mg/kg/day) became significantly higher in the former patients from day 2 onwards and remained significantly elevated throughout the first year (achieving equal target C_0).



47.8% of *CYP3A5*1/POR*28CT/TT* genotype carriers had a C_0 below 10ng/mL on day 3 (vs. 3.7% *CYP3A5*1/POR*28CC*-carriers, $p<0.0001$) and needed significantly more days to achieve this minimum target (3.3±1.7 vs. 1.9±1.9 days; p=0.001).



Patients carrying at least one *CYP3A5*1*-allele together with at least one *POR*28 T*-allele persistently displayed approximately 25% higher TDReq compared to homozygous *POR*28 CC*- CYP3A5 expressers. Compared with CYP3A5 non-expressers, TDReq in the former recipients was almost constantly 100% higher. Multivariate analyses in the group of *CYP3A5*1*-allele carriers showed that *POR*28* genotype (p=0.009) and patient age (p=0.0006) were independently associated with TDReq.
Conclusion: These observations indicate that the *POR*28* SNP is associated with early Tac underexposure and additional increases in TDReq in patients already carrying a *CYP3A5*1*-allele. Whether the *POR*28* SNP will affect clinical efficacy needs to be determined in prospective studies.

RO-349 IMMUNE MONITORING DURING TOL101-ANTI-αβTCR MONOCLONAL ANTIBODY THERAPY PHASE 2 RENAL TRANSPLANT TRIALS

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Background: Current biological induction agents used in clinical transplantation are well known for their broad immune modulating activity and, in particular, their prolonged depletion of several lymphocyte subpopulations. TOL101 is a novel monoclonal IgM antibody that is specific for the αβ TCR, and is currently in First in Man Phase 2a/b testing in the United States. This analysis describes the kinetics of peripheral blood leukocytes in subjects treated with several different doses of TOL101 and undergoing an initial kidney transplant.
Methods: Multiple cohorts of primary kidney recipients received TOL101 daily for 5-9 days at escalating doses beginning with 1/10 the Minimum Anticipated Biologic Effect Level. Maintenance therapy included tacrolimus, mycophenolate mofetil, and steroids. Multi–parametric flow cytometry was performed on peripheral blood samples, and the presence of pro-inflammatory cytokines IFNγ, TNF, IL-1β, IL-6, and IL-10 was determined by multiplex ELISA (Luminex). The pharmacokinetics of TOL101, the pharmacodynamic effects on lymphocyte subsets, and HAMA formation were assessed using ELISA.
Results: TOL101 specifically down-modulated the CD3 receptor complex on αβ-TCR+ T cells in a dose-dependent fashion. In contrast, γδ-TCR+ T cells, B cells, NK cells, granulocytes, and monocytes in the peripheral blood appear to remain baseline following TOL101 treatment. Modulation of the T cell receptor complex, as opposed to deletion of T cells, appeared to be the predominant mechanism of T cell inactivity. The pharmacokinetic profile of TOL101 correlated with the CD3+ T cell pharmacodynamic marker. Notably, inflammatory cytokine production was not observed following the T cell modulation during or after initial TOL101 infusion.
Conclusions: At the doses tested, TOL101 is capable of specifically modulating αβ-TCR+ T cells, having little effect on other immune cell subsets and no clinically significant pro-inflammatory cytokine release.

RO-350 CONVERSION FROM TACROLIMUS CAPSULES TWICE DAILY TO TACROLIMUS TABLETS ONCE DAILY IN STABLE KIDNEY TRANSPLANT PATIENTS: EFFICACY RESULTS FROM A PHASE III, OPEN-LABEL, MULTICENTER, PROSPECTIVE, RANDOMIZED STUDY

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Background: Phase II studies of de novo and stable renal and liver recipients showed improved pharmacokinetic (PK) parameters and a tendency toward fewer treatment failures and serious adverse events (SAEs) for extended-release tacrolimus tablets (LCP-Tacro™) administered once-daily (qd) vs. standard tacrolimus capsules (Prograf®) administered twice-daily (bid). Here we report efficacy results from a Phase III trial of stable renal transplant recipients converted from Prograf bid to LCP-Tacro qd.
Methods: Kidney transplant recipients 3- 60 months post-transplant taking oral Prograf bid with tacrolimus trough levels 4-15 ng/mL were randomized to receive LCP-Tacro qd or to maintain their Prograf regimen for 12 months. The primary efficacy endpoint was a composite of death, graft failure, biopsy-proven acute rejection (BPAR) or loss to follow-up within 12 months of randomization. Initial LCP-Tacro dose was 30% lower (15% for African Americans) than the pre-conversion Prograf total daily dose. Subsequently, trough levels of 4-15 ng/mL were targeted in both drugs.
Results: 324 patients were randomized; mITT population was analyzed (LCP-Tacro: n=162; Prograf: n=162). The groups were similar in demographics and mean days post-transplant. Mean (SD) daily drug doses were: LCP-Tacro: 4.7 mg (3.2), Prograf: 4.9 (3.0); mean trough levels were similar between the groups throughout the study. The primary composite endpoint was met by 4 patients in each group, p>0.999.
Conclusion: LCP-Tacro qd-based therapy was noninferior to Prograf bid-based therapy in stable renal recipients. These results and the previous PK results suggest that LCP-Tacro may be an attractive alternative to Prograf. Whether the improved PK and qd dosing translate into fewer dose changes and SAEs; and improved compliance warrant further testing.

Efficacy Results, LCP-Tacro vs. Prograf

	Local Pathology Reading	
	LCP-Tacro* (n=162)	Prograf* (n=162)
Primary endpoint, n (%)	4 (2.5)	4 (2.5)
Treatment Difference (95% CI)	0% (–4.2, +4.2)	
p-value	>0.999	
Individual Efficacy Components		
Death, n (%)	2 (1.2)	1 (0.6)
Graft Loss, n (%)	0 (0.0)	0 (0.0)
Lost to f/u, n (%)	0 (0.0)	1 (0.6)
BPAR, n (%)	2 (1.2)	2 (1.2)
	Central Pathology Reading	
	LCP-Tacro	Prograf
Primary endpoint, n (%)	3 (1.9)	6 (3.7)
Treatment Difference (95% CI)	–1.85% (–6.51, +2.30)	
p-value	0.502	
Individual Efficacy Components		
Death, n (%)	2 (1.2)	1 (0.6)
Graft Loss, n (%)	0 (0.0)	0 (0.0)
Lost to f/u, n (%)	0 (0.0)	1 (0.6)
BPAR, n (%)	1 (0.6)	4 (2.5)

*Modified Intention-To-Treat (mITT): received ≥1 dose of study drug. The pre-specified non-inferiority margin was 9%.

RO-351 IMMUNOSUPPRESSION MONITORING BY Cylex Immuknow TEST AFTER LIVER TRANSPLANTATION: PRELIMINARY RESULTS OF RANDOMIZED PROSPECTIVE TRIAL

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Background: The Immuknow assay (IA) determines cellular immunity by quantitative measurement of intracellular ATP level in CD4+ lymphocytes and it may be applied to modulate immunosuppresion after liver transplantation (LT).
Methods: We performed a prospective randomized trial where the study group (A) modulated the immunosuppression (tacrolimus and steroids) according to IA and the control group (B) had a standard monitoring with a IA blinded.
Primary endpoint was to evaluate the correlation among IA and infection/rejection episodes.
Results: 101 patients were enrolled during 2008-2010: 48 in therapy group (group A) and 53 in control group (group B). The two groups had comparable recipient and donor clinical features, such as the pre-transplant IA. Patients enrolled have a significantly lower pre-transplant cellular immune response compared to healthy controls (96±241 vs. 408±184 ng/ml p=0.02), while patients with MELD>25 had a significantly lower immune function (median 54 vs. 109 ng/m ATP, p<0.05).
Rejection episodes (biopsy proven) were 5 in the therapy group vs. 7 in the control group (p= n.s.) and infection were 11 in group A vs. 24 patients in group B (p<0.05).
Patients who developed infections in the post-op. course had a significantly lower Cylex text at the day of transplant (median 25 vs. 126 ng/m ATP, p<0.01).
Patient survival was comparable between the two groups (87% vs. 82%), as was the graft survival (85% group A vs. 76% group B).
Conclusions: Patients awaiting LT have an impaired immune response compared to healthy controls, in particular if MELD score was high. The IA showed a correlation with the infective episodes and the immunosuppression modulation according to IA reduced the infections in the study group.

RO-352 ECULIZUMAB THERAPY IN REFRACTORY RECURRENCE OF THROMBOTIC MICRO ANGIOPATHY ASSOCIATED TO ANTI-PHOSPHOLIPID ANTIBODIES AFTER RENAL TRANSPLANTATION

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Renal thrombotic micro angiopathy (TMA) is a serious complication of systemic lupus erythematosus (SLE) associated with the presence of anti-phospholipid antibodies (aPL). In his most fulminant form, TMA can lead to a rapid irreversible end stage renal disease. Eculizumab is a novel therapy of choice for patients suffering from paroxysmal nocturnal hemoglobinuria (PNH) and

for atypical hemolytic uremic syndrome. Recently, Eculizumab was successful to prevent recurrence of catastrophic anti-phospholipid antibody syndrome (CAPS) in a patient after transplantation. The effect of Eculizumab in recurrence of TMA in presence of aPL remains to be demonstrated. We report the case of a 27-year-old woman who was referred to our institution for evaluation for a renal transplantation. The kidney biopsy showed severe TMA, complete glomerular scarring and diffuse tubule-interstitial fibrosis. The presence aPL antibodies (lupus anticoagulant, IgG anti cardiolipine and IgG anti B2 glycoprotein type I), anti-nuclear and anti-nucleosome antibodies at high titer and a reduce level of C3 level was compatible with the diagnosis of fulminant TMA in a SLE patient in presence of aPL. The patient underwent living related kidney transplantation. The graft produced urine immediately. As serum creatinine remained at 172μmol/L at day 6, a graft biopsy was performed. Isolated diffuse glomerular and arteriolar TMA was seen leading to daily plasma exchange, from day 7 to 10). The patient developed oligoanuria and weekly Eculizumab perfusion was administered. Renal function begun to improve after the third Eculizumab perfusion. Three months post transplant, serum creatinine is 100μmol/L, without proteinuria aPL antibodies are undetectable. Graft biopsy revealed complete resolution of TMA without sequel.This case report demonstrates the benefit of Eculizumab therapy in a fulminant recurrence of TMA, refractory to classical therapy after kidney transplantation.

RO-353 PRESERVATION OF RENAL FUNCTION IN LIVER TRANSPLANT RECIPIENTS WITH CERTICAN-BASED VS CNI-BASED THERAPY: THE PROTECT STUDY

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Introduction: With current CNI-based immunosuppressive regimens acute rejection (AR) has become less important as it rarely causes graft loss and death. In fact, excess immunosuppression (IS) is the greater concern which shifted the focus to avoiding long-term complications of IS, especially nephrotoxicity and recurrent liver disease. Thus, the introduction of everolimus (EVR) may improve renal function and other safety outcomes by allowing for minimization and later elimination of CNIs early post-transplantation.
Methods: In this 11 month multicenter, prospective, open label study 203 de novo LTx patients with good renal function (calculated glomerular filtration rate ≥50mL/min) 4-8 weeks after transplantation were randomized into two groups. Group A continued CNI treatment (n=102; standard CNI dose [tacrolimus or cyclosporine] ±steroids). Group B was switched to everolimus ± steroids (n=101). Everolimus was given.5mg bid initially, later adjusted to target trough level of 5-12ng/mL and CNI was withdrawn stepwise until week 16 post randomization.
Results: The primary end point of an inter group-difference of 8mL/min) in change in GFR calculated by Cockcroft-Gault in the intent-to-treat (ITT) analysis from baseline to Month 11 was not reached. However, the mean difference in GFR calculated by MDRD at Month 11 between the everolimus group and the CNI group was 7.778 mL/min (p=0.0209, ITT population). Further, conversion to an everolimus-based regimen showed comparable efficacy at Month 11 evaluations for incidence of Biopsy Proven Acute Rejection (BPAR), graft loss or death.

Conversion to everolimus: efficacy assessments

Efficacy end point	Everolimus, n=96 (%)	CNI, n=98, (%)
Month 1–11		
BPAR	17 (17.7)	15 (15.3)
Graft loss	2 (2.1)	2 (2.0)
Death	4 (4.2)	4 (4.1)

The adverse effect profile in everolimus group was consistent with earlier transplant studies.
Conclusions: These results demonstrate that in liver transplant recipients with good renal function 4-8 weeks posttransplant, conversion to everolimus (mostly monotherapy) can be achieved without compromising efficacy and may lead to an improvement in renal function during the first postoperative year.

RO-354 TEN YEARS IMMUNOSUPPRESSION AVOIDANCE IMPROVE THE NATURAL COURSE OF CIRRHOSIS RECURRENCE IN HCV LIVER TRANSPLANT RECIPIENTS

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Background: The present study describes the histological outcome over 10 years of follow-up of HCV liver transplant (LT) recipients who successfully discontinue immunosuppression (IS).
Methods: Thirty-four patients (25M/9F, 62±6.4 years) transplanted for HCV-end stage liver disease, were enrolled in a prospective study with the aim to achieve a sustained IS-free state [Tisone et al, J Hep 2006]. Herein the 10 years histological course of the recurrent disease was analyzed in terms of fibrosis and inflammation score.
Results: After a mean follow up of 115 (range 100–124) months, out of the 34 originally patients enrolled, 29 remained alive [7 Tolerant (TOL) and 22 non tolerant (non-TOL)] and are routinely followed. One patients in TOL group had IS resumption due to kidney transplantation. The 10-years patients survival rate was comparable (89% vs. 87.5%, p=n.s.). Comparing baseline and 10 years biopsies, TOL group showed an improvement in grading [5.5 (SD 1.6) to 3 (SD 1.6) (*p=0.001*)] and no differences in staging [2.7 (SD 0.9) vs 2 (SD 1.5), *p=n.s.*] vs non-TOL who have showed and improvement of grading score [4.8 (SD 1.8) to 2.5 (SD 1.2), *p=0.0003*] and an increasing of staging [2.3 (SD 0.9) to 3.1 (SD 1.8), *p=0.03*]. The fibrosis progression rate calculated for TOL and non-TOL group was -0.06 (SD 0.12) and 0.08 (SD 0.18) respectively (*p=0.06.*). Furthermore at the last biopsy, 14/22 non-TOL (63%) showed feature of advanced fibrosis vs none in the TOL group (*p:0.006*). No evidence of chronic rejection was observed during the follow-up.
Conclusions: After a 10-year follow up, the IS avoidance remains safe and seems to improve the histological course of the disease recurrence in HCV LT recipient.

RO-355 IMMUNOGENETICS TO INDIVIDUALIZE INDUCTION IMMUNOSUPPRESSION

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Introduction: Previously we have correlated early kidney allograft loss with a limited number of mismatched HLA class I alloepitopes recognized by recipient in a self-HLA-DR-restricted manner and described nine immunogenic HLA combinations. Here we investigate the efficacy of induction therapy with anti-CD25 monoclonal antibodies to prevent the rejection of deceased donor kidney (DDK) allografts transplanted with or without immunogenic HLA combination.
Methods: All DDK transplants studied (n=388) were performed in our clinic and followed up prospectively. The recipients were treated (intention to treat) with neoral + aza + steroids (n=138) or neoral + mmf + steroids (n=250). To prevent episodes of acute rejection anti-CD25 monoclonal antibodies were given to 49 (13%) patients (for zenapax, n=36; for simulect, n=13). Donor-recipient pairs were investigated for possible immunogenic HLA combinations retrospectively. There appeared to be 144 (37%) transplants at risk. To assess the effect of immunogenic HLA combinations one-year transplant period was analyzed. The Kaplan-Meier method was used to estimate probability of graft survival. The log-rank test was used to compare the estimates.
Results: The results are shown in Table. The induction therapy with anti-CD25 monoclonal antibodies did not benefit the survival of kidneys grafted in the absence of any immunogenic HLA combination (row 1 vs row 2 p=NS). On the contrary, the survival of the grafts at risk improved significantly (row 3 vs row 4 p=0.04) when the therapy was supplemented with anti-CD25 prophylaxis.

1-yr graft survival

Immunogenic HLA combination	Anti-CD25 induction	n	Survival, %	p
–	–	216	88	NS
–	+	28	89	
+	–	123	71	0.04
+	+	21	91	

Conclusion: Our study suggests that induction therapy with anti-CD25 monoclonal antibodies did improve the survival of not all DDK grafts but only the ones transplanted in the presence of immunogenic HLA combinations.

RO-356 STEROID FREE IMMUNOSUPPRESSION IN KIDNEY TRANSPLANTATION: A USEFUL ALTERNATIVE

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Background: To study the safety and efficacy of steroid free protocol in living donor transplantation with IL-2RA induction with tacrolimus/MMF maintenance.

Patient & Methods: We prospectively evaluated 59 renal transplants on steroid free protocol. All patients in the group received IL2RA induction and IV Methylprednisolone 500 mg then oral prednisolone which was stopped by day 5. All patients received Tacrolimus and MMF maintenance. Outcome measures were acute rejections, infections, graft loss, PTDM, requirement of antihypertensive medications, S. Cholesterol and LDL levels. We compared patients on steroid free protocol with 80 patients who received IL-2RA, Tacrolimus, MMF and steroids. Fisher exact test' and Chi Square were used for statistical analysis and a p value <0.05 was considered significant.

Results: The study group had 59 patients (30 males & 19 females), mean age was 39.4 ± 12.5 years. The control group was similar (mean age 40.9 ± 13.5 yrs, 31 males and 9 females).The mean follow up was14.03 ± 7.04 months. Eight patients (13.5%) had an episode of Acute Rejection in steroid free group which was similar to those on steroid based protocols 10/80 (12.5%) (p=0.9). 11/59 had infections with UTI being the commonest (9/11) which was similar to the control group (10/80, 12.5%) (p=0.53). 3 (3.3%) of these 59 patients developed NODAT as compared to 11/80 in the control gp (p=0.11). The incidence of graft loss and death were similar in the two groups. Of the 59 patients, 31.3% did not require antihypertensive medications. The cholesterol and LDL levels in both groups were similar.

Conclusions: This study suggests that steroid free immunosuppression is safe and efficacious without any increased incidence of acute rejection.

RO-357 INFLAMMATORY CYTOKINES PROFILE AFTER ONCE-DAILY TACROLIMUS CONVERSION IN STABLE KIDNEY TRANSPLANT RECIPIENTS

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Stable renal transplant patients (sRT) can be safely converted from tacrolimus-twice-daily (Tac-T) to Tac once-daily (Tac-O) formulation. This conversion is followed by Tac trough levels (Ttl) reduction of about 20-30%. In these cases no modifications of renal function (RF) has been observed but an issue is raised about the development of subclinical rejection, characterized by alterations of inflammatory cytokines and C-reactive protein (CRP) in the absence of creatinine alterations.

Aim: Aim of our study was to assess Ttl, RF, CRP and cytokines among sRT converted from a Tac-T to a Tac-O.

Methods: January 2009-October 2010, enrollement of 46 consecutive sRT (3-5 years post-transplant) treated with Tac-T+MMF+steroids. Patients were converted to Tac-O 1mg:1mg. Ttl, serum creatinine (sCr), glomerular filtration rate using the Modification of Diet in Renal Disease formula (MDRD), CRP, and clinical assessment were performed monthly for 12 months before (retrospectively) and after conversion (prospectively). Each patient served as his own control based upon values before versus after conversion.

Plasma samples were collected at 3 and 12 months after conversion to assess a panel of 27 cytokines, including IL-2, IL-6, IFN-γ, TGF-α.

Results: We observed a significant reduction in Ttl after conversion (p=0.000,CI 95% 1.96-2.31). RF evaluated by sCr and MDRD were not significantly different after conversion as well as CRP.

Among the whole group,14 patients (30,4%) did not modify Ttl (GroupA), wihle 32 (69,6%) showed Tac-O Ttl significantly lower than Tac-T (GroupB).

RF and CRP did not show modification in both Groups A and B. The assessment of cytokines did not show any significant difference between the 2 Groups. No episodes of acute rejection occurred.

Conclusion: The reduction of Ttl after conversion to Tac-O is not associated with graft dysfunction neither increase in inflammatory parameters compatible with subclinical rejection.